Primary Myelofibrosis in the Young

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ABSTRACT

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Primary myelofibrosis is a clonal disorder of a multipotent hematopoietic stem cell of unknown etiology and is one of the least common myeloproliferative neoplasms (MPN).[1] It primarily affects men in their sixth decade or later.[1] We are presenting a young lady who presented with anemia and massive splenomegaly diagnosed as Primary myelofibrosis.

Keywords: Primary Myelofibrosis

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INTRODUCTION

Primary myelofibrosis is a clonal disorder of a multipotent hematopoietic stem cell of unknown etiology characterised by marrow fibrosis, extramedullary haematopoiesis and splenomegaly.[1] It is one of the least common myeloproliferative neoplasms (MPN). In contrast to other myeloproliferative neoplasms (MPN) and so-called acute or malignant myelofibrosis, which can occur at any age, Primary myelofibrosis primarily afflicts men in their sixth decade or later.

CASE REPORT

A 34 year old female presented with loss of appetite and generalised tiredness since 5 years and a progressive abdominal lump since 1 year. There was a past history of Hyperthyroidism for which had taken treatment for some time.

General examination showed pallor and systemic examination revealed massive splenomegaly. Blood investigations revealed normocytic normochromic anaemia (Hb-6.8) with high ESR (63mm/1st hour). PBS- tear drop RBCs, leucoerythroblastic picture with adequate number of platelets and WBCs. All other blood investigations including TSH, anti-TPO, S. Ferritin, S.Iron were normal.

Based on the history and physical examination in the presence of a leucoerythroblastic blood picture, a provisional diagnosis of Primary myelofibrosis was made though the patient was young.

USG abdomen showed massive splenomegaly. X-ray pelvis and lumbar spine **(figure 1)** revealed osteosclerotic lesions. CT abdomen- same findings as reported in USG with osteosclerotic lesions in the pelvis and vertebra l bones. Bone marrow study done which was dry tap on aspiration and biopsy showed marrow fibrous tissue composed of reticulin fibres and collagen suggestive of primary myelofibrosis. JAK 2 mutation was found to be positive which further confirmed the diagnosis.

This is a case of Primary myelofibrosis in a young female.

DISCUSSION

Myelofibrosis is a rare, serious myeloid malignancy classified as one of the Philadelphia chromosome negative myeloproliferative neoplasms (MPN).[2] It is the least common chronic myeloproliferative neoplasms (MPN).

It is a clonal disorder of multipotent stem cell of unknown etiology, characterised by marrow fibrosis, extramedullary haematopoiesis and splenomegaly.

Dysregulation of JAK-STAT pathway is the key contributor to the clinical phenotype of the disease regardless of the absence or presence of the JAKV617F mutation.[2] JAK-STAT pathway plays a pivotal role in the differentiation and development of haematopoietic cells and functioning of the immune system.[6]

Extramedullary hematopoiesis is a well-recognized phenomenon of this disease process. Although typically

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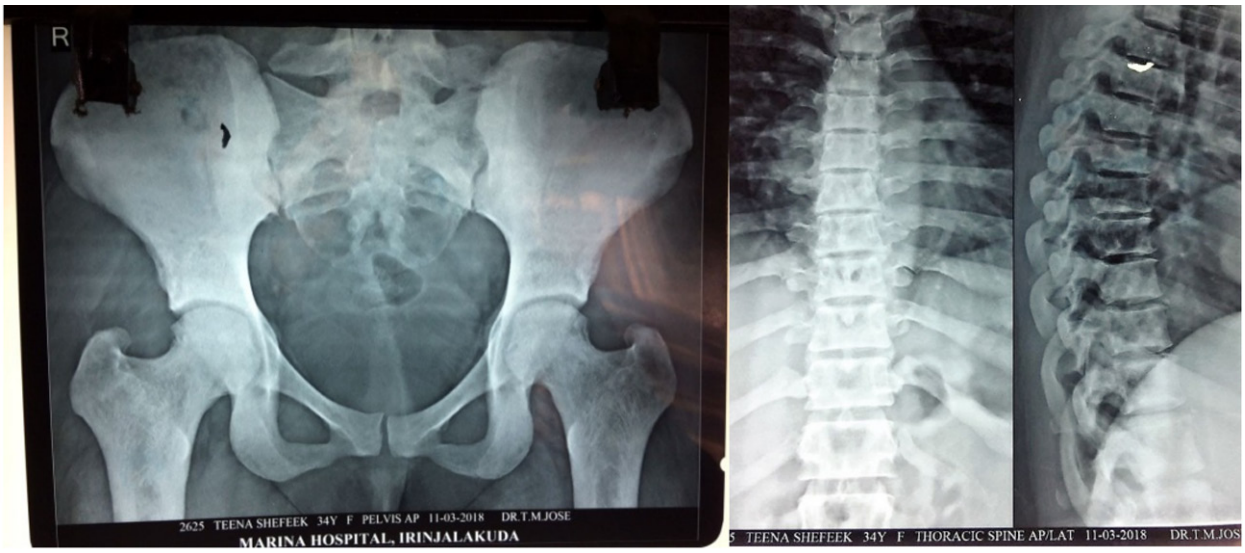

Figure 1. **X-ray pelvis and spine showing osteosclerotic lesions**

seen in sites of fetal hematopoiesis, it can be found in any organ and present in a myriad of different ways.[5]

CLINICAL FEATURES

85% or more of myelofibrosis patients present with palpable splenomegaly at the time of diagnosis.[2] 50% have hepatomegaly and other symptoms including constitutional symptoms like fatigue, night sweats, pruritis, bone/muscle pain and cachexia.

Complications

Ascites, portal hypertension, spinal cord compression, skin nodules.

It is a diagnosis of exclusion which requires that the diseases listed in the **table 2** be ruled out.

Diagnosis is based on bone marrow morphology. The presence of JAK2, CAL or MPL mutation is supportive but not essential for diagnosis; approximately 90% of patients carry one of these mutations and 10% are "triple-negative"[3]

The diagnosis of primary myelofibrosis is facilitated using WHO criteria listed in the **(table 1)**

Table 1. Diagnostic criteria of primary myelofibrosis

Major criteria(all are required)	Minor criteria (must meet 2)
Megakaryocyte proliferation and atypia- reticulin or collagen fibrosis	Anaemia, palpable spleno-megaly
Does not meet criteria of other clonal disorders (Polycythemia vera, CML)	Increase in serum LDH
Clonal marker (JAK2 V617F/ MPLW515K/L) or evidence of secondary myelofibrosis	Leucoerythroblastosis

PBS will show tear drooped RBCs, nucleated RBCs, myelocytes, dysplastic megakaryocytes. Cytopenia usually dominates the picture in the advanced stage. Bone marrow is in-aspirable and biopsy will reveal marrow fibrosis consists of reticulin fibres and collagen. There is an increased number of circulating CD-34 positive cells for unknown reasons.

Most patients eventually die from the disease, with a median survival ranging from approximately 5–7 years.[4]

There is no specific treatment. Erythropoietin, androgens, steroids, low-dose thalidomide can be tried for cytopenias.

In case of splenomegaly/ constitutional symptoms, either of the following agents is advised.

- Ruxolitinib (JAK1/2 inhibitors)
- Hydroxyurea
- Peg IFN
- Splenectomy/splenic irradiation

However, allogeneic stem cell transplantation is the curable way of treatment.

Table 2. Causes of Secondary myelofibrosis

Malignant	Non-malignant
Acute leukemia, CML Hairy cell leukemia	HIV infection
Hodgkin's disease, lymphoma	Hyperparathyroidism, renal osteodystrophy, vitamin D deficiency
Primary myelofibrosis	Tuberculosis
Multiple myeloma, myelodysplasia, metastatic carcinoma, polycythemia vera, systemic mastocytosis	Thorium dioxide exposure, Gray platelet syndrome

END NOTE

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