Primary Myelofibrosis in the Young

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ABSTRACT

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). It primarily affects men in their sixth decade or later. We are presenting a young lady who presented with anemia and massive splenomegaly diagnosed as Primary myelofibrosis.

Keywords: Primary Myelofibrosis

INTRODUCTION

Primary myelofibrosis is a clonal disorder of a multipotent hematopoietic stem cell of unknown etiology characterised by marrow fibrosis, extramedullary haematopoiesis and splenomegaly. 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). 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. JAK-STAT pathway plays a pivotal role in the differentiation and development of haematopoietic cells and functioning of the immune system.

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

*See End Note for complete author details

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seen in sites of fetal hematopoiesis, it can be found in any organ and present in a myriad of different ways.³

**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)

PBS will show tear drooped RBCs, nucleated RBCs, myelocytes, dysplastic megakaryocytes. Cytopenia usually dominates the picture in the advanced stage. Bone marrow is in-asprialble 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.

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<thead>
<tr>
<th>Table 1. Diagnostic criteria of primary myelofibrosis</th>
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<td><strong>Major criteria (all are required)</strong></td>
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<tr>
<td>Megakaryocyte proliferation and atypia- reticulin or collagen fibrosis</td>
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<tr>
<td>Does not meet criteria of other clonal disorders (Polycythemia vera, CML)</td>
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<tr>
<td>Clonal marker (JAK2 V617F/ MPLW515K/L) or evidence of secondary myelofibrosis</td>
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<tr>
<td><strong>Minor criteria (must meet 2)</strong></td>
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<tr>
<td>Anaemia, palpable splenomegaly</td>
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<td>Increase in serum LDH</td>
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<td>Leucoerythroblastosis</td>
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<th>Table 2. Causes of Secondary myelofibrosis</th>
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<td><strong>Malignant</strong></td>
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<tr>
<td>Acute leukemia, CML Hairy cell leukemia</td>
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<td>Hodgkin’s disease, lymphoma</td>
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<tr>
<td>Primary myelofibrosis</td>
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<tr>
<td>Multiple myeloma, myelodysplasia, metastatic carcinoma, polycythemia vera, systemic mastocytosis</td>
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<tr>
<td><strong>Non-malignant</strong></td>
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<tr>
<td>HIV infection</td>
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<tr>
<td>Hyperparathyroidism, renal osteodystrophy, vitamin D deficiency</td>
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<tr>
<td>Tuberculosis</td>
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<td>Thorium dioxide exposure, Gray platelet syndrome</td>
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Figure 1. X-ray pelvis and spine showing osteosclerotic lesions
END NOTE

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Conflict of Interest: None declared

REFERENCES