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A CLINICAL CASE STUDY ON PRIMARY MYELOFIBROSIS

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ABSTRACT

Primary myelofibrosis (PMF) is a chronic myeloproliferative neoplasm marked by bone marrow fibrosis, leading to cytopenias and extramedullary hematopoiesis. This case report describes a 55-year-old male with hypothyroidism and portal hypertension, presenting with severe anemia, hepatosplenomegaly, and fatigue. Diagnostic findings included pancytopenia, elevated LDH, JAK2V617F mutation, and bone marrow biopsy confirming overt fibrosis. Treatment with ruxolitinib was initiated. PMF progresses through prefibrotic and fibrotic stages, with the latter carrying a poor prognosis (3–5 years survival). Management focuses on symptom relief, as curative allogeneic stem cell transplant is limited by patient age. This case underscores the importance of early diagnosis and targeted therapy in PMF.

CASE REPORT

History

A 55-year-old male with a history of hypothyroidism and portal hypertension accompanied by splenomegaly for nine years presented with generalized weakness and abdominal distension over the past two months. No significant family history was noted.

General Examination

The patient was conscious and oriented, with normal temperature, pulse, and blood pressure. Severe pallor was observed. Abdominal examination revealed mild hepatomegaly and massive splenomegaly.

Investigations

- **Complete Blood Count (CBC):** Hemoglobin (Hb) – 4.8 g/dL, white blood cells (WBC) – 6.5 × 10^3/cmm, red blood cells (RBC) – 1.57 × 10^6/cmm, platelets – 42 × 10^3/cmm. Blood indices: MCV – 96 fl, MCH – 30.7 pg, MCHC – 31.6 g/dL, RDW – 30%.
- **Peripheral Smear:** -Dimorphic picture with normocytic normochromic and macrocytic normochromic RBCs; 5% normoblasts showing dyserythropoietic changes.

Other Tests: Renal and liver function tests were normal. ESR – 48 mm/hr, serum LDH > 1995, vitamin B12 – 176 pg/mL, TSH – 11.35 uIU/mL, free T3 – 1.99 pg/mL, T4 – 1.13 ng/dL, serum iron – 111.0 µg/dL, ferritin – 144 ng/mL, corrected reticulocyte count – 0.16%. Coagulation profile and Coombs tests were negative.

Imaging: CECT abdomen and pelvis confirmed hepatosplenomegaly without focal lesions, dilated portal and splenic veins, and no lymphadenopathy or ascites.

Bone Marrow Biopsy: Cellularity 40-45%, increased and atypical megakaryocytes with clustering, suppressed myeloid precursors and neutrophils, normoblastic erythroid maturation, and marrow fibrosis with fibroblast streaming, consistent with overt myelofibrosis.

Genetic Testing: JAK2V617F mutation detected.

Treatment

The patient was initiated on the JAK1/2 inhibitor ruxolitinib at 5 mg orally.

DISCUSSION

In PMF, abnormal hematopoietic cells, particularly megakaryocytes, secrete cytokines like fibroblast growth factor, leading to bone marrow fibrosis. This displaces normal hematopoietic tissue, causing extramedullary hematopoiesis, primarily in the liver and spleen, resulting in organ enlargement. Splenomegaly exacerbates pancytopenia, especially thrombocytopenia and anemia. Massive splenomegaly may also lead to subcapsular infarcts.

Stages of PMF:

1. Prefibrotic Stage: Mild normocytic anemia, poikilocytosis, tear-drop cells, nucleated RBCs, thrombocytosis, and mild leukocytosis. Bone marrow shows hypercellularity with abnormal megakaryocyte clustering.
2. Overt Fibrotic Stage: Reticulin or collagen fibrosis (grades 2 or 3) with megakaryocytic proliferation and atypia.

Diagnostic Criteria:

Prefibrotic Stage: Requires all three major criteria (megakaryocyte proliferation/atypia without fibrosis, exclusion of other myeloproliferative disorders, and presence of JAK2/CALR/MPL mutation) plus at least two minor criteria (leukoerythroblastosis, elevated LDH, anemia, or splenomegaly).

Overt Fibrotic Stage: All three major criteria (megakaryocyte proliferation/atypia with fibrosis, exclusion of other disorders, and clonal marker evidence) plus at least one minor criterion (anemia, leukocytosis, splenomegaly, elevated LDH, or leukoerythroblastosis).

Prognosis:

PMF has the worst prognosis among myeloproliferative neoplasms. Survival is approximately 10-15 years in the prefibrotic stage and 3-5 years in the overt fibrotic stage. Risks include leukemic transformation, thrombohemorrhagic events, and infections.

Treatment:

Allogeneic stem cell transplantation (alloSCT) is the only curative option, but most patients are ineligible due to age. For others, treatment focuses on symptom management, such as addressing anemia or splenomegaly.

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