A CASE OF CHRONIC IDIOPATHIC MYELOFIBROSIS
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Abstract:
Idiopathic myelofibrosis is a chronic clonal myeloid disorder characterized by anemia, splenomegaly, immature granulocytes, erythroblasts, and teardrop-shaped red cells in the blood, marrow fibrosis, and osteosclerosis. Myelofibrosis with myeloid metaplasia and idiopathic myelofibrosis currently are the two most frequently used terms for the disease. Idiopathic myelofibrosis characteristically occurs after age 50 years. The median age at diagnosis is approximately 65 years. The incidence of the disease is approximately 0.5-1.5 cases per 1,00,000 per year and a median age of onset of 67 years. Here we are presenting this patient 62 years old male, farmer by occupation, who was admitted in our hospital with massive splenomegaly.

Keyword:
Myelofibrosis, splenomegaly, tear drop cells, marrow fibrosis, JAK2 mutation

CASE REPORT:
62 Year old male patient Muthukamatchi presented with complaints of Easy fatiguability, giddiness for the past 1 month. He had left sided upper quadrant abdominal distension for 1 month which was gradually increasing. He also complained of exertional dyspnoea and loss weight for 1 month duration. He did not have loss appetite, low grade fever, abdominal pain, bony pain, cough with expectoration. He did not have loss of appetite, fever, cough with expectoration and bleeding manifestations in the form of epistaxis, bleeding gums, hematemesis, melena. On general examination he was found to have severe pallor. Apart from that all other findings were normal.

On examination of abdomen, on inspection he was found to have left upper quadrant fullness. There were no dilated veins or scars over abdomen. On palpation he had massive splenomegaly of about 20 cms in size, extended upto midline. He did not have hepatomegaly or free fluid in the abdomen. Other systems including cardiovascular, respiratory, central nervous system examination were normal. His complete hemogram showed Hb of 7.2 gms%, RBC of 2.80 millions/cu.mm, TC of 2800 cells/cu.mm and platelets of about 75000 cells/cu.mm, PCV of 21.

His basic blood investigations like blood sugar, urea creatinine, liver function test and routine urine examination were normal except for increased Serum LDH which was about 764 IU/L. On imaging of abdomen by USG he had splenomegaly of 21 cm size with calcifications. His liver, pancreas, gall bladder were normal with few peripancreatic collaterals and portal vein size was 1.6 cm. CT abdomen of the patient showed massive splenomegaly of 22 cm size with normal sized liver and pancreas.

His peripheral blood smear showed pancytopenia with reduction in all 3 lineages. His RBCs showed anisopoikilocytosis and hypochromic microcytes. There were numerous tear drop cells, target cells seen in his smear.

Peripheral smear showing tear drop cells

Bone marrow aspiration was dry tap. Subsequently we proceeded with bone marrow biopsy which showed thickened and sclerotic bony trabeculae, with erythroid, myeloid and groups of megakaryocytes. Bone marrow also showed Fibrous Tissue proliferation.

Bone marrow showing extensive fibrosis
His liver biopsy specimen showed normal architecture of liver parenchyma with evidence of extra medullary hematopoiesis with nodular collection of megakaryocytes, erythroid and myeloid cells in sinusoidal spaces. There were no evidence of cirrhosis.

OGD scopy of this patient was normal. Finally mutation analysis study for JAK 2 MUTATION was done. In that V617F mutation in JAK2 gene was detected.

DISCUSSION:
According to WHO Criteria for diagnosing IMF[1] Major criteria: 1. Presence of megakaryocyte proliferation and atypia usually accompanied by either collagen or reticulin fibrosis 2. Does not meet criteria for PV, CML, MDS and other myeloid neoplasm 3. Demonstration of JAK2 V617F mutation or other clonal marker Minor criteria: 1. Leukoerythroblastosis 2. Elevated serum LDH 3. Anemia 4. Palpable splenomegaly To diagnose idiopathic myelofibrosis all 3 major and at least 2 minor criteria should be met. In our case all 3 major and 3 minor criteria were met. So we made out the diagnosis of idiopathic myelofibrosis in this patient.

Our patient presented with 1. pancytopenia 2. Massive splenomegaly 3. Tear drop cells in smear 4. Bone marrow fibrosis. He was asymptomatic for many years before presenting with mild symptoms. In view of massive splenomegaly[3,4,5] with pancytopenia, long asymptomatic period, there are only few differential diagnosis for this presentation. But in the background of dry bone marrow tap we proceeded with bone marrow biopsy which showed thickened, sclerotic bony trabeculae with fibrous tissue proliferation[6,7] suggestive of myelofibrosis. Liver biopsy showed extramedullary haematopoiesis. Finally the diagnosis was confirmed with JAK 2 MUTATION ASSAY which showed V617F mutation in JAK2 gene.[8,9] Treatment may include hydroxyurea for thrombocytosis and massive splenomegaly, red cell transfusions for severe anemia, local irradiation of fibrohematopoietic tumors or of the spleen, and splenectomy. Portosystemic shunt surgery may be required for gastroesophageal variceal bleeding [10,11]

The disease may remain indolent for years or may progress rapidly by further deterioration in hematopoiesis, by massive splenic enlargement and its sequelae, or by transformation to acute myelogenous leukemia. Overall median survival is approximately 5 years.

The major causes of death are infection, hemorrhage, post-splenectomy mortality, and acute leukemic transformation[12,13]. An increased risk of progression to leukemia has been reported in splenectomized patients.

CONCLUSION:
We are presenting this case for its rarity. The incidence of the disease is approximately 0.5-1.5 cases per 1,00,000 per year and a median age of onset of 67 years. IMF should be considered as an important differential diagnosis in patients presenting massive splenomegaly with mild symptoms or in asymptomatic patients. These patient has to be followed up for years to find out the development portal hypertension and leukemic transformation.

REFERENCES:
1. WHO Diagnostic criteria for PMF 2008