Case Report

Ascites in CML - A Rare Extramedullary Manifestation

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ABSTRACT

Ascites in chronic myeloid leukaemia (CML) as an extramedullary manifestation is rarely reported in the literature. We report here a case of Chronic myeloid leukaemia presenting with extramedullary disease as massive ascites in a 23-yr old female. All stages of granulocytes and a few blasts were present in both the ascitic fluid and a peripheral blood smear. Based on bone marrow examination, ascitic fluid cytology and ultrasonography of abdomen she was diagnosed as a case of Chronic myeloid leukaemia in chronic phase with extramedullary disease as massive ascites. After starting treatment with Imatinib mesylate favourable response was observed.

Key Words : Ascites, Chronic myeloid leukemia, Extramedullary, Imatinib mesylate.

Introduction -

Chronic myeloid leukaemia (CML) is a clonal myelo proliferative stem cell disorder, characterized by expansion of myeloid, erythroid, and megakaryocytic cells. CML accounts for 15% of adult leukaemia's with an incidence of 12 cases per 100,000 population.

The clinical course of chronic myeloid leukaemia (CML) is characterized by two different clinical phases: the initial chronic phase, and the subsequent acute phase or blast crisis. After a 2 to 4 year chronic phase, the disease accelerates with an increase in the percentage of blast cells in the peripheral blood and bone marrow[1]

Some proportion of patients with CML develop extramedullary disease caused by the infiltration of blast cells; this condition is called extramedullary blast crisis. The incidence of extramedullary blast crisis is reportedly 7 to 17 percent in patients with blast crisis[2].

We hereby report a patient of CML in chronic phase who developed extramedullary blast crisis in the form of massive ascites with no increase in blast cells in the bone marrow, and who was put on Imatinib mesylate with a favourable response.

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Case Report -

A 23 years female presented with history of generalised weakness and easy fatigability of 3 months duration, pain and distension of abdomen since 15 days and difficulty in breathing since 3 days due to abdominal distension. .She had no history of fever, cough, jaundice, decreased urine output, chest pain, palpitations or any bleeding tendency. On physical examination, patient was emaciated, afebrile, pulse was 90/min, regular, blood pressure was 110/70 mmHg, tachypnoeic with respiratory rate of 24/min and Spo2 was 92 % on room air. She was pale. No other positive findings like icterus, cyanosis, oedema feet, lymphadenopathy, petechiae, purpura or ecchymotic patches, sternal tenderness or any signs of liver cell failure were observed. Abdominal examination revealed tense ascites and splenomegaly about 20 cms extending upto umbilicus. Normal peristaltic sounds were audible. Rest of the systemic examination was within normal limits.

Laboratory investigations revealed HB : 7.0 gm% PS : TLC- > 2,00,000 /mm3, DLC: N-58%, L-7%, M-7%, E-3%, B-3%, promyelocyte-2%, myelocyte 10%, metamyelocyte-4%, blast-6%, platelets-5,08,000/ mm3. ***(Figure 1)*** Bone marrow examination showed hypercellular marrow containing cells at all stages of granulocytic hyperplasia and 6% blasts. ***(Figure 2)*** Ascitic fluid analysis revealed glucose 109 mg/dL, protein 5.2

g/dL (serum protein 6.6 g/dL), albumin 2.9g/dL (serum albumin 3.2 g/dL). Ascitic fliud microscopy revealed WBC count 2,390 /mm3 (N-57%, L-6%, E-2%, B-3%, promyelocyte 3%, myelocyte 17%, metamyelocyte 7%, blast 5%) ***(Figure 3)***. The ascitic fluid was negative for Gram stain and acid fast bacilli. Ultrasound examination of abdomen revealed gross ascites with splenomegaly, with spleen measuring 19.3 cms along its longest axis. Liver and portal vein were within normal limits.

Patient's coagulation profile, serum electrolytes, liver and kidney function tests were within normal limits. Patient was found to be negative for HIV and HBsag infection.

Patient was diagnosed as a case of CML in chronic phase with extramedullary disease as massive ascites. Patient was started on tablet Imatinib 400 mg OD and a favourable response was seen.

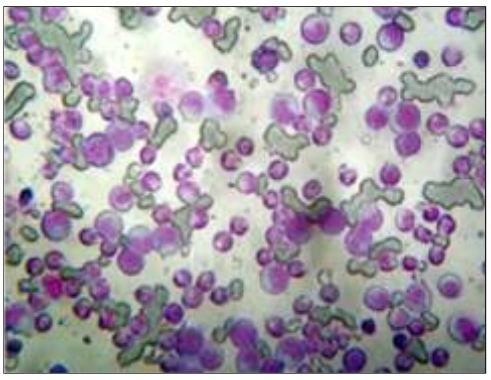

Fig. 1 : **Peripheral smear shows a full spectrum of cells in the granulocyte series, ranging from blast forms to mature neutrophils, with intermediate myelocytes and neutrophils**

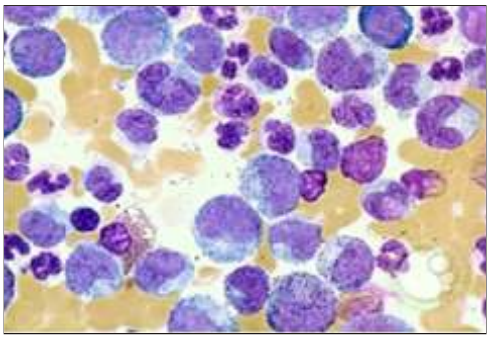

Fig. 2 : **Smear of marrow aspirate showing an increased number of granulocytes in all stages of development and blasts (Wright-Giemsa stain)**

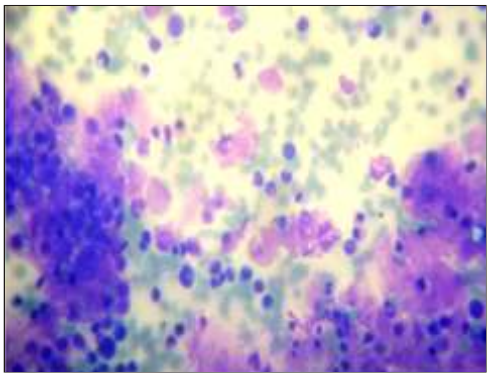

Fig. 3 : **Smear from ascitic fluid showed a dense infiltrate of immature granulocytic precursors along with a few eosinophils and basophils in the background of RBCs**

Discussion -

Although extramedullary blast crisis is generally accompanied by increasing blasts in the bone marrow or peripheral blood, it may precede medullary disease progression[2]. Extramedullary blast crisis is the first manifestation of accelerated phase in approximately 10 percent of patients with CML[3].

Lymph nodes, serosal surfaces, skin and soft tissue, breast, gastrointestinal or genitourinary tract, bone and central nervous system are among the principal areas involved[3]. Case reports of pleural effusion[4], pericardial effusion and cardiac tamponade in patients with CML have been reported. Ascites in chronic myeloid leukaemia (CML) is rarely reported.

Umesh das et al have proposed four mechanisms for the development of pleural effusion in patients with CML[4]. Hyun woo kim et al also proposed similar mechanism for the development of pleural effusion in CML[5]. The first mechanism is leukemic infiltration into the pleura. In these cases, pleural fluid analysis revealed variable stages of granulocytes and leukemic blasts. The ascitic fluid cytology in our patient had similar findings. The second mechanism is pleural reaction secondary to bleeding into the pleural cavities that may cause pleural effusion in the patient with CML. Predisposing factor such as leukostasis and platelet dysfunction may have a role in hemorrhagic

effusion. Thus, the cytological findings in the effusion will be due to leukemic cell contamination and pleural reaction as a result of bleeding into the pleural cavity. If this is true, the ratio of red blood cells to nucleated cells in the blood and ascitic fluid should be similar. In our patient, however, the ratio of red blood cells to nucleated cells was higher in the blood than in the ascitic fluid, and thus it is more likely that the large numbers of nucleated cells in the ascitic fluid originated from the peritoneal cavitiy[5]. A third possible mechanism underlying effusion is pleural extramedullary haematopoiesis. It can present as a discrete mass in almost any organ, including the liver, spleen, breasts, lymph nodes, kidneys, thyroid, pancreas, endometrium, and mediastinum, or in the serous effusion. But, unlike pleural leukemic infiltration, extramedullary haematopoiesis includes hematopoietic cells of the erythroid, myeloid, and megakaryocytic cells, although one lineage can predominate[5]. A fourth mechanism causing effusion is non malignant causes, such as infection. Therefore, the possibility of infectious process must be excluded and the presence of necrotic debris and/or the positive identification of microorganisms by special stains may suggest an infectious process[5].

On the basis of these proposed mechanisms, our clinical and laboratory findings we concluded that leukemic infiltration into peritoneal cavity was the cause of ascites in our patient.

Generally the median time from diagnosis of extramedullary blast crisis to marrow blast crisis is 4 months, and the median survival after development of extramedullary transformation is 5 months[6]. Extramedullary disease in CML is considered as an indicator of poor prognosis, which should lead to a change in therapy and to the institution of treatment usually reserved for blast crisis[5].

Imatinib mesylate, a competitive inhibitor of the Bcr-Abl tyrosine kinase, is highly effective in treating chronic phase CML, but less effective against CML in its advanced phases. However, the efficacy of Imatinib mesylate for extramedullary blast crisis of CML has yet to be fully elucidated[2]. To the best of our knowledge, there has been only a single case report of Chronic myeloid leukaemia presenting with extramedullary disease as massive ascites responding to Imatinib mesylate[6].

In conclusion, patients with CML should be considered at risk for development of extramedullary manifestations of blast crisis while the bone marrow remains in the chronic phase. Extramedullary blast crisis of CML can occur at anytime and circulating stem cells can be seen anywhere. In CML patient with ascites, bleeding into peritoneal cavity and extramedullary hematopoiesis should first be considered. If these causes are ruled out, the presence of leukemic cells in the ascitic fluid may denote leukemic involvement of peritoneum.

Conflicts of interest : None reported

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