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Oncology

EXTRAMEDULLARY MANIFESTATIONS OF CHRONIC MYELOID LEUKEMIA – OUR EXPERIENCE OF 2 CASES

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ABSTRACT Chronic Myeloid leukemia (CML) is a myeloproliferative disorder characterized by the dysregulated production and uncontrolled proliferation of mature and maturing granulocytes with fairly normal differentiation. It is associated with the fusion of two genes: BCR (on chromosome 22) and ABL1 (on chromosome 9) resulting in the BCR:ABL1 fusion gene. In the absence of treatment, CML has a triphasic or biphasic clinical course as it progresses from a chronic phase (CP) to an accelerated phase (AP)and on to a terminal blast crisis. Extramedullary involvement is uncommon at initial presentation or relapse, mostly occurs in accelerated or blast phase and it is rarely associated with pleural and peritoneal involvement. Only few cases of CML with ascites and pleural effusion have so far been reported world wide. Out of these, chronic phase cases are very few. Here we report 2 cases of CML CP, out of which one patient presented which massive ascites and another patient with pleural effusion. Cytology smears of ascitic fluid and pleural fluid showed collections of myeloid precursors with CML CP picture in peripheral blood and bone marrow. Finally diagnosed as having CML CP with serous cavity involvement.

KEYWORDS : CML, chronic phase, Extramedullary, ascites.

INTRODUCTION:

CML accounts for approximately 15 to 20 percent of leukemias in adults [1].The clinical hallmark of CML is the uncontrolled production of mature and maturing granulocytes. It has an annual incidence of 1 to 2 cases per 100,000, with a slight male predominance [2-4].CML has a triphasic clinical course –Chronic phase, accelerated phase and blast crisis. At diagnosis, 20 to 50 percent of patients are asymptomatic, with the disease first being suspected from routine blood tests [5,6]. Among symptomatic patients, systemic symptoms such as fatigue (34 percent), malaise (3 percent), weight loss (20 percent), excessive sweating (15 percent), abdominal fullness (15 percent), and bleeding episodes due to platelet dysfunction (21 percent) are common [6]. Extramedullary involvement mostly occurs during the accelerated phase or the blast phase in the bone marrow and peripheral blood but rarely in the chronic phase. Here we report 2 cases of CML CP presented with extramedullary involvement.

Case Reports

Case 1 –

A 52 year old male diagnosed as CML – CP in 2017 and received Imatinib irregularly for 4 years and stopped on his own. He came to our hospital with gross abdominal distension. On examination his ECOG (Eastern Cooperative Oncology Group) Performance status was 2 and had fluid thrill. On evaluation, complete blood picture revealed total WBC count of 3,57,030 cells/mm3, hemoglobin of 6.3 g/dL, and a platelet count of 3.73 Lakhs/mm3. Peripheral smear showed markedly raised total count with myelocyte bulge and 3 to 5% blasts suggestive of CML-CP (Figure 1). All other blood parameters were normal except serum albumin which was low (2.7g/dl). USG abdomen revealed hepatosplenomegaly and gross ascites. Chest x ray was normal. Bone marrow aspiration (Figure 2A and 2B) revealed elevated myeloid erythroid ratio of 8.1 with myeloid cell proliferation and <3% blasts suggesting CML – CP. Bone marrow biopsy reported as myeloid hyperplasia compatible with CML. Karyotyping was abnormal – 46 XY t(9;22)(q34;q11.2). BCR ABL Quantitative RT PCR reported as P210 – positive – IS % - 40. SAAG(Serum ascites albumin gradient) was 1.6 G/dl. Ascitic fluid cytology smears showed collections of myeloid precursors with occasional mesothelial cells – seen myelocytes, metamyelocytes and neutrophils suggesting serous cavity involvement by CML (Figure 3).

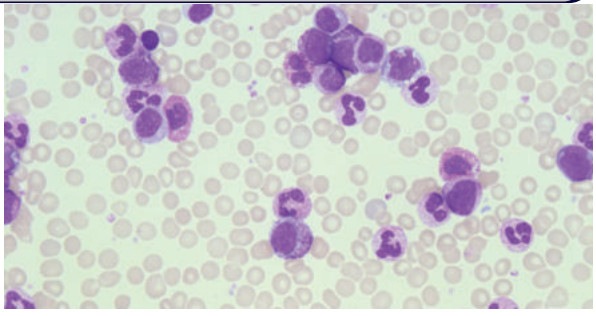

Figure 1: Peripheral Smear Shows leucocytosis with myeloid left shift

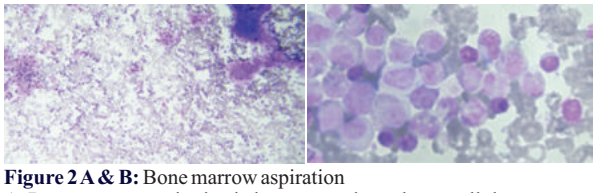

Figure 2 A & B: Bone marrow aspiration
A: Bone marrow aspiration in low power shows hypercellular marrow
B: Bone marrow aspiration in high power shows increased myeloid and erythroid ratio

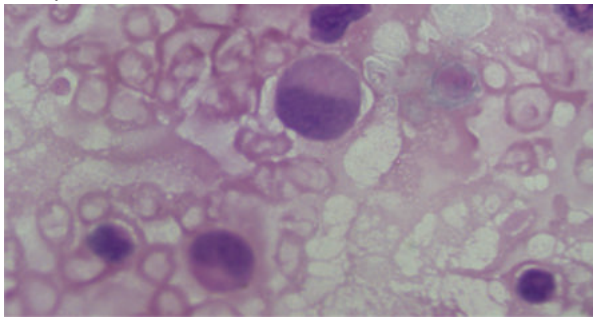

Figure 3 : Ascitic fluid cytology smear showing collections of myeloid precursors

Case 2 –

A 45 year old female presented with hyperleukocytosis and moderate pleural effusion. Her complete blood picture revealed Total WBC count of 2,30,270 cells/mm3, hemoglobin of 7.3 g/dL, and a platelet count of 5.40 Lakhs/mm3. The peripheral blood and bone marrow aspiration showed CML – CP picture. BCR ABL qualitative RT PCR (P210) – positive. Karyotyping revealed only t(9:22) translocation. Pleural fluid cytology showed collections of myeloid cells like myelocytes and metamyelocytes. She was started treatment with Imatinib 600 mg OD.

DISCUSSION:

Some patients of CML develop extramedullary disease caused by the infiltration of blast cells; this condition is called extramedullary(EM) blast crisis. Its incidence is 7 to 17 % [7] and mostly occurs during the accelerated phase or the blast phase but rarely in the chronic phase. It may precede medullary disease progression [7] and may be first manifestation of AP in approximately 10% of patients [8] It is an indicator of poor prognosis. Common sites involved are lymph nodes, serosal surfaces, genitourinary tract, breast, gastrointestinal tract, skin and soft tissue, bone and central nervous system (CNS). Case reports of CML with pericardial effusion, pleural effusion and cardiac tamponade have been reported.[9][11] Ascites in CML patients is rarely reported.

Four mechanisms were proposed for the development of effusions in CML by Umesh das et al and Hyun woo kim et al. [9][10]

1. Leukemic infiltration into the visceral cavity
2. Reaction secondary to bleeding into the cavities – If this is the cause, the ratio of red blood cells to nucleated cells in the blood and ascitic fluid should be similar.
3. Extramedullary haematopoiesis
4. Non malignant causes like infection – Presence of necrotic debris and identification of microorganisms support infectious process.

Based on clinical and laboratory findings, we concluded that leukemic infiltration into visceral cavity is the cause for development of ascites and pleural effusion in our cases. Many such cases were reported showing favourable response to BCR ABL tyrosine kinase inhibtors.[12] Aleem and Siddiqui reported a patient with massive ascites and bone marrow in CML CP, and favorable response to imatinib.[13] Bansod *et al*. had reported a patient who presented with massive ascites and massive splenomegaly and was diagnosed with EM blast crisis without bone marrow involvement and showed a favorable response to imatinib therapy.[14]

CONCLUSION:

Ascites and pleural effusion in CML CP are reported very rarely. Proper cytological examination of ascitic and pleural fluid is essential. Patients with CML can develop EM blast crisis while the marrow still remains in chronic phase. EM blast crisis is almost always followed by haematological blast crisis after a few months. Hence such cases should be followed closely for future development of blast crisis.

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