Scholars Academic Journal of Biosciences (SAJB) **ISSN 2321-6883 (Online)**
Sch. Acad. J. Biosci., 2014; 2(12C): 987-990 **ISSN 2347-9515 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI:** 10.36347/sajb.2014.v02i12.028

Case Report

Chronic Myeloid Leukemia (CML) Infiltrating Pleura: A Bad Prognostic Sign: Case Report with Review of Literature

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Abstract: Pleural effusion in chronic myeloid leukemia (CML) is poorly understood and rarely reported in the literature. CML has been reported to show extra medullary involvement in only 10% cases that involves lymph nodes and spleen. Pleura are extremely uncommon site of extra medullary involvement in CML. When the pleural effusion is caused by leukemic pleural infiltration, the differential white blood cell count of the effusion becomes identical to that of the peripheral blood, fluid cytology revealing leukemic blasts. We report a case of 40 years old male patient who was referred to our hospital with 10 days history of fever, dyspnoea and cough. He was diagnosed one year ago as a case of chronic phase CML with Philadelphia chromosome (Ph) and *BCR/ABL* gene translocation positive, since one year he is on imatinib. X-Ray chest and computerized tomography (CT) chest demonstrated gross left sided pleural effusion. Diagnostic thoracocentesis revealed pleural effusion infiltrated by myeloblasts which are suggestive of extramedullary blast crisis.
Keywords: Chronic Myeloid Leukemia, Philadelphia Chromosome (Ph), Extramedullary Blast Crisis, BCR/ABL Fusion Gene, Pleural Effusion.

INTRODUCTION

Very few hematologic malignancies have been reported in the literature with development of pleural effusion during the pathogenesis and spread of the disease.

Pleural effusions are most frequently associated with Hodgkin's Lymphoma (HL) and Non- Hodgkin's Lymphoma (NHL), Myelodysplastic Syndromes (MDS), rarely in Acute and Chronic Leukemia [1]. Pleural involvement in CML generally appears shortly before transformation to acute leukemia [2]. Development of extramedullary disease in the pleura of patients with CML is found to be frequently associated with increased blasts in the pleural fluid. Though analysis of pleural fluid always does not exhibit excess blasts. It has been found that in some cases, all stages of granulocytes and blasts are present in the pleural fluid [3, 4].

CASE REPORT

A 40year old male presented with dyspnoea, cough, and high grade fever. He was a known case of CML on imatinib 400mg since one year. No past history of tuberculosis, bronchial asthma, hypertension or diabetes. No recent history of trauma to the chest wall.

Physical examination revealed moderate pallor, vitals –Normal, No clubbing or cyanosis and No lymphadenopathy.

Systemic examination revealed decreased breath sounds on left side of chest, moderate splenomegaly without liver enlargement.

Table 1: Lab investigations

Investigation	Findings
Complete Blood Picture (CBP)	Hemoglobin (Hb %) – 8.5gm% (Normal Range : 12 gm % - 16 gm%) White Blood Cell Count-71,800/cu.mm (Normal Range : 4,000 to 11,000/cu.mm) Myeloblasts -02% (Not seen normally) Promyelocytes -10% (Not seen normally) Myelocytes -18% (Not seen normally) Metamyelocytes -10% Not seen normally) Neutrophils -34% (Normal Range: 40-70 %) Lymphocytes -07% (Normal Range: 20-40 %) Eosinophils -06% (Normal Range: 01-06 %) Basophils -01% (Normal Range: 01-02 %) Monocytes -07% (Normal Range: 02-10 %) Platelet count :- 60,000/cu.mm (Normal Range: 1.5 Lakh -4.0 Lakh/cu.mm) (Fig. 1)
Chest X-Ray	Moderate Left sided pleural effusion
Ultrasonography	Left gross pleural effusion with internal echoes and septations with left lung collapse and Splenomegaly
CT-Chest	Moderate to gross pleural effusion with adjacent lung collapse. Patchy nodular areas of increased attenuation with fibrotic bands noted in bilateral upper lobes.
RT-PCR : BCR / ABL translocation	Positive
Pleural Fluid Analysis	2ml in quantity , Hemorrhagic (Fig. 2) Cell Count and Morphology:Total cell count >80,000/cu.mm. Loaded with cells comprising of myeloid series of cells comprising of blasts, promyelocytes, myelocytes, metamyelocytes and plenty of lymphocytes, RBC's and few nucleated RBC's (Fig. 3 & 4)

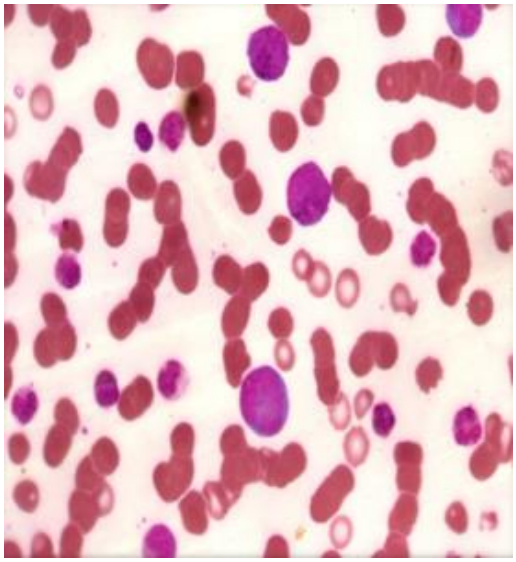

Fig. 1: Peripheral blood smear showing Microcytic Hypochromic RBC's and Myeloblasts

Fig. 2: Hemorrhagic Pleural effusion

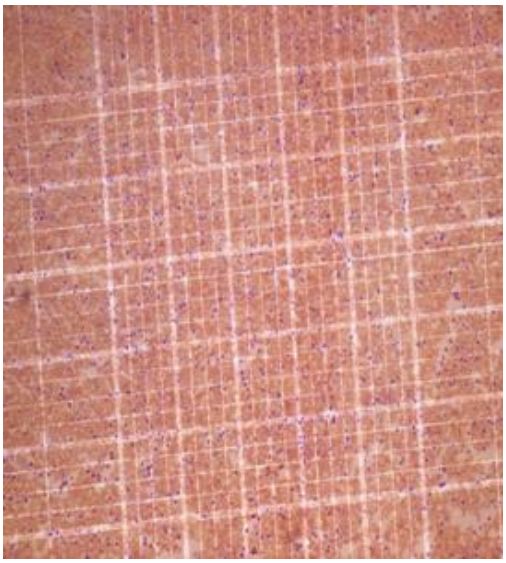

Fig. 3: Neubaur chamber loaded with pleural fluid showing myeloid series of blast cells and loaded with RBC's (Low Power View)

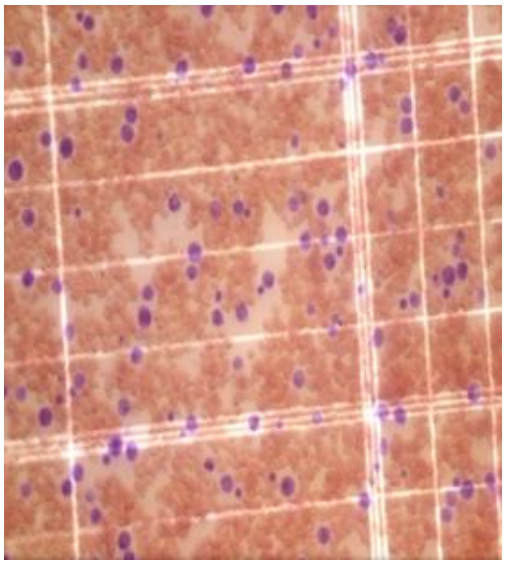

Fig. 4: Neubaur chamber showing myeloid series of blast cells and loaded RBC'S (High Power View)

DISCUSSION

Chronic myeloid leukemia (CML) involving pleura and causing pleural effusion is not clearly understood, generally occurring during the accelerated phase or blast crisis [4].

Several possible mechanisms have been proposed for exudative pleural effusion in CML patients.

- First mechanism is leukemic infiltration into the pleura usually occuring at the time of or just prior to bone marrow evolution to blast crisis phase involving lymph nodes, bone, nervous system, brain, testis, skin, breast, soft tissues, synovia, gastrointestinal tract, ovaries, kidneys and pleura [5-7, 9].

- Second mechanism is pleural reaction that is secondary to bleeding into the pleural cavities, may cause pleural effusion in the patient with CML [8]. Predisposing factors like leukostasis and platelet dysfunction may have a role in hemorrhagic effusion [9].

- Third possible mechanism is pleural extramedullary hematopoiesis that can present as a discrete mass in organs such as liver, spleen, breasts, lymph nodes, kidneys, thyroid, pancreas, endometrium, and mediastinum, or in the serous effusion [9, 10].

- Fourth possible mechanism is nonmalignant causes like infection [9].

- Fifth mechanism pleural effusion is a complication of dasatinib therapy in CML, usually mild or moderate and more frequent among patients in advanced CML phases and those who are treated at daily doses of 140 mg or higher, particularly with a twice-daily schedule. But with adequate management, most patients can continue therapy with dasatinib [11].

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 [7]. In our case patient reported with pleural effusion after one year of diagnosis.

Extramedullary disease is considered as an indicator of poor prognosis that should lead to a change in therapy and to the institution of treatments usually reserved for blast crisis. However, effective standard therapy for pleural effusion in CML is not there [7]. Literature survey has shown fewer cases with isolated pleural infiltration of CML.

CONCLUSION

To conclude patients with CML should be considered at risk for the development of extramedullary manifestations of blast crisis while the bone marrow remains in the chronic phase [9].

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