Chronic myelogenous leukemia presented as blast transformation phase

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Abstract
Chronic Myelogenous Leukemia (CML) is a chronic myeloproliferative neoplasm characterised by uncontrolled proliferation of mature and maturating granulocytes. In our case 42 year male over a period of 13 months showed blastic transformation with severe thrombocytopenia, disseminated intravascular coagulation and bleeding. Herewith we present this case for its clinical behaviour, hematological findings and disease course.

Keyword: Myeloproliferative Neoplasms, Blast crisis, Leukemia.

Introduction
CML is a pleuripotent myeloproliferative neoplasm associated with BCR-ABL1 fusion gene in a Philadelphia chromosome. In most of patients is characterised by a chronic phase which gradually goes through an accelerated phase.[1] For CML with blast transformation requires molecular cytogenetic study for presence of t(9,22)(q34;q11) Philadelphia chromosome or BCR gene (22q11 and ABL gene (9q34) fusion transcript along with blood or bone marrow showing >20% blasts or extramedullary blast proliferation. In bone marrow biopsy shows a large focus of blasts. In our case showed above findings with severe thrombocytopenia.

The progression of CML to accelerated / blastic phase may originate in precursor cells like granulocytic macrophage progenitor pool rather than hemopoietic stem cells.

Case Report
A 45 year male presented with history of abdominal pain, severe nausea, vomiting of 2 days associated with blurring of vision, fatigue, shortness of breath, chest pain and pain in extremities. He was a known case of CML which was detected 13 months back and was on treatment. On physical examination he had mild splenomegaly and hepatomegaly. Abdominal tenderness was noted. Severe pain in both the extremities were noted.

On investigation complete blood count showed Hb – 14.4 gm%, total leukocyte count – 5,33,000/mm^3, platelet count – 60000/mm^3. The differential count showed myeloblast – 88%, stab form – 2%, neutrophils – 6%, lymphocyte – 4%. (Fig. 1-3.) Prothrombin time and INR was raised.

Previous 1 month back bone marrow finding revealed hypercellularity, increased myeloid series (M:E – 12:1) with 10% myeloblast and granulocytes in all stages of maturation. Basophils are elevated and small hypolobated megakaryocytes were noted. Erythroid series cells showed normoblastic erythropoiesis. On peripheral blood smear and bone marrow findings were suggestive of CML with mild fibrosis.

Cytogenetic study showed BCR-ABL1 fusion gene in Philadelphia chromosome, type of transcript – P210 (B3A2.B2A2) major transcript detected.

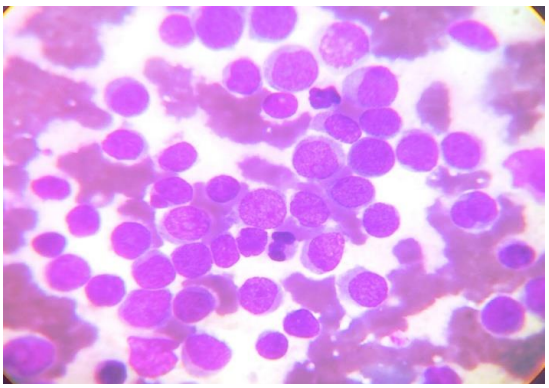

Fig. 1: Peripheral blood smear showing numerous blasts, and few stab and neutrophils. (Leishman stain, 400x)

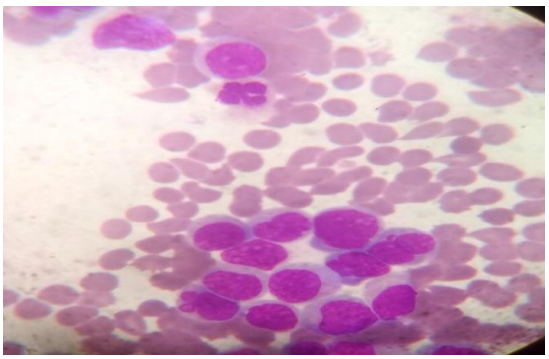

Fig. 2: Peripheral blood smear showing large blasts with round to oval nuclei and 2-3 prominent nucleoli. (Leishman stain, 1000x)

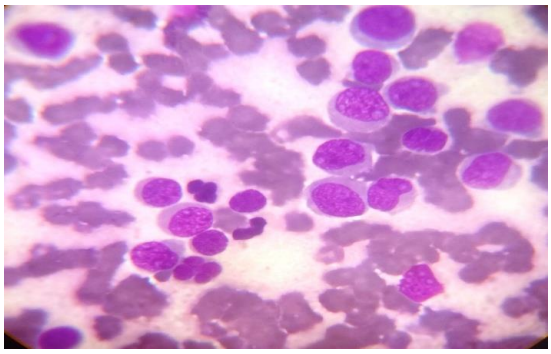

Fig. 3: Peripheral blood smear showing myeloblasts with round to oval nuclei and 2-3 prominent nucleoli, and few neutrophils (Leishman stain, 1000x)

Discussion

CML is called as chronic myeloid leukemia/ chronic granulocytic leukemia. I t is commonly seen as chronic myeloproliferative neoplasm with overall incidence of 10-20 cases per million annually. In Indian population CML is one of the commonest adult leukemia accounting for 30% to 60% of all adult leukemias[2]. It commonly affect (median age) in 5th-6th decade of life.[3]

Clinically presents with insidious onset having anemia, weakness, easy fatiguability, weight loss, abdominal pain or dragging sensation.[4] About 20-40% cases remain asymptomatic or diagnosed incidentally on routine hematological investigation having high leukocyte count.

In our case patient had sudden pain abdomen, vomiting and presented with clinical and laboratory finding of disseminated intravascular coagulation and bleeding.

The CML disease progress in 3 phases as chronic phase in most of patients of variable duration of 2–5 years. The half of cases have accelerated phase which shows persistent or gradually increasing leucocytosis, thrombocytosis, basophilia or splenomegaly.

In usual course the progress of disease occurs from chronic phase to an accelerated phase and then to blast phase / blast crisis. The terminal phase of blast crisis is noted in about 70% of cases. The clinical course is similar to that of acute leukemia.

In our case it showed transition to blast transformation phase with severe DIC. The blast crisis arises in patients with known CML, but it can be the initial presentation of the disease. In this situation, if there is no previous history of leukocytosis or splenomegaly the distinction between CML-BC and de novo *BCR-ABL1*+ AML is a diagnostic dilemma.

The mean of 3 years after diagnosis of CML is observed, to develop blast transformation phase. The blast transformation phase usually shows transition to myeloid blast in 70% of cases and 20-30% to lymphoid blast. In rare cases transformation to erythroid blast or extramedullary blast in tumor mass in soft tissue, lymphoid tissue is noted.[5,6]

In our case showed > 88% of myeloid blast on peripheral smear. LAP (Leukocyte alkaline phosphatase) score was low indicating abnormal neutrophil maturation. Patient developed bleeding and related to severe thrombocytopenia and coagulopathy related to severe leucocytosis (TLC-5.33 lakhs/mm^3).

The cases of CML in chronic phase without effective treatment will go to accelerated phase and then to blast phase in 3-4 years after diagnosis.

The treatment of CML is to reduce signs and symptoms of splenomegaly, treat systemic or metabolic complications, control of severe leucocytosis and chemotherapy. Imatinib mesylate which shows 90-95% complete hematological remission and in 60% cases cytogenetic response. For Imatinib resistance patients second generation protein kinase inhibitors may be given. Only curative approach is stem cell transplant for better management of these cases.[7]

Overall 5-year relative survival increased from 27 to 49%. Patients with CML-BP have a median survival of approximately 6 months. Leukemia carry a considerable risk of morbidity as well as mortality.[8-10]

The lymphoblastic blast crisis cases are noted in 15-30% individuals. Usually there are younger age group, lower leucocyte count and respond better to chemotherapy than myeloid crisis.

Conclusion

Our case showed sudden severe clinical manifestation of coagulopathy related to CML in blast transformation phase. The patients having more blasts, increased basophils, high leukocyte count and splenomegaly will rapidly transformed to blast phase.

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