

CASE REPORT

Blast phase transformation of chronic myelogenous leukemia presenting with central nervous system manifestation

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ABSTRACT

Chronic myelogenous leukemia (CML) is the most common of all leukemia constituting 15–20% of all leukemia. The clinical course of the diseases runs in two to three phases, initial chronic phase followed by accelerated phase or blast phase. Blast phase most commonly presents clinically as fever, splenomegaly, and bone pain. Here, we present a case of CML in blast phase presenting with central nervous system manifestation in a 55-year-old patient with a brief review of the literature.

Key words: Blast phase, cerebral infarct, chronic myeloid leukemia, thrombosis

Introduction

Chronic myelogenous leukemia (CML) is the most common of all leukemia constituting 15–20% of all leukemia. It is a disease of the bone marrow arising from the abnormal pluripotent stem cell and in 90% of the cases it is associated with Philadelphia chromosomes. The clinical course of the diseases runs in two to three phases, initial chronic phase followed by accelerated phase or blast phase.^[1,2] Blast phase may be myeloid (70%) or lymphoid (30%). Blast phase most commonly presents clinically as fever, splenomegaly, and bone pain. Occurrence of central nervous system (CNS) manifestations due to blast phase is rare.^[2] We report such a case in a 55-year-old male with a brief review of the literature.

Case Report

A 55-year-old male patient presented to emergency department with a history of sudden weakness of left half of the body along

with headache, altered sensorium, and deviation of angle of mouth to the right side since 1-day. He was a known case of CML on imatinib treatment. His Philadelphia chromosome status was more than 100% at the time of diagnosis. He was not a known diabetic or hypertensive. On examination, pallor was present. CNS examination revealed E2M2V4; he was in altered sensorium, the power decreased on the left half of the body (2/5), and left plantar was up going. Per abdomen examination showed splenomegaly and other systems were within normal limits. Fundus examination showed papilledema. Computerized tomography scan (CT scan) revealed a hypodense area in right frontal – temporal region with areas of the infarct [Figure 1a]. Routine blood investigations showed hemoglobin - 10.4%, total leukocyte count was 37,860/cu mm, platelet count was 98,000/cu mm. Peripheral smear showed microcytic hypochromic red blood cells with increased white blood cell counts, which predominantly showed myeloblast (30%) and monoblast (30%), basophils constituted 8%, rest of the myeloid series constituted 32% [Figure 1b-d]. Biochemical investigations were within normal limits. With the above findings, a diagnosis of CML in blast phase to acute myeloid leukemia (AML) M4 (By French American British classification) with cerebral infarct was made. Cerebrospinal fluid (CSF) examination was planned, but the patient expired. Patient relatives did not give consent for postmortem CSF examination.

Discussion

Hematologically, CML is characterized by the presence of immature granulocytes, basophils, eosinophils, thrombocytosis, thrombocytopenia, and anemia. Clinically, course of CML is bi or triphasic; initial chronic phase is followed by accelerated phase or blast phase.^[2] World Health Organization (WHO) laid down

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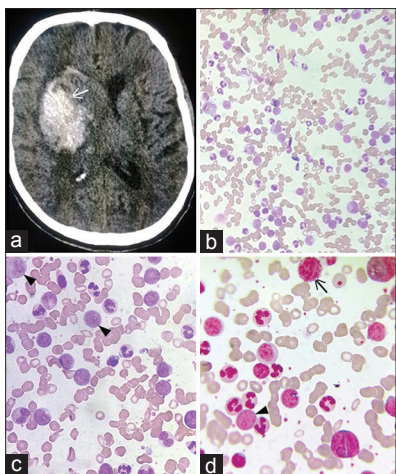


Figure 1: (a) Computerized tomography scan showing hypodense area in right frontal –temporal region with areas of the infarct (arrow). (b) Peripheral smear showing microcytic hypochromic red blood cells with increased white blood cell (WBC) count and decreased platelet (Leishman, \times obj. 40). (c and d) Peripheral smear showing increased WBC with blasts (arrow head). Note the presence of basophil (arrow) (Leishman, \times obj. 100)

criteria for diagnosis of blast phase, it is diagnosed when one or more of the following criteria are present: (1) Blast $>20\%$ of peripheral blood leukocytes or nucleated bone marrow cells. (2) Extramedullary blast (EMB) proliferation and (3) Large foci of clusters of the blast in the bone marrow biopsy.^[1]

Clinically, conversion of chronic phase to blast phase presents with varied symptoms such as unexplained fever without underlying infection, bone pain, abdominal pain due to splenic enlargement or infarct, loss of well-being, unexplained weight loss, extramedullary enlarging masses, arthralgia not responding to treatment, and rarely CNS infarct (as observed in our case).^[3]

In a study by Alwan^[2] on 53 patients of CML, 21 developed blast crisis. The most common clinical presentation was unexplained fever (95%) followed by splenic enlargement (66%) and bone pain in 57% of the patient. Only one patient (5%) presented with hemiplegia. CT scan showed thrombosis of the vessel (as observed in our case).

CNS involvement in CML occurs due to many causes; it may be due to EMB crisis or vascular injury or platelet abnormality.^[4,5] EMB crisis is defined as a proliferation of the blast outside the bone marrow, this may or may not be preceded by bone marrow blast crisis. CNS is one of the favored organs for EMB due to the poor penetration of imatinib mesylate. Imatinib mesylate is the gold standard drug for CML, and it is effective against all the phases of CML. It has shown 90% hematological and 60% cytogenetic response in cases of CML; however the main disadvantage is poor CNS penetration by the drug and its metabolites.^[4] Studies by Wolff *et al.*^[6] Petzer *et al.*^[7] Neville *et al.*^[8] and cases reported by Radhika *et al.*^[4] supported the poor penetration of imatinib and its

metabolites to CNS. In addition, Wolff *et al.*^[6] also documented that level of drug in CSF was 1% less than plasma, and it was $1/3^{\text{rd}}$ of the concentration required to inhibit 50% of proliferating blast.

The proliferating blasts, especially of monoblastic lineage, because of their large size, increase the viscosity of the blood, which leads to stasis of blood, tissue hypoxia, and endothelial injury predisposing to thrombosis. AML M3 (by French American British Classification) contain procoagulant granules which on institution of chemotherapy leads to disseminated intravascular coagulation and consumption of clotting factors and platelet causing hemorrhage. Hemorrhage in cases of leukemia may also occur due to qualitative or quantitative defects of the platelets.^[5]

The prognosis of CML in blast phase is poor with a median survival of 6 months myeloid type and for lymphoid type is 12 months. The prognosis is grave if the patient develops CNS manifestation.^[2]

Conclusion

Blast crisis should be kept in the differential diagnosis in any patient presenting with CNS manifestation in a known case of CML, and the prognosis of these patients is usually poor with short survival.

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