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Case Report

Transformation of CML Blast Phase to T Cell Acute Lymphoblastic Leukemia: A Rare Case Presentation

PS Ghalaut[1], Sudhir Kumar Atri[2], Isha Pahuja[3], Naresh Gaur[3], Arvind Chahal[3], Divya Sahni[3],
[1]Senior professor & Head, Department of Medicine, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana-124001
[2]Professor, Department of Medicine,Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana-124001
[3]Post Graduate Residents, Department of Medicine,Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana-124001

***Corresponding author**
Naresh Gaur
Email: nareshgaur13@gmail.com

Abstract: We are presenting this case that was a follow up case of chronic myeloid leukemia and presented in blast phase to the Department of clinical Hematology and Oncology of our institute. The patient was properly evaluated further with repeated complete haemogram, Immunophenotyping, Bone marrow biopsy examination and found to be CML to T Cell ALL transformation that is quite rare situation. The patient was then treated with ALL protocols. We concluded that every patient of CML blast phase needs complete work up for proper management.
Keywords: CML, IRMA, ALL, Blast phase.

INTRODUCTION

Chronic myeloid leukaemia (CML) is a clonal stem cell disorder, which results from the neoplastic transformation of the hemopoietic stem cell and is characterized by an increased proliferation of myeloid elements at all stages of maturation. The course of the disease is characteristically triphasic: a chronic phase (CP) lasting three to six years is followed by transformation to an accelerated phase (AP) and then a terminal blast phase of short duration. Most of the patients who progressed to blast crisis belong to AML. Rest belongs to B cell ALL. We are reporting a case with CML to T cell ALL conversion which is quite rare in the course of CML. With introduction of imatinib as first line therapy prognosis is drastically improved and conversion to blast phase has decreased significantly.

CASE REPORT

A 50 year female patient of CML since 1 yron regular t/t with imatinib therapy 400mg once daily and with complete hematological response, presented to our hematology clinic with generalized weakness since 21 days, bleeding spots all over the body which were sudden and spontaneous in onset progressive in nature and not associated with any trauma. It was associated with bleeding gums since 14 days and fever since 7 days. Fever was low grade, intermittent in nature and associated with decreased appetite without any system specific symptoms. On General physical examination patient vitals were stable. Pallor and sternal tenderness were present.Skin examination showed multiple, diffuse, reddish to bluish, soft, flat, smooth surface, irregular ecchymotic patches of variable size varying from 1x1 cm to 4x3 cm were present over bilateral upper and lower limbs, chest and abdomen. Per abdomen examination showed 4 cm palpable spleen. Rest of the systemic examination was normal.

On investigating the patient complete blood count showed Hb7.8 g/dl, TLC 55000 /mm3, DLC N5/L7/M1/E1B/2, APC < 20,000 and peripheral smear showed dimorphic picture with 80% blasts. Bone marrow biopsy revealed marked decrease in normal hematopoitic elements and marrow was full of lymphoblasts. Her liver function and kidney function tests were within normal limits. Bcl-abl was 100% positive. Immunophenotyping analysis is shown in this table 1.

Table 1: Immunophenotyping analysis

Marker	Result	Marker	Positivity
CD3	strong +ve	CD19	-ve
CD5	strong +ve	CD20	-ve
CD7	strong +ve	CD22	-ve
CD10	-ve	CD33	-ve
CD13	-ve	CD117	-ve
CD45	+ve	MPO	-ve
HLA-DR	-ve	Tdt	-ve

This is suggestive of T cell ALL. IRMA(imatinibresistance mutational analysis) was done but it was inconclusive. According to patient performance status she was started on BFM protocol of ALL but during chemotherapy patient developed intracranial bleed due to severe thrombocytopenia and expired.

DISCUSSION

CML is a myeloproliferative disorder associated with philaldelphia chromosome t(9;22) (q34;q11) or BCR-ABL fusion gene which results in formation of a gene product that has constitutively active tyrosine kinase activity. Philaldelphia positive CML has 3 phases- chronic, accelerated and blast. Chronic phase(CP) in CML is defined as presence of <10% of blasts in blood or marrow. Accelerated phase in CML is defined as blasts in blood or marrow >10-19%, basophils in blood >20%, persistent thrombocytopenia (< lac/ul), thrombocytosis (>10 lac/ul), Blast phase in cml is defined as presence of >20% of blasts in peripheral blood or bone marrow and the demonstration of extra medullary blastic infiltrates [1]. Resistance mutations in late CP are associated with greater likelihood of progression to blast phase, confirming the significance of BCR-ABL for the development of mutations and of genetic instability for disease progression [2]. The most frequently observed genetic aberrations are a second Philadelphia chromosome, trisomy 8, isochromosome 17, trisomy 19, alone or in various combinations, and complex aberrations. Up to 80% of BC patients show some forms of chromosomal changes. Cytogenetic evolution appears to be the most consistent predictor of blastic transformation.

The most frequently observed mutations involve p53 (in 25% of myeloid BC) and p16/AKT (in about 50% of lymphoid BC) [3, 4]. In contrast to BCR-ABL positive B-ALL,BCR-ABL positive T-ALL is extremely rare with very few cases reported [5].

CONCLUSION

In preimatinib era conversion of cml to blast crises was 20% per year. But with the introduction of imatinib conversion of cml to blast crises reduces only to 1% per year. Out of this 1%, 70- 80% convert to AML(Acute Myeloid Leukemia) and 20% to ALL(Acute Lymphoid Leukemia). Out of this 20% of ALL, 95% convert to B cell ALL and only 2-3% convert to T cell ALL [6]. Sudden blastic transformation occurring in patients in complete hematologic transformation is less common and among these patients conversion to T cell ALL is very rare which has bad prognosis and requires aggressive treatment. Therefore all patients with blast phase should be properly evaluated because treatment and prognosis vary according to type of transformation.

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