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Case Report

Chronic Myeloid Leukemia in Myeloblastic Crisis Under 18 Months of Age-Case Report

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Abstract

Chronic Myelogenous Leukemia (CML) is rare in childhood. It constitutes three to five percent of leukemia in paediatric age of less than fifteen years. Estimated annual incidence is 0.6-1 cases/million. In adult CML, myeloid lineage is more common with 20-30% being lymphoblastic in blast phase. But in paediatric, blast phase is commonly lymphoblastic. This case is being reported because of its extremely uncommon incidence in age less than eighteen months. To the best of our knowledge, this is the first case report of CML in myeloid blast crisis under eighteen months of age.

Keywords: Chronic myeloid leukemia; Chronic phase; Children

Abbreviations: CML: Chronic Myeloid Leukemia; ECG: Electrocardiography; 2D ECHO: 2-Dimensional Echocardiogram; BP: Blast Phase; ALL: Acute Lymphoblastic Leukemia; Ph Chromosome: Philadelphia Chromosome; HSCT: Hematopoietic Stem Cell Transplantation

Introduction

Chronic Myelogenous Leukemia (CML) is rare in childhood. It constitutes three to five percent of leukemia in paediatric of age less than fifteen-years [1]. The annual incidence is 0.6-1 cases per million [1]. In adult CML, myeloid lineage is more common with 20-30% being lymphoblastic in blast phase. But in paediatric, blast phase is commonly lymphoblastic. To the best of our knowledge, there is no case report of myeloid crisis of CML under the age of two years. Hence, we report this unique case of myeloid crisis in a fifteen-month-old girl baby.

Case Report

15month old girl baby presented with complaints of fever on and off for 7 months and abdominal distension for 5 months. She is second born to nonconsanguineous parents. Her development was appropriate for age. On examination she had pallor, splenohepatomegaly (spleen was palpable 8 cm below left costal margin, liver 6 cm below right costal margin). Blood counts at diagnosis were haemoglobin of 6.1 gm per dl, total count of 3,40,000 cells per cubic millimetre with platelet of 1.05 lakhs per cubic millimeter.

Peripheral smear showed markedly increased number of white blood cells with marked shift to left with neutrophilic lineage, with blast cells being 4% and basophil 12%. Biochemistry was normal except lactate dehydrogenase, 292U/L. ECG, 2D ECHO, chest X ray was normal. Ultrasound abdomen revealed hepatosplenomegaly. Haemoglobin electrophoresis was normal for age (haemoglobin adult 96%, haemoglobin A2 3.2%). Bone marrow morphology was hypercellular with myeloid hyperplasia, with blasts of 20%. These blasts were medium sized cells with fine chromatin, granular cytoplasm, suggestive of acute myeloid leukemia. Karyotyping was 46, XX, t(9,22) (q34,q11). Flow cytometry was positive for MPO, CD 13, CD 33, CD 117, CD 64, HLA DR - suggestive of acute myeloid leukemia (M2 type). PCR in peripheral blood positive for BCR-ABL (p 210) fusion. These features were suggestive of chronic myeloid leukemia in myeloid blast crisis.

In view of myeloid blast crisis, she was managed with daunorubicin and cytosine arabinoside (3+7) protocol. Two cycles of induction followed by three consolidations with high dose cytosine arabinoside along with TKI (dasatinib) (Table 1).

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Table 1:

	UPFRONT	POST INDUCTION1	POST INDUCTION2	POST HIDAC 1	POST HIDAC 2	POST HIDAC 3
CYTOGENETICS	t(9,22) (q34,q11)	t(9,22) (q34,q11)	t(9,22) (q34,q11)	t(9,22) (q34,q11)	t(9,22) (q34,q11)	t(9,22) (q34,q11)
BCR: ABL	94.54%	6.38%	3.893%	1.542%	0.162%	0.76%
MRD	N/A	0.015%	0.013%	0.009%	0.05%	0.01%

Discussion

CML is a rare disease in children. It accounts for 3-5% of all leukemia in children less than fifteen years of age [(1)]. In children CML is common in female whereas in adulthood it is common in male [2]. Splenomegaly, hepatomegaly, hyperleukocytosis, anemia and leukostatic signs and symptoms are more frequent in children [3]. Percentage of circulating blasts and spleen size are important predictors of long-term survival [4].

The WHO classification definition for Blast Phase (BP) is ≥ 20% blast cells in the peripheral blood or bone marrow, or extramedullary blast proliferation [5]. In adult CML, myeloid lineage is more common with 20-30% being lymphoblastic in blast phase. But in paediatric, blast phase is commonly lymphoblastic [6]. An international registry of CML in children (n=479) reported blast in seventeen children, with 70% being lymphoblastic [6]. To the best of our knowledge no patient with CML in myeloblastic crisis under 2 years of age was reported.

Within the major break point cluster, CML patients there is transcript phenotypes with an e13a2 0r e14a2 junction [7]. Clinical presentation of splenomegaly with increased white blood cell counts in a well child should raise the suspicion of CML. CML blast phase shares clinical picture of acute leukemia. CML blast crisis is difficult to distinguish from Ph positive Acute Lymphoblastic Leukemia (ALL). In CML there is massive splenomegaly, basophilia and p210 fusion gene (p190 in Ph positive ALL). In CML lymphoid blast crisis, Philadelphia chromosome (Ph) will be in the lymphoblasts and neutrophils, whereas in Ph positive ALL, it is present only in lymphoid cells.

After the induction phase, parents were counselled for HSCT, however parents refused. Now one year post consolidation, patient is on dasatinib and regular follow-up.

Author Statements

Conflict of Interest

No conflict of interest for all the authors.

Declaration of Patient Consent Form

Consent form attached in supplementary material.

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