



Case Report

# Chronic myeloid leukemia in childhood: a case report

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## ABSTRACT

Chronic myeloid leukemia is a rare hematological malignancy in the pediatric age group. It is a clonal hematopoietic stem cell disorder in which granulocytes are the major proliferative components with the presence of the BCR-ABL1 fusion gene. Here, we report a case of CML in a three - year child with a clinical presentation of fever and abdominal distension. The diagnosis was made based on bone marrow aspiration findings and molecular study.

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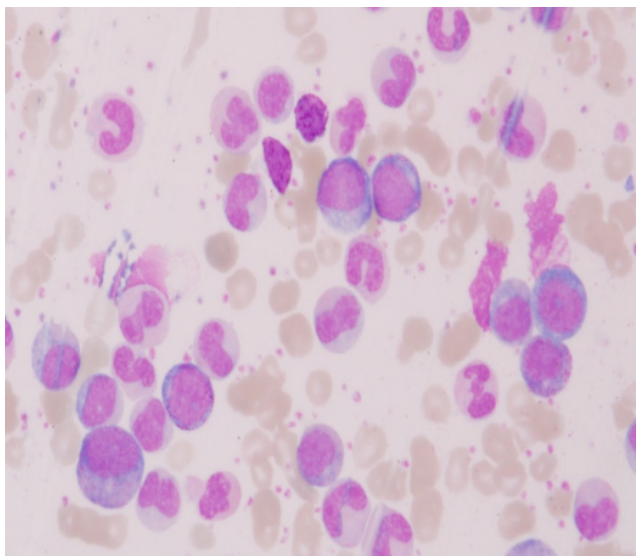
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## INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by the presence of the BCR/ABL1 fusion transcript encoded by the Philadelphia (Ph) chromosome, a result of a reciprocal translocation between chromosomes 9 and 22.<sup>1</sup> The median age at diagnosis of CML is 60 to 65 years and is rare among children and adolescents. CML constitutes 2% of all leukemias in children younger than 15 years with an annual incidence of 1 case per million.<sup>2</sup> Recent data highlight the distinct biological differences between adult and pediatric CML. Pediatric CML patients typically have higher mean WBC counts, more pronounced splenomegaly, and pursue a more aggressive clinical course when compared to adult CML patients.<sup>3</sup> Here, we report a case of CML in a three-year patient because of its uncommon incidence in childhood.

## CASE REPORT

A three- year child presented with complaints of low-grade fever and weight loss. There was gradual abdominal



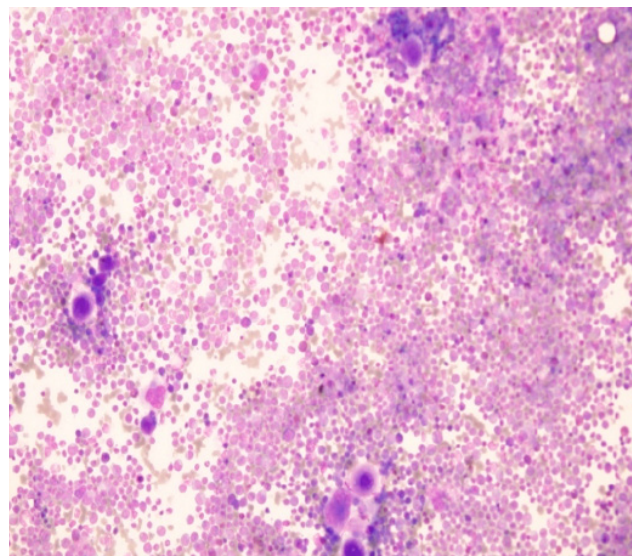
**Figure 1:** Photograph of peripheral blood smear of patient showing left shift in maturation (Wright stain, 1000x)

distension for one month. Local examination revealed a hard and distended abdomen. Splenomegaly was noted. The patient was admitted to the pediatric ward with a differential diagnosis of acute leukemia and storage disorder. Biochemical parameters showed increased serum LDH. A routine hemogram was carried out, which revealed hemoglobin (Hb) 5.5 gm/dl with a markedly elevated total leukocyte count of 21,200/mm<sup>3</sup>. A peripheral differential count revealed a shift to the left (fig. 1). Basophilia and eosinophilia were noted. Platelet count was normal with 2,62,000/mm<sup>3</sup>. On peripheral smear examination, the diagnosis of Myeloproliferative neoplasm was given.

Bone marrow aspiration was carried out under all aseptic precautions, which revealed hypercellular bone marrow with myeloid predominance with the differential count of Blast = 01%, Myelocytes = 20%, Metamyelocytes = 12%, Neutrophils with band forms = 43%, Monocytes = 03%, Eosinophils = 05% and Basophils = 08%. Erythroid and lymphoid series were suppressed (Erythroid = 05% and Lymphocytes = 03%). Megakaryocytes were increased in number with micromegakaryocyte (fig. 2). With peripheral smear and bone marrow findings, differential diagnoses of chronic myeloid leukemia - chronic phase and juvenile myelomonocytic leukemia were made.

The cytogenetic study was carried out, which was positive for 46XX,t(9,22)(q34;q11.2). 98% of the cells were positive for BCR-ABL1 by fluorescence in situ hybridization (FISH) method. Thus the diagnosis of CML in three years old female patient was confirmed and the patient was started on chemotherapy with regular follow-up.

## DISCUSSION



**Figure 2:** Bone marrow smear shows hypercellular marrow with myeloid predominance and increased megakaryocytes with micromegakaryocytes (Wright stain, 200x)

Leukemia is the most common cancer in children and teens. Most childhood leukemias are acute lymphoblastic leukemia (ALL) followed by acute myeloid leukemia (AML). CML is a rare disease among children with an aggressive clinical course.<sup>4</sup> This case report aims to highlight this rare entity and discuss the recent advances and researches in it. CML is characterized by a translocation between chromosomes 9 and 22, resulting in the formation of the Philadelphia (Ph) chromosome. This translocation generates breakpoint cluster region (BCR)-ABL1 chimera messenger RN and results in leukemic cells with growth advantages. CML usually presents in the age group of 60-65 years. The natural history of untreated CML is biphasic or triphasic with most cases diagnosed in the initial CML-chronic phase (CP) followed by an accelerated phase (AP), a blast phase (BP), or both. The common symptoms are fatigue, weight loss, abdominal fullness, bleeding, purpura, splenomegaly, leucocytosis, anemia, and thrombocytosis.<sup>5</sup>

Juvenile myelomonocytic leukemia (JMML) is also a myeloproliferative neoplasm of childhood characterized by a proliferation of the granulocytic and monocytic lineage with peripheral blood monocytes > 1 x 10<sup>9</sup>/L. In contrast to CML, in JMML there is no basophilia and Philadelphia chromosome or BCR-ABL1 fusion.<sup>5</sup> Thus, a molecular study is mandatory for the diagnosis of CML. The hallmark karyotypic abnormality of CML is t(9;22)(q34;q11), yet complex translocations, such as t(6;9;22), are seen in 5-10 % of cases. The resulting BCR-ABL1 fusion protein is sensitive to tyrosine kinase inhibitors (TKIs). The use of these agents has vastly improved prognosis; however, a subset of patients progress to AP or BP despite adequate treatment, and the prognosis for CML-BP remains poor.<sup>6</sup>

There are significant differences in pediatric and adult

CML. Biologically, in adult CML, there is a single breakpoint cluster within the first centromeric 1.5 kb of the BCR, whereas, in pediatric CML, there is a bimodal breakpoint distribution which is similar to adult Ph+ acute lymphoblastic leukemia with M-BCR rearrangement.<sup>1</sup> These differences in the genomic landscape may contribute to the more aggressive clinical characteristics in pediatric CML. Hijjiya et.al<sup>2</sup> assumed that CML in an eight-month-old, which may also involve congenital factors, will have different biology from CML in a 70-year-old, though there is little data to support this. Host differences in adult patients compared with rapidly developing pediatric and adolescent patients may affect CML development, response to treatment, and adverse effects of treatment.<sup>2</sup> A retrospective analysis found that children and young adults had an inferior complete cytogenetic response (CCyR), major molecular response, and complete molecular response compared to older patients although there were no differences in survival.<sup>1</sup> Allogenic bone marrow transplant is the most successful therapy if a suitable HLA identical donor is available for chronic phase CML. For patients without a suitable donor, control of the disease with chemotherapy is the best current alternative.<sup>7,8</sup> In a study from China by Cai Y et.al concluded the median age at diagnosis of CML in the pediatric population is 9-years. Most of all patients are CML-CP. 5 years overall survival and event-free survivals are 100% and 89.1%.<sup>4</sup>

## CONCLUSIONS

CML in children has more aggressive clinical features. Treatment-free remission though well established in adults at present is not applicable in pediatric CML. Recent work has begun to reveal differences in CML biology in adults and children that may account for the clinical differences in CML presentation, progression, and response to treatment.

**Conflict of Interest:** None

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