

Chronic Myeloid Leukemia in a 14-Year-Old: A Rare Case with Unique Clinical Challenges

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ABSTRACT

Chronic myeloid leukemia (CML) is a rare myeloproliferative disorder in children, accounting for only 2% of pediatric leukemias. This case report presents a 14-year-old male diagnosed with CML, highlighting the unique clinical and molecular characteristics of pediatric CML. The patient exhibited symptoms of low-grade fever, abdominal discomfort, splenomegaly and leukocytosis. Peripheral blood smear and bone marrow aspiration confirmed a myeloid predominance and cytogenetic analysis identified the Philadelphia (Ph) chromosome with BCR-ABL1 fusion. Although CML predominantly affects older adults, pediatric cases often follow a more aggressive course with unique genomic features. Tyrosine kinase inhibitors (TKIs) have improved outcomes, but pediatric patients may still exhibit suboptimal responses or disease progression. This report emphasizes the importance of early diagnosis, molecular confirmation and individualized treatment strategies, including the role of bone marrow transplantation in managing pediatric CML.

Keywords: Pediatric chronic myeloid leukemia (CML), Philadelphia chromosome, Bcr-Abl1 fusion gene, Tyrosine kinase inhibitors (TKIS), Allogenic bone marrow transplantation.

Introduction

Chronic Myeloid Leukemia (CML) is a type of myeloproliferative disorder caused by the BCR-ABL1 fusion gene, which results from a reciprocal translocation between chromosomes 9 and 22, forming the Philadelphia (Ph)

chromosome¹. The median age for CML diagnosis ranges between 60 and 65 years, making it relatively rare in children and adolescents. Among individuals younger than 15 years, CML accounts for only 2% of all leukemia cases, with an estimated incidence of 1 case per million annually².

Research indicates that pediatric CML differs biologically from its adult counterpart. Children with CML often present with higher white blood cell counts, more significant splenomegaly and tend to follow a more aggressive disease course compared to adults³. In this report, we describe a rare case of CML in a 14-year-old boy, underscoring the uncommon occurrence of this disease in young patients.

Case Presentation

A 14-year-old male presented with a week-long history of low-grade fever, loss of appetite and dull abdominal pain. On examination, his abdomen was soft and non-tender, with notable splenomegaly. The patient was admitted for further evaluation. Laboratory investigations revealed elevated lactate dehydrogenase (LDH) at 743 mg/dL and an abnormal coagulation profile (APTT>60). A peripheral blood smear showed significant leukocytosis, thrombocytosis and anemia, along with a left-shifted differential count. Basophilia and eosinophilia were also observed (**Table 1**). These findings raised suspicion of a myeloproliferative disorder.

Bone marrow aspiration, performed under sterile conditions, revealed hypercellularity with a predominance of myeloid cells. The differential cell count included 2% blasts, 25% myelocytes, 14% metamyelocytes, 45% segmented neutrophils, 1% monocytes, 1% eosinophils and 2% basophils. The erythroid and lymphoid series were notably suppressed, with erythroid cells comprising 9% and lymphocytes 1% of the count. There was also an increase in megakaryocytes. Based on these bone marrow and peripheral blood findings, the patient was diagnosed with chronic myeloid leukemia (CML).

Cytogenetic analysis confirmed the diagnosis, showing the presence of the Philadelphia chromosome with a translocation t(9;22) (q34;q11.2). Additionally, fluorescence in situ hybridization (FISH) demonstrated that 96% of the patient’s cells were positive for the BCR-ABL1 fusion gene. The patient was subsequently referred to the oncology department for appropriate treatment and long-term follow-up.

Table1: Peripheral Smear report.

Labs	Result	Reference Range
WBC (x10 ³ /µl)	186.45	04-11
Platelets Count (x10 ³ /µl)	773	150-450
RBC(x10 ⁶ /µl)	3.68	4.5-5.8
HB (gm/dl)	9.9	12.8-17.5
HCT (%)	28.6	45-55
MCV (fL)	77.7	80-100
RDW (%)	16.9	11.5-14.6
Blast Cells (%)	3%	Nil
Basophils (%)	2%	0.1.5
Eosinophils (%)	1.93	0-0.8

Discussion

Leukemia is the most prevalent cancer among children and adolescents, with the majority of cases classified as acute lymphoblastic leukemia (ALL), followed by acute myeloid leukemia (AML). In contrast, chronic myeloid leukemia (CML) is a rare entity in children and exhibits a more aggressive clinical behavior⁴. This report aims to explore this uncommon condition, emphasizing recent research developments and advancements in its management.

CML is distinguished by a specific chromosomal abnormality—a translocation between chromosomes 9 and 22—resulting in the formation of the Philadelphia (Ph) chromosome. This mutation produces the BCR-ABL1 fusion gene, leading to uncontrolled cell growth with a proliferative advantage. Although CML is primarily diagnosed in adults between 60–65 years, its occurrence in children follows a unique biological and clinical pattern. The disease generally progresses through three stages: chronic phase (CP), followed by accelerated phase (AP) and ultimately blast phase (BP) if left untreated. Early symptoms include fatigue, weight loss, splenomegaly, purpura, abdominal discomfort, anemia, thrombocytosis, leukocytosis and bleeding⁵.

Differentiating Cml from Juvenile Myelomonocytic Leukemia (JMML)

Another significant childhood myeloproliferative disorder is juvenile myelomonocytic leukemia (JMML), marked by increased granulocytic and monocytic proliferation. Unlike CML, JMML lacks both basophilia and the Philadelphia chromosome. Molecular diagnostic tools are essential to confirm CML, as its hallmark abnormality is the t(9;22) (q34;q11) translocation, with occasional complex variations such as t(6;9;22) found in 5–10% of cases. The BCR-ABL1 fusion protein is highly responsive to tyrosine kinase inhibitors (TKIs), which have transformed the prognosis for CML. However, despite effective treatment, some patients progress to advanced phases, where outcomes remain poor, particularly in the blast phase⁶.

Pediatric CML: Unique Clinical and Molecular Features

There are important biological and clinical distinctions between pediatric and adult CML. In adults, the breakpoint in the BCR gene is typically confined to a small region, whereas pediatric cases show a more varied distribution, similar to Ph-positive ALL with M-BCR rearrangements¹. This distinct genomic landscape may explain the more aggressive nature of pediatric CML. Hijiya et al. suggested that cases in very young children, such as infants, may involve unique biological factors distinct from those seen in older adults, though limited data are available to validate this hypothesis. Variations in patient age may also influence disease progression, treatment outcomes and side effects².

A retrospective study indicated that children and young adults exhibit lower rates of complete cytogenetic response (CCyR), major molecular response (MMR) and complete molecular response (CMR) compared to older individuals, although survival rates remain comparable¹.

Treatment Approaches and Prognosis

Allogenic bone marrow transplantation remains the most effective treatment option for pediatric CML, provided an HLA-matched donor is available. For patients lacking a suitable donor, chemotherapy serves as the primary alternative for disease control. A study conducted in China by Cai et al. reported that the median age of diagnosis among pediatric CML patients was nine years, with most cases identified in the chronic phase. The study also highlighted promising outcomes, with five-year overall survival and event-free survival rates of 100% and 89.1%, respectively⁴.

In summary, while TKIs have revolutionized the treatment of CML, challenges remain, especially in pediatric cases that may

not respond optimally or progress to advanced phases. Early diagnosis and individualized therapeutic strategies are essential to improving outcomes in this rare pediatric malignancy.

Conclusion

This case highlights the uncommon presentation of chronic myeloid leukemia (CML) in a 14-year-old patient, reinforcing the importance of recognizing its distinct clinical and biological features in pediatric populations. Although rare, pediatric CML often exhibits a more aggressive course compared to adult cases, with higher leukocyte counts and significant splenomegaly, as observed in this patient. The presence of the Philadelphia chromosome and BCR-ABL1 fusion gene, confirmed through cytogenetic analysis, remains the cornerstone for diagnosis and management. Despite advancements in treatment with tyrosine kinase inhibitors (TKIs), the risk of progression to advanced disease phases still poses a challenge. Allogeneic bone marrow transplantation offers the best chance for long-term remission, especially in younger patients, provided a compatible donor is available. This case underscores the need for early detection, timely referral and individualized treatment strategies to improve outcomes in pediatric CML, emphasizing the critical role of long-term follow-up and monitoring for disease progression.

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