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(Case Report)

# Rare case of Chronic Myeloid Leukemia (chronic phase) in pediatric age group: Diagnostic and pathological perspective

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## Abstract

Pediatric chronic myeloid leukemia is a rare childhood malignancy, accounting for 3-5% of all childhood cancers. Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm characterized by the presence of the Philadelphia chromosome (BCR-ABL1 fusion gene). While CML predominantly affects adults, pediatric cases are uncommon. This case report outlines the clinical presentation, diagnostic findings, and pathological features of CML in a 19-year-old female, who presented with marked leukocytosis, 61% basophilia, a myelocyte-metamyelocyte peak, and 2% blasts in the differential count. The leukocyte alkaline phosphatase score was reduced, and the p210 transcript of BCR-ABL1 was identified by polymerase chain reaction. Bone marrow was hypercellular with increased granulopoiesis and dysplastic megakaryocytes.

**Keywords:** Chronic myeloid leukemia (CML); Pediatric; Philadelphia chromosome (Ph); Breakpoint cluster region-Abelson murine leukemia 1 gene (BCR-ABL1); Juvenile myelomonocytic leukemia

## 1. Introduction

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm, accounting for approximately 15% of new leukemia cases in adults. It is quite rare in children, constituting only 3-5% of all childhood malignancies [1][2]. CML is characterized by the acquisition of the Philadelphia chromosome (Ph) by leukemic cells in both adults and children. The molecular pathogenesis involves a balanced reciprocal translocation of genes between chromosomes 9 and 22. The ABL1 gene on chromosome 9 fuses with the BCR gene on chromosome 22, leading to the expression of the BCR-ABL1 oncoprotein, which is a constitutively active tyrosine kinase that promotes leukemogenesis via upregulation of the RAS, RAF, JUN, MYC, and STAT kinases [1]. Children with CML are exposed to tyrosine kinase inhibitors during their growth years, leading to a higher burden of morbidities that differ from those in adults and require careful monitoring [1][3].

## 2. Case report

A 19-year-old female presented with complaints of low-grade fever, weight loss, and abdominal distention for one month. Local examination revealed a hard and distended abdomen. Hepatomegaly and splenomegaly were noted. Blood counts revealed hemoglobin of 12.3 g/dl and marked leukocytosis (total leukocyte count: 120 x $10^3$/µL). Differential counts showed a myelocyte peak (promyelocytes: 4%, myelocytes: 30%, metamyelocytes: 5%, band forms: 20%), a blast count of 2%, and basophilia (2%). Platelet count was adequate (2.2 lacs/cumm). Bone marrow aspiration was performed under aseptic precautions, revealing a myelocyte peak (40%), blast count of 2%, and basophilia (8%).

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Megakaryocytes were increased in number, with the presence of micromegakaryocytes. Based on the peripheral smear and bone marrow findings, a diagnosis of chronic myeloid leukemia in the chronic phase was made, which was confirmed by FISH (fluorescence in situ hybridization). Treatment was initiated with adequate transfusion support. The patient tolerated the treatment well and was discharged after two weeks.

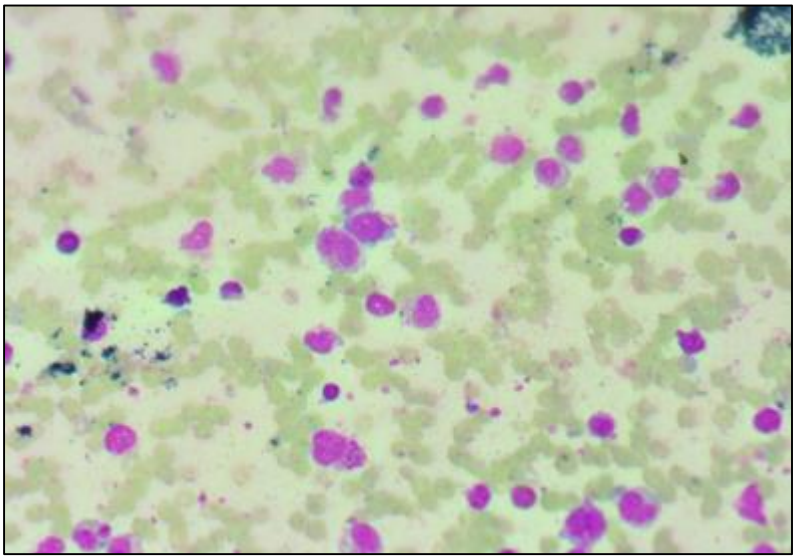

**Figure 1** Peripheral blood smear showing promyelocyte, myelocyte, metamyelocyte and band forms

## 3. Discussion

Most childhood leukemias are acute lymphoblastic leukemia (ALL), followed by acute myeloid leukemia (AML). CML is a rare disease in children and has an aggressive clinical course[4].

CML is characterized by a translocation between chromosomes 9 and 22, resulting in the formation of the Philadelphia (Ph) chromosome. This translocation generates the breakpoint cluster region (BCR)-ABL1 chimera messenger RNA, giving leukemic cells a growth advantage. CML typically presents in individuals aged 60-65 years. The natural history of untreated CML is biphasic or triphasic, with most cases diagnosed in the initial chronic phase (CP), followed by an accelerated phase (AP), a blast phase (BP), or both. Common symptoms include fatigue, weight loss, abdominal fullness, bleeding, purpura, splenomegaly, leukocytosis, anemia, and thrombocytosis[5]. Fluorescence in situ hybridization (FISH) is the most commonly used test for detecting BCR-ABL1 fusion in the diagnosis of CML. Reverse transcriptase-polymerase chain reaction (RT-PCR) is employed to detect the breakpoint and quantify transcripts, which serve as a baseline for disease monitoring.

The differential diagnosis of CML in pediatric age groups includes leukemoid reaction and juvenile myelomonocytic leukemia (JMML). Leukemoid reactions present with high TLC but lack a myelocyte bulge. Toxic granulation and normal or raised leukocyte esterase levels help exclude a diagnosis of CML. Juvenile myelomonocytic leukemia (JMML) is another myeloproliferative neoplasm of childhood, characterized by the proliferation of granulocytic and monocytic lineages, with peripheral blood monocytes > 1 x 10^9 /L. In contrast to CML, JMML does not exhibit basophilia, the Philadelphia chromosome, or BCR-ABL1 fusion[5]. Therefore, molecular studies are essential for diagnosing CML. The hallmark karyotypic abnormality of CML is t(9;22)(q34;q11), though complex translocations, such as t(6;9;22), are observed in 5–10% of cases. The resulting BCR-ABL1 fusion protein is sensitive to tyrosine kinase inhibitors (TKIs). Although the use of TKIs has vastly improved the prognosis, a subset of patients still progress to the accelerated phase or blastic phase despite adequate treatment, and the prognosis for CML in the blastic phase remains poor[6]. In adult CML, there is a single breakpoint cluster within the first centromeric 1.5 kb of the BCR, while pediatric CML shows a bimodal breakpoint distribution similar to adult Ph+ acute lymphoblastic leukemia with M-BCR rearrangement. These differences in the genomic landscape may contribute to the more aggressive clinical characteristics seen in pediatric CML. The risk of tumor lysis syndrome in pediatric CML is low; however, patients are managed with oral hydration, allopurinol, and hydroxyurea until the diagnosis is confirmed. Imatinib has been shown to be an effective tyrosine kinase inhibitor (TKI) in the pediatric population. Allogeneic 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, disease control with chemotherapy is the best current alternative [7][8].

## 4. Conclusion

Pediatric CML is a rare disease and differs significantly from adult CML in terms of clinical presentation, disease biology, and outcomes. The first-line therapy is tyrosine kinase inhibitors (TKIs); however, long-term use in pediatric patients raises concerns regarding their effects on bone growth, endocrine function, vaccination, and future fertility. While treatment-free remission is well established in adults, it is not yet applicable in pediatric CML.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

## References

[1] Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2018 update on diagnosis, therapy and monitoring. Am J Hematol. 2018;93(3):442–459.

[2] Ekwere TA, Abudu EK. BCR-ABL Positive Childhood Chronic Myeloid Leukemia. J Case Reports. 2017 Aug 15;289–292.

[3] Hijiya N, Schultz KR, Metzler M, Millot F, Suttorp M. Pediatric chronic myeloid leukemia is a unique disease that requires a different approach. *Blood.* 2016;127(4):392–399.

[4] Cai Y, Liu C, Guo Y, et al. Analysis of 48 Cases Pediatric Chronic Myeloid Leukemia from China: Results from a Single Institute in China. Blood. 2019;134: 5911.

[5] Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J. (ed.) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th ed. Lyon, IARC; 2017. pp439.

[6] Lewen M, Gresh R, Queenan M, et al. Pediatric chronic myeloid leukemia with transformation : a case report. Biomark Res. 2016;1- 6.

[7] Hossain MZ, Hasan P, Ahmed B, et al. Two cases of chronic myeloid leukemia in pediatric and young adolescent age group. Journal of Dhaka Medical College. 2016; 25:74-76.

[8] Nikumbh DB, Wader JV , Kshirsagar VY, et al. Adult Type Chronic Myeloid Leukemia in Childhood : A Case Report JKIMSU. 2012; 1:113-1.