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Chronic Myeloid Leukemia (CML) in A 14-Year-Old

Catherine Halim[1]*, Leonardo Trisnarizki[2], Sisca[3]
Universitas Kristen Satya Wacana, Indonesia[1,2]
Universitas Trisakti, Indonesia[3]
Email: catherine.halim@uksw.edu[1]*

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child, anemia, leukocytosis, splenomegaly, myeloid cell predominance

Abstract
Chronic Myeloid Leukemia (CML) is a myeloproliferative disorder accounting for approximately 2-3% of leukemias in children and adolescents, with an annual incidence of 1 in 1,000,000 individuals (approximately 10% of all CML cases). The median age of onset in children is 11-12 years. CML is caused by a reciprocal translocation of genes on chromosomes 9 and 22, resulting in the formation of the Breakpoint Cluster Region (BCR) gene on chromosome 22 with the Abelson leukemia virus (ABL) gene. The BCR-ABL protein has constitutive tyrosine kinase activity, leading to the activation of intracellular signal transduction pathways such as STAT, RAS, JUN, MYC, and Phosphatidylinositol-3 kinase. This case report concerns a 14-year-old girl with CML, a rare hematologic malignancy in children. The patient presented with abdominal enlargement and hardening for 2 months, abdominal pain, fever, and vomiting. Physical examination revealed splenomegaly (Schuffner 4). Laboratory tests revealed anemia (hemoglobin 7.3 g/dL) and leukocytosis (291,890 WBCs/mm³). Peripheral blood smear showed myeloid blasts and all stages of granulocyte maturation with basophilia and eosinophilia. Bone marrow aspiration confirmed chronic myeloid leukemia in the chronic phase with an M/E ratio of 25.5. BCR-ABL molecular testing revealed positive fusion of B2A2 and B3A2. This case highlights the aggressive presentation of pediatric CML characterized by massive splenomegaly and extreme leukocytosis, which differs from adult CML. Early recognition and timely diagnosis are essential to prevent disease progression and life-threatening complications such as leukostasis, bleeding, and splenic rupture.

INTRODUCTION

Chronic Myeloid Leukemia (CML) is a myeloproliferative disorder caused by the BCR::ABL1 gene fusion, resulting from a translocation between chromosomes 9 and 22, forming the Philadelphia chromosome (Ph).

The average age of CML patients is 60 – 65 years, making it relatively rare in children and adolescents (Ford et al., 2022; Millot et al., 2025; Nevejan et al., 2024; Sembill et al., 2023; Suttorp et al., 2023). The prevalence of CML in children under 15 years of age is 2% – 3%, with an estimated incidence of 1 per 1 million children annually.

CML cases in children from 2020 to 2024 accounted for 2.72% of all childhood cancer cases in Indonesia (Al-Qerem et al., 2025; Huang et al., 2025; Iqhrammullah et al., 2025). The predisposing factors for CML in children are not yet clearly understood. Approximately 90% of CML patients have the reciprocal translocation t(9;22) (q34;q11.2), which causes shortening of chromosome 22, known as the Philadelphia chromosome, which contains the BCR::ABL1 oncogene.

The chronic phase of CML is the most common phase in patients and can last for several years (Berman, 2022; García-Gutiérrez et al., 2022; Held & Atallah, 2023; Senapati et al., 2023). In the chronic phase, myeloid cells continue to differentiate, with blast cells comprising less than 10% of the bone marrow.

The diagnosis of CML is generally confirmed by leukocytosis, the presence of the Philadelphia chromosome (Ph), or BCR::ABL1 molecular abnormalities (Mulyadi et al., 2024).

The purpose of this case study is to determine the clinical and laboratory characteristics of pediatric CML patients in Surakarta, Indonesia.

The urgency of this case report is driven by several factors. First, the rarity of pediatric CML (1 per 1 million children annually) means that many clinicians may never encounter this condition, leading to potential delays in diagnosis. Second, the aggressive presentation of pediatric CML, characterized by massive splenomegaly and extreme leukocytosis, can lead to life-threatening complications such as leukostasis, splenic rupture, and bleeding if not promptly recognized and managed. Third, the availability of effective tyrosine kinase inhibitor (TKI) therapy makes early diagnosis particularly important, as timely treatment can prevent disease progression and achieve long-term remission. Fourth, the lack of published case reports from Indonesia limits the availability of local data for clinicians and policymakers. This case report aims to fill this gap by providing detailed clinical and laboratory data from a pediatric CML patient in Surakarta, Indonesia.

The novelty of this case report lies in several aspects. First, this report provides detailed documentation of pediatric CML from Indonesia, contributing to the limited Southeast Asian literature on this rare disease. Second, the case report provides comprehensive diagnostic data, including peripheral blood smear findings, bone marrow aspiration results, and BCR::ABL1 molecular confirmation, serving as a reference for clinicians. Third, the report highlights the aggressive clinical presentation of pediatric CML (Schuffner grade IV splenomegaly and leukocytosis of 291,890/mm^3), which differs from the more indolent presentation commonly observed in adults. Fourth, the case discussion integrates recent literature from 2024 – 2026, providing an up-to-date review of pediatric CML management.

The purpose of this case report is to describe the clinical and laboratory characteristics of a pediatric CML patient in Surakarta, Indonesia, and to review the current literature on the diagnosis and management of CML in children and adolescents. The specific objectives are: (1) to present a detailed case of a 14-year-old girl with CML in the chronic phase; (2) to describe the diagnostic workup, including physical examination, laboratory tests, peripheral blood smear, bone marrow aspiration, and BCR::ABL1 molecular testing; (3) to discuss the clinical presentation and management challenges of pediatric CML; and (4) to provide recommendations for the early recognition and timely management of pediatric CML based on current guidelines.

METHOD

A 14-year-old girl presented with abdominal enlargement for the past 2 months. She had abdominal pain for 4 days, accompanied by fever for 4 days, and vomiting.

On examination, the abdomen appeared enlarged and hardened, with abdominal tenderness (epigastric, umbilical, bilateral hypochondriacal) and splenomegaly (Schuffner 4). The patient was admitted for further evaluation.

Laboratory tests revealed decreased hemoglobin and hematocrit (Hemoglobin 7.3 g/dL and Hematocrit 20.3%), and increased leukocyte count (291,890 WBCs/mm3). A peripheral blood smear showed anemia, leukocytosis, myeloid blasts, and all stages of granulocyte maturation, along with increased basophils and eosinophils (basophilia and eosinophilia). These findings raised suspicion of a myeloproliferative disorder, namely CML.

The patient also underwent a multi-slice computed tomography (MSCT) of the abdomen, which revealed hepatosplenomegaly, bilateral cystic ovarian masses, ascites, and a comb sign suggestive of inflammatory bowel disease.

Bone Marrow Puncture (BMP) examination showed chronic myeloid leukemia in the chronic phase.

Table 1. Hematology Examination Results

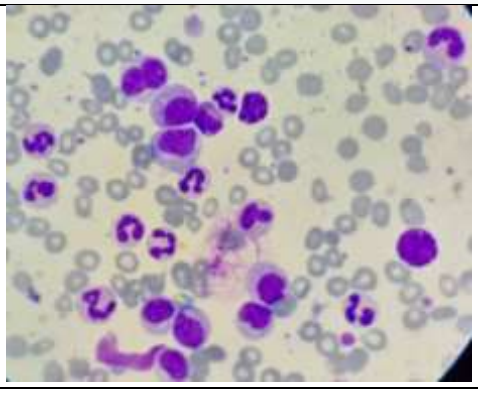
January 25 th 2026		January 25 th 2026	
Hemoglobin	7.3 g/dL	Hemoglobin	6.0 g/dL
Hematocrit	20.3 %	Hematocrit	16.9 %
Leucocytes	291,890 / mm3	Leucocytes	231,940 / mm3
Erythrocytes	2.76 milions / mm3	Erythrocytes	2.3 juta / mm3
Platelets	406,000 / mm3	Platelets	349,000 / mm3

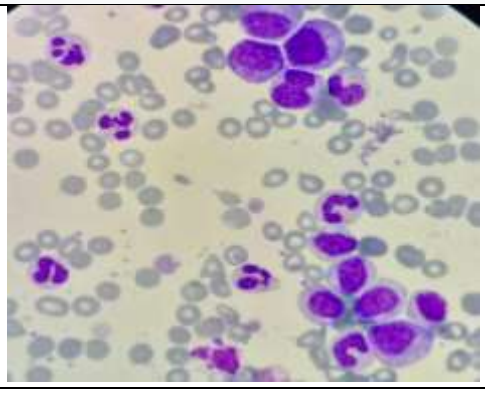
Leukocyte Differential Count: Myeloblasts 14%, Promyelocytes 7%, Myelocytes 4%, Metamyelocytes 3%, Stab 6%, Segments 63%, Eosinophils 3%.

Table 2. Peripheral Blood Screening (PBC) Results

Erythrocyte	Anisopoikilocytosis, Microcytes, Normocytes, Macrocytes, Target Cells, Pencil Cells, Tear Drop Cells, Hypochromic, Polychromacy.
Leucocyte	Increased Number, In 100 Leukocyte Cells Found Myeloblasts, Dominance of Granulopoietic Series (Promyelocytes, Myelocytes, Metamyelocytes).
Platelet	Number Within Normal Limits, Even Distribution, Morphology Within Normal Limits
Conclusion	Hypochromic Microcytic Anemia and Leukocytosis Suspected Chronic Hematologic Malignancy of Myeloid Series.
Suggestion	BMP, BCR - ABL

Table 3. Microscopic Results of Peripheral Blood Screening





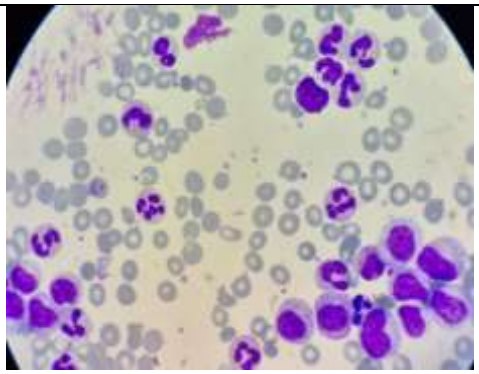
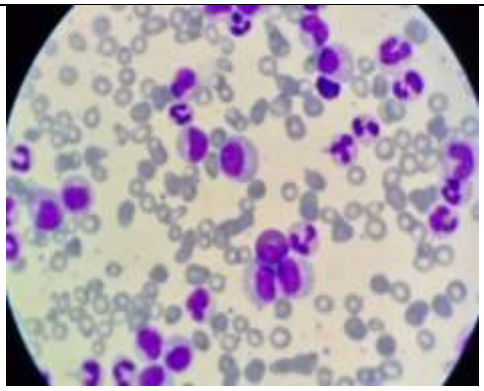



Table 4. Bone Marrow (BMP) Results :

Location	SIAS (S)
Cellularity	Hypercellularity
Consistency	Dense
M/E Ratio	25.5 (Increased)
Granulopoietic System	Increased activity, all stages of granulopoietic maturation are present: Myeloblasts (2%), Promyelocytes (4.4%).
Thrombopoietic System	Normal activity, mature megakaryocytes readily present.
Lymphopoietic System	Decreased activity, normal maturation
Conclusion	Current bone marrow aspiration findings are consistent with Chronic Myeloid Leukemia in Chronic Phase
Recommendations	BCR ABL, Routine Blood Monitoring and Peripheral Blood Screening

Table 5. BCR ABL Results

BCR ABL	Positive Fusion of B2A2 and B3A2

RESULTS AND DISCUSSION

Chronic myeloid leukemia (CML) is a rare hematologic malignancy in children, with a prevalence of approximately 2–3% of all childhood leukemias. The incidence rate in Kuwait is approximately 6 cases per 100,000 individuals and globally, it is 1–2 cases per million per year. This rarity in the pediatric population poses challenges in understanding the characteristics of the disease and optimizing appropriate therapy. (Bourusly, M et al., 2025)

CML is a hematologic malignancy characterized by the presence of the Philadelphia chromosome (pH), a tyrosine kinase fusion with BCR-ABL1, which causes myeloid proliferation and genomic instability. The disease progresses through three clinically defined phases: the chronic phase (CP), the accelerated phase (AP), and the blast phase (BP).

CML in children often presents with more aggressive symptoms than adults. Children have proportionally larger spleens (median 8 cm below the ribcage; range 0-25 cm) and higher leukocyte counts (median 250 × 10^9/L). The patient in this case had similar characteristics, marked by Schuffner IV splenomegaly and leukocytosis of 291,890/mm3.

Epidemiology

The median age of onset of CML is 60-65 years, and CML is rare in children and adolescents. The prevalence of CML is 2% of all leukemias in children under 15 years of age and 9% of all leukemias in adolescents between 15 and 19 years of age, with an annual incidence of 1 and 2.2 cases per million in these two age groups. Differences in CML in adults and children are related to host factors and the biology of the leukemia cells. (Hijiya, N et al., 2016)

CML is rare in children and adolescents, accounting for approximately 2% and 9% of all leukemias in children under 15 years of age and in adolescents between 15 and 19 years of age, respectively. The annual incidence increases with age: 1 per million in children under 15 years of age and 2.5 per million in adolescents.

Pathophysiology

Several studies have reported that children and adolescents tend to have a more aggressive clinical presentation than adults. This is due to differences in leukemia cells or host biology. Children with CML share the same genetic characteristics as adults: the balanced translocation t(9;22)(q34;q11), which causes the fusion of the ABL1 oncogene located on chromosome 9 to the BCR gene region (M-BCR) on chromosome 22, resulting in a constitutively dysregulated ABL1 tyrosine kinase, with a 210 kDa or 190 kDa region. However, the distribution of BCR gene breakpoints differs in pediatric CML. The distribution pattern in children is similar to that observed in adult Philadelphia-positive acute lymphoblastic leukemia (Ph1 ALL) with the M-BCR arrangement. Similar to adults, nearly all children and adolescents with CML exhibit e13a2 (b2a2) or/and e14a2 (b3a2) junctions (Giona, F et al., 2022).

Diagnosis

Children and adolescents, as well as young adults, with CML-CP tend to have a more aggressive clinical presentation. The disease exhibits aggressive clinical characteristics in children and young adults compared to older adults. A study of 2,784 patients aged 18-29 years and older showed more frequent splenomegaly and larger spleens than in older adults.

CML in children presents with a more aggressive presentation, with larger spleens, higher white blood cell (WBC) counts, a higher frequency of accelerated phase (AP) or blast phase (BP), and a distinct genetic profile compared to adult CML.

Transcriptome studies of CD34+ CML cells analyzed by RNA sequencing revealed that more genes in the Rho pathway are differentially expressed in pediatric CML cells compared to adult CML cells, which may contribute to the distinct clinical presentation.

Genome sequencing also revealed a higher frequency of ASXL1 somatic mutations and germline variants associated with clonal hematopoiesis in pediatric CML compared to adult CML, although their impact on prognosis remains unclear.

The National Comprehensive Cancer Network (NCCN) guidelines recommend testing for the diagnosis of CML, including a history and physical examination, spleen size (cm below the ribcage), complete blood count (CBC) with leukocyte differential count, chemistry profile, bone marrow (BM) aspirate and biopsy, and quantitative RT-PCR (Q-RT-PCR) using the international scale from peripheral blood. On aspirate, required tests include morphology with blast and basophil percentages, karyotype, fluorescent in situ hybridization (FISH), and qualitative RT-PCR for BCR-ABL. Cerebrospinal fluid (CSF) studies are not necessary in patients with chronic phase (CP) CML unless clinically indicated or in patients with suspected

blast phase (BP). This recommendation is also supported by the Chronic Myeloid Leukemia Committee of the International Berlin Frankfurt Munster (I-BFM) Study Group.

Childhood CML presents unique host factors, including the potential use of tyrosine kinase inhibitors (TKIs) for decades and the unknown long-term impact of TKIs. The breakpoint of the ABL gene on chromosome 9 is located in exon a2. In 95% of cases, the breakpoint of the BCR gene on chromosome 22 occurs in the major BCR (M-BCR), either in exon e13 (b2) or exon e14 (b3), resulting in two slightly different chimeric transcripts. These breakpoints give rise to various BCR-ABL rearrangements, the most common being e13a2 (b2a2) and e14a2 (b3a2), which encode the p210 protein. In some cases, there is coexpression of these transcripts due to alternative splicing (b2a2+b3a2).

Management

Treatment strategies for children and adolescents with chronic myeloid leukemia (CML-CP) have evolved from allogeneic hematopoietic stem cell transplantation (HSCT) to tyrosine kinase inhibitors (TKIs). Treatment recommendations are based on initiation of therapy with a first or second generation TKI according to the patient's European Treatment and Outcome Study (EUTOS) risk group.

The next step, based on the recommended monitoring results, is switching to a TKI or another drug if resistance or toxicity develops. The panel also provides recommendations regarding criteria for discontinuing TKIs in children and adolescents who have achieved a therapeutic response. Allogeneic stem cell transplantation (HSCT) is not recommended as first-line treatment for children with CML-CP, but should be considered if progression to advanced phase or failure of multiple treatment lines occurs.

Imatinib is a TKI approved for first-line therapy in children with CML. Dasatinib is approved as first and second line therapy for pediatric patients with CP CML. Nilotinib was also approved in 2018 as first and second line therapy for pediatric patients with CML aged one year or older. (Heng, J et al., 2026).

Management of laboratory findings of hyperleukocytosis in children with suspected pCML-CP consists of hydration and hydroxyurea as the first prophylactic step in patients without clinical signs of leukostasis, which can prevent the development of clinical leukostasis in the first week after hospitalization. TKIs at an appropriate dose should be initiated as soon as the diagnosis of CML is confirmed.

Table 5. Rate of leukoreduction in CML therapy

Drug/Measure	Time required for a 50% reduction of white cell count
Hydroxyurea (25–50 mg/kg/day in 2–3 divided doses)	1–2 weeks
TKIs	1–2 weeks
Low-dose Ara-C (100 mg IV 24 hours)	3–5 days
Low-dose Ara-C plus thioguanine (1 mg/kg, max. 40 mg once daily)	3 days
Leukapheresis/Exchange transfusion	30%–50%–80% reduction within hours

Patients with clinical symptoms of leukostasis, hydration plus hydroxyurea therapy should be simultaneously augmented with more rapidly acting cytoreductive measures.

In organ-threatening emergencies, such as priapism in men, leukoapheresis or exchange transfusion is the most rapid procedure. However, the clearance efficiency of therapeutic leukoapheresis is lower in patients with CML than in patients with acute leukemia. Possible reasons include an enlarged spleen in CML and increased myelocytic precursor cells that are difficult to separate from whole blood by centrifugation. Therefore, to increase efficiency, more than one cycle of leukoapheresis may be necessary. Leukoapheresis or exchange transfusion can sometimes be associated with complications such as bleeding and electrolyte abnormalities. Furthermore, in situations where access to such invasive procedures is difficult, exchange transfusion may be an alternative. It is also recommended to initiate low-dose cytosine arabinoside (Ara-C) along with hyperhydration (doubling or tripling of maintenance fluids), hydroxyurea, and TKIs to reduce blood cell counts. (Athale, U. et al., 2019)

Complications

Chronic myeloid leukemia (CML) is rare during the first two decades of life. Most pediatric patients with chronic CML experience massive hyperleukocytosis. Although rare, problems such as leukostasis, thrombocytosis, and splenomegaly, or a combination of these, can require emergency life- and organ-saving interventions.

Leukostasis can commonly occlude small blood vessels in the cerebral microvasculature, lungs, heart, retina, auditory canal, bones, kidneys, fingers, and penis (in males). Combination chemotherapy with leukoapheresis or exchange transfusion is necessary in selected cases. Despite the presence of thrombocytosis, no thrombotic complications have been observed in pediatric CML, but signs of bleeding have been observed. These complications include intracerebral hemorrhage, soft tissue bruising, epistaxis, gum bleeding, gastrointestinal or genitourinary bleeding, and menorrhagia, with von Willebrand syndrome. The routine use of low-dose acetylsalicylic acid as prophylaxis in children with thrombocytosis is not recommended. Splenomegaly is complicated by the presence of splenic infarction, which varies from asymptomatic infarction to hemorrhagic shock secondary to massive subcapsular hemorrhage with splenic rupture. (Moulik, N, R et al., 2025)

CONCLUSION

This case report describes a 14-year-old girl diagnosed with chronic-phase Chronic Myeloid Leukemia (CML), a rare pediatric hematologic malignancy characterized by massive splenomegaly (Schuffner grade IV), extreme leukocytosis (291,890/mm^3), and anemia, reflecting the more aggressive clinical presentation commonly observed in children. The diagnosis was established through peripheral blood smear examination, bone marrow aspiration demonstrating hypercellularity with a markedly increased myeloid-to-erythroid (M/E) ratio of 25.5, and BCR::ABL1 molecular testing showing positive B2A2 and B3A2 fusion transcripts corresponding to the p210 protein, consistent with current NCCN and I-BFM pediatric CML guidelines. This case emphasizes the importance of early recognition of pediatric CML in children presenting with abdominal enlargement, splenomegaly, and marked hematologic abnormalities, as prompt diagnosis and initiation of tyrosine kinase inhibitor (TKI) therapy are essential to prevent disease progression and serious complications such as leukostasis, bleeding, and splenic rupture. Furthermore, this report highlights the need for a multidisciplinary approach in managing pediatric CML and suggests that future research should focus on long-

term treatment outcomes, molecular response patterns, and the quality of life of pediatric patients receiving TKI therapy, particularly in resource-limited settings.

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