CASE REPORT

Case Report on Acute Lymphoblastic Leukemia in a Child Presented with Migratory Polyarthritis with Normal Peripheral Blood Smear

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ABSTRACT

Patients with leukemia can present with polyarthritis and polyarthralgia mimicking juvenile rheumatoid arthritis, diagnosis and treatment of leukemia can be delayed with disastrous effects. A 14-year-old boy with a history of pre-B ALL, diagnosed in 2019, presented seventeen months after treatment completion due to symptoms of migratory polyarthritis lasting for one month, with raised ASO titer, but not fulfilling criteria for acute rheumatic fever. He presented to EAR multiple times, with a wide range of autoimmune-like phenomena, but his rheumatoid factors, ANA profile, and inflammatory markers like ESR and CRP were normal. Peripheral blood smears were repeatedly without pathological changes. It is unusual for acute leukemia to present with normal CBC and peripheral blood smear, however, bone marrow should be advised if the clinical symptoms /signs are suggestive of acute leukemia after ruling out the other common differentials.

Keywords: *Migratory polyarthritis, leukemia, blood smear, polyarthritis, juvenile idiopathic arthritis.*

INTRODUCTION

Acute leukemia is the most common malignancy of childhood and can present with a wide spectrum of clinical manifestations. There are underlying 3 pathological mechanisms for the whole clinical spectrum [1-3]. First; bone marrow failure due to extensive infiltration by blast cells, manifested clinically by anemia/pallor, hemorrhages /thrombocytopenia, second, infiltration of other tissues like lymph nodes, liver, spleen, CNS and testes by leukemic cells/blasts, presenting with lymphadenopathy, hepatosplenomegaly and signs of CNS involvement like seizures and headache. Third, systemic effects of cytokines released by tumor cells, such as fever, malaise, fatigue, and nausea. Acute leukemia can present in children with polyarthritis/arthralgias mimicking the pattern of juvenile arthritis, thereby delaying the diagnosis of the disease and the start of treatment [4]. It can present with migratory arthritis with aleukemic peripheral blood smear, mimicking acute rheumatic fever [5]. We are presenting a case report of a 14-year-old child having migratory polyarthritis and fever, mimicking acute rheumatic fever with repeatedly normal peripheral blood smears. Diagnosis of acute leukemia was confirmed by bone marrow examination.

CASE REPORT

A 14-year-old child, who completed his treatment for pre-B ALL in February 2023 presented to Shaukat Khanum Cancer Hospital, Peshawar in August 2024 with a history of fever and migratory arthritis, involving left knee, right elbow, and left shoulder, subsequently. Besides the inflamed joints involved, the physical examination was normal. His ASO titer was raised, ESR and CRP were on the upper normal limit, and peripheral blood smears were repeatedly normal. Although the criteria for acute rheumatic fever were not fulfilled, he started prophylactic therapy with benzathine penicillin due to the high risk of acute rheumatic fever. Over the subsequent few weeks, he developed other autoimmune-like phenomena like pleurisy along with the existing arthralgia. RA (rheumatoid factor) and ANA (antinuclear antibodies) were negative. Afterward, he developed severe backache, lasting for one month. Repeated CBCs showed normal values of all three lineages: WBC 6700, Hgb 13.5 and Platelet count 250000, without atypical cells. Upon reviewing the record, when ALL was diagnosed, in 2019, it was revealed that he had the same onset of illness, with polyarthritis in 8-10 months, receiving methotrexate as DMARDs, along with steroids. Therapy was conducted for 8 months, without resolution of arthritis symptoms. Bone marrow examination was performed and diagnosis of pre-B ALL was established, molecular cytogenetics detected no high-risk translocations and HR gene rearrangement (TEL/AML translocation, BCR-ABL translocation, and MLL gene rearrangements are negative). Karyotype howed GTG banding 59~62<3n>,XXY,+X,+Y,-2,-3,i(7)(q10),-9,-11,-12,-13,-16,-19,20,+21[cp12]/46,XY[8]; Abnormal Male Karyotype. He was successfully treated according to UK ALL 2011 guidelines regimen B: the induction phase involved 4 drugs, excluding methotrexate and steroids, due to previous treatment of suspected RA. The therapy was completed in February 2023.

Based on the record and current severe backache, we justified the bone marrow aspiration, confirming the ALL relapse, showing 52% of blasts. The flow cytometry showed 30% of total cellular events expressing CD45

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variable (- to +), HLA DR+, CD19+, CD10++, CD38++, TdT dim+, CD79a++. This population of cells was MPO and cCD3 negative. Molecular genetics was negative for high-risk translocations and HR gene rearrangements. Chromosomal analysis for hematological disorders showed GTG banding 63,XXY,+X,+Y,-2,-3,i(7)(q10),-8,-9,-11,-12,-13,-16,-19,-20,+21,+21[cp3]/46,XY[18]; Abnormal Male Karyotype. The boy was diagnosed with late combined (medullar and testicular) relapse and started chemotherapy according to R3 protocol, So far, he completed R3 induction, R3 consolidation, intensification phase 3, received interim maintenance phase, and has undergone testicular irradiation. Remission was established on October 17, 2024, with negative MRD (minimal residual/measurable disease) on bone marrow for Pre B ALL. Currently, he has been doing well on maintenance phase therapy since June 11, 2025.

DISCUSSION

Acute leukemia can manifest with various symptoms and signs, most frequently with hepatomegaly, splenomegaly, pallor, fever, and bruising, present in more than 50% of cases [6]. Other features like recurrent infections, fatigue, limb pain, lymphadenopathy, bleeding tendency, and rash can be seen in about one-third to one-half of the patients [6]. Osteoarticular manifestations are present in 10-30% of children [7]. Arthritis can occur in leukemia at any stage of the disease, even several months before the diagnosis [8-10]. In such cases, patients have normal CBC, without the presence of blasts in peripheral smear, and diagnosis is usually established by bone marrow aspiration.

Our patient had a history of arthritis-like symptoms and signs, lasting 8-10 months before the initial ALL diagnosis, having normal CBC and peripheral blood smear. Since the treatment with methotrexate and steroids lacked the response, with persistent polyarthritis symptoms and signs. We emphasize the importance of early diagnosis since the patient developed cytopenia after 10 months of treatment, leading to bone marrow examination and delayed ALL diagnosis. At the presentation of relapsed disease, he, again, had migratory polyarthritis, lasting for one month, accompanied by fever and later backache over the next month. We prompted the bone marrow aspiration, despite the repeatedly normal CBC and peripheral blood smears, and established the diagnosis of relapse, with 52% of blast cells. A subset of patients may have aleukemic leukemia with no peripheral blast cells and normal leukocyte counts, however, in such cases, the other cell count may be suppressed, resulting in thrombocytopenia and anemia or there may be other clinical manifestations strongly suggestive of acute leukemia/hematological malignancies [5].

The whole emphasis in this case report for the clinicians is placed on the fact that one should not follow only the results of peripheral blood counts if clinical manifestations are suggestive of acute leukemias. Bone marrow examination should be performed to avoid unnecessary delays in treatment. The literature shows the osteoarticular manifestations of ALL, with fever (80%) and surprisingly normal blood counts (30%) and blasts population in the bone marrow [11, 12].

CONCLUSION

Acute leukemias are sometimes challenging to diagnose, especially with autoimmune and paraneoplastic presentations, like osteoarticular presentations, with normal blood counts and peripheral blood smear morphology, however, general pediatricians should keep in mind the arthritis as one of the clinical presentations of ALL. In case of persistent symptoms and signs, we should search for other typical clinical manifestations among the spectrum, like bone pains to justify bone marrow examination. Clinicians should not stop investigating for ALL in cases of normal peripheral blood smear.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the guardians of the patient for publication of this case report.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Declared none.

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