

Myeloid Sarcoma Preceding Clinically Recognized Acute Myeloid Leukemia in a Child: A Case Report

Shiva Shadani

North Khorasan University of Medical Sciences

Mohsen Rahmanian

m.rahmanian.md@gmail.com

North Khorasan University of Medical Sciences

Arian Aminzadeh

North Khorasan University of Medical Sciences

Kourosh Yousefi Hassanabad

Imam Reza Hospital, North Khorasan University of Medical Sciences

Case Report

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Abstract

Background

Myeloid sarcoma is an uncommon extramedullary manifestation of a myeloid neoplasm that may occur concurrently with acute myeloid leukemia (AML) or precede clinically recognized marrow disease. Its variable clinical and histopathologic appearance can result in diagnostic confusion, particularly when presenting as an isolated-appearing soft-tissue lesion in children.

Case Presentation:

A 7-year-old boy presented with fever, generalized petechiae and purpura, weakness, severe pancytopenia, and a recurrent painful left-forearm mass. The lesion had first appeared approximately 18 months earlier and was initially considered a hemangioma on ultrasonography. Subsequent histopathologic examination and a limited immunohistochemical panel suggested a lymphoproliferative disorder and later probable precursor lymphoblastic lymphoma. Following development of overt marrow disease, bone-marrow examination demonstrated 40% blasts, while flow cytometry supported AML with aberrant CD7 expression. Re-evaluation of the forearm specimen using a broader immunohistochemical panel demonstrated weak myeloperoxidase, CD7, CD117, and CD99 expression, resulting in reclassification as myeloid sarcoma. Treatment with daunorubicin, cytarabine, and thioguanine was initiated. Gemtuzumab ozogamicin was not administered because of low CD33 expression. Following the first induction course, the patient achieved remission with undetectable measurable residual disease by next-generation flow cytometry.

Conclusion

Persistent or recurrent pediatric soft-tissue lesions with atypical clinical behavior require adequate tissue sampling, broad lineage-directed immunophenotyping, and timely correlation with marrow findings. This case illustrates how myeloid sarcoma can precede clinically recognized AML and mimic both benign vascular and lymphoid lesions, while also demonstrating a favorable early response to AML-directed systemic therapy.

Introduction

Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy characterized by clonal expansion of myeloid precursors and disruption of normal hematopoiesis. Pediatric AML differs biologically from adult disease, with age-specific genomic features that influence classification, risk stratification, treatment response, and prognosis [1–3]. Marrow failure commonly produces anemia, thrombocytopenia, and neutropenia, causing pallor, bleeding, fever, and infection. Although outcomes

have improved through risk-adapted chemotherapy, molecular diagnostics, response assessment, and supportive care, relapse remains the principal cause of treatment failure [3, 4].

Myeloid sarcoma (MS), historically termed granulocytic sarcoma or chloroma, is a tissue-based manifestation of a myeloid neoplasm characterized by a mass of myeloid blasts outside the bone marrow [1, 2]. It most often occurs concurrently with AML but may also present during relapse, accompany other myeloid neoplasms, or precede clinically recognized leukemia [1, 2, 5]. Pediatric MS most frequently involves the skin, soft tissues, bone, and orbit, although lymph nodes, the gastrointestinal tract, central nervous system, and testis may also be affected [2, 5]. Its clinical, radiologic, and histologic appearances vary by anatomical site and degree of differentiation; consequently, MS may mimic benign or inflammatory lesions, lymphoma, or other small round-cell tumors [5].

When MS precedes recognized marrow disease, nonspecific morphology or an incomplete immunohistochemical panel may delay correct lineage assignment. Diagnosis requires integration of tissue morphology with broad immunophenotyping, bone-marrow examination, flow cytometry, and cytogenetic or molecular studies [1, 5]. We report a child with a slowly progressive subcutaneous forearm lesion initially considered a hemangioma and subsequently interpreted as a lymphoproliferative disorder and probable precursor lymphoblastic lymphoma. Re-evaluation after the development of pancytopenia and marrow disease established MS associated with AML showing aberrant CD7 expression. This case highlights the need to reconsider persistent or recurrent pediatric soft-tissue lesions when their clinical course is inconsistent with the initial diagnosis.

Case Presentation

A 7-year-old boy was admitted to Imam Reza Hospital in Bojnord with a 2-day history of fever, generalized petechial and purpuric skin lesions, weakness, and lethargy. He also had a painful swelling over the anterior aspect of the left forearm that had recently increased in size.

According to his parents, the forearm lesion had followed a prolonged, initially indolent course. Approximately 18 months before admission, focal thickening and induration developed over the upper one-third of the left forearm. Nearly 1 year later, progressive swelling at the same site became clinically apparent as a palpable mass. Ultrasonography performed on October 7, 2025, demonstrated an irregular, ill-defined, solid hypoechoic lesion measuring approximately 21 × 5 mm in the subcutaneous soft tissue along the lateral aspect of the upper one-third of the forearm. The lesion contained fatty components and tubular vascular structures, and hemangioma was initially considered the most likely radiologic diagnosis. The patient's medical, family, and psychosocial history revealed no significant findings or known genetic predispositions to hematologic malignancies.

An earlier complete blood count available from this phase of the clinical course showed mild leukopenia, with a white blood cell count of 3,160/ μ L, but preserved hemoglobin and platelet levels of 12.9 g/dL and 169,000/ μ L, respectively. The erythrocyte sedimentation rate was 10 mm/h, C-reactive protein was 0.1

mg/L, and blood cultures showed no growth after 72 hours. Bone marrow examination was not performed at that time; therefore, the presence or absence of early marrow involvement could not be established.

As the lesion became painful, surgical excision was attempted. A substantial portion of the mass was removed, but complete resection was not feasible because of adherence to adjacent vessels and deeper soft tissues. Gross examination showed a cream-yellow soft-tissue specimen measuring $2 \times 2 \times 1$ cm that contained a lymph node measuring approximately 1 cm in diameter. Histologic examination demonstrated marked effacement of the lymph-node architecture by an infiltrate of small- to medium-sized lymphoid-appearing cells with mildly irregular nuclei and scant cytoplasm. Mild vascular proliferation, mitotic activity, focal necrosis, and crush artifact were present. No Reed-Sternberg or Hodgkin-like cells were identified, and the lymph-node sinuses were largely obliterated. The initial interpretation was suspicious for a lymphoproliferative disorder versus a reactive process, and additional immunohistochemical assessment and second-opinion review were recommended.

Diagnostic follow-up was delayed. Approximately 2 months before admission, the patient developed severe diffuse myalgia, sweating, progressive weakness, and lethargy. Concurrently, the lesion at the previous operative site increased in size, became discolored, and was painful on palpation (Fig. 1). Repeat ultrasonography on May 6, 2026, demonstrated inflammatory changes in the subcutaneous tissue and a residual or recurrent lesion measuring approximately 17×6 mm.

The original tissue block was subsequently evaluated using a limited immunohistochemical panel. The neoplastic cells showed strong and diffuse expression of leukocyte common antigen and CD99, with a Ki-67 proliferation index of approximately 55%. CD3, CD10, and CD20 were negative. Based on this limited profile, the lesion was interpreted as a high-grade immature nodal or extranodal lymphoma, most compatible with precursor lymphoblastic lymphoma of probable T-cell or null-cell lineage.

At admission, the patient was fully conscious but appeared acutely ill. Physical examination revealed marked conjunctival pallor and generalized petechiae and purpura involving the trunk and extremities (Fig. 2). Small cervical lymph nodes were palpable in the anterior, posterior, and submandibular chains. The abdomen was soft and non-tender, although hepatosplenomegaly was detected on deep palpation. Respiratory and testicular examinations were unremarkable.

Initial laboratory evaluation demonstrated severe pancytopenia: the white blood cell count was $2.9 \times 10^3/\mu\text{L}$, hemoglobin 4.4 g/dL, hematocrit 13.4%, and platelet count $34 \times 10^3/\mu\text{L}$. The differential count showed 5.5% neutrophils and 90.4% lymphocytes. Cervical ultrasonography demonstrated multiple small lymph nodes with preserved morphology and a maximum short-axis diameter of 6 mm. Abdominal ultrasonography confirmed hepatomegaly, with a midclavicular liver length of 150 mm, and moderate splenomegaly, with a craniocaudal length of 152 mm. No para-aortic or mesenteric lymphadenopathy was identified. Scrotal ultrasonography showed normal bilateral testicular echogenicity and vascularity without a focal lesion.

Bone marrow aspiration and trephine biopsy were subsequently performed. Differential counting of the aspirate demonstrated 40% blasts, 44% lymphocytes, 5% erythroid cells, and markedly reduced maturing myeloid elements. The reported myeloid-to-erythroid ratio was 1.5:1. Erythroid maturation was markedly reduced, and myeloid maturation arrest was observed. The trephine biopsy was markedly hypercellular, with approximately 90% cellularity, and showed extensive replacement of the marrow spaces by a monotonous population of mononuclear blast-like cells. Erythroid precursors and megakaryocytes were decreased, and multiple mitotic figures, including atypical forms, were present. These findings were considered consistent with acute leukemia.

Flow-cytometric immunophenotyping identified a predominant blast population expressing HLA-DR in 72% of cells, CD13 in 42%, CD7 in 30%, and CD117 in 18%. CD33 was expressed in 5.3% of cells. CD19, CD20, TdT, CD2, CD3, CD14, CD64, and CD34 were each expressed in fewer than 1% of cells, whereas CD5, CD56, and CD138 were negative. The findings favored acute myeloid leukemia, reported as non-M3 AML, with aberrant CD7 expression.

Bone marrow immunohistochemistry demonstrated weak expression of myeloperoxidase and CD7 and CD117 positivity in approximately 20% of cells. CD3, CD19, TdT, CD68, CD64, and CD34 were negative. These findings supported the diagnosis of acute myeloblastic leukemia with aberrant CD7 expression.

Following establishment of the marrow diagnosis, the forearm lesion was re-evaluated using a broader immunohistochemical panel. The neoplastic cells were strongly positive for leukocyte common antigen and weakly positive for myeloperoxidase, CD7, CD117, and CD99. The Ki-67 proliferation index was approximately 40%. CD3, CD20, TdT, CD68, and CD34 were negative. Second-opinion histopathologic review described a neoplastic proliferation of atypical cells with convoluted nuclei, occasional prominent nucleoli, and pleomorphic features. The lesion was consequently reclassified as granulocytic sarcoma, currently termed myeloid sarcoma.

Real-time polymerase chain reaction testing of the bone marrow was negative for DEK::NUP214 (DEK-CAN), RUNX1::RUNX1T1 (AML1-ETO), CBFB::MYH11, and BCR::ABL1 p190 and p210. The tumor-board documentation additionally recorded negative results for NPM1, CEBPA, FLT3-ITD, WT1, and KIT. Collectively, the clinical, morphologic, immunophenotypic, and molecular findings established a diagnosis of pediatric acute myeloid leukemia with aberrant CD7 expression, preceded clinically by a subcutaneous myeloid sarcoma of the left forearm.

Treatment was initiated according to a newly diagnosed pediatric AML protocol using daunorubicin, cytarabine, and thioguanine (DAT). Gemtuzumab ozogamicin was not administered because CD33 expression was low, being detected in only 5.3% of the blast population. During hospitalization, severe thrombocytopenia necessitated platelet transfusion. The patient developed an anaphylactic reaction during transfusion, requiring temporary discontinuation. After modification of the transfusion protocol, subsequent platelet transfusions were administered without recurrence of anaphylaxis, allowing continuation of supportive care. Following the first induction course, the patient achieved remission, and

measurable residual disease (MRD) assessment by next-generation flow cytometry showed no detectable residual disease, representing a favorable early treatment response.

Discussion

The distinguishing feature of this case is a subcutaneous forearm MS that was evident approximately 18 months before overt marrow failure and recognition of AML. Its slow enlargement and tubular vascular structures on ultrasonography favored hemangioma, while incomplete excision and delayed diagnostic follow-up prolonged uncertainty. The complete blood count showed mild leukopenia, with preserved hemoglobin and platelet counts; however, no marrow examination was performed. Accordingly, the lesion can be described as preceding recognized AML, but not as proven isolated MS, which requires absence of marrow involvement [5–7]. This distinction is relevant because morphologically normal marrow may still harbor low-level clonal abnormalities [1].

The sequential pathologic interpretations demonstrate the overlap between MS and lymphoid or other small round-cell neoplasms. The initial specimen appeared lymphoid, and a limited panel showing strong leukocyte common antigen and CD99 expression, a high Ki-67 index, and negative B- and T-cell markers led to a provisional diagnosis of probable precursor lymphoblastic lymphoma. This did not establish precursor lymphoid differentiation or myeloid lineage. Reassessment demonstrated weak MPO and CD117 immunoreactivity and negative TdT; aberrant CD7 expression was present in both the lesion and marrow. When morphology is ambiguous, a lineage-directed panel incorporating CD43, MPO, lysozyme, CD117, CD68 or CD163, CD34, and B- and T-cell markers, integrated with marrow flow cytometry, improves diagnostic accuracy [5–8].

MS should prompt immediate marrow, cytogenetic, and molecular evaluation even when peripheral blood is not frankly leukemic [1, 5]. Pediatric MS is associated particularly with core-binding-factor and chromosome 11/KMT2A abnormalities, but prognostic effects differ across anatomical sites and molecular subgroups [2, 6]. In this patient, the tested recurrent AML-associated rearrangements and mutations were negative. Their absence alone does not establish high-risk disease: contemporary pediatric AML risk assessment integrates the complete cytomolecular profile with treatment response and measurable residual disease [3, 4].

AML-type systemic chemotherapy is recommended for MS, including apparently isolated presentations, because surgery or radiotherapy alone does not address occult or subsequent systemic disease [5–7]. Surgery is mainly diagnostic or reserved for selected complications, while radiotherapy may be considered for symptomatic, compressive, or residual local disease [5–7]. This case therefore supports early adequate biopsy, broad immunophenotyping, and multidisciplinary radiologic-pathologic-hematologic review of persistent or recurrent pediatric soft-tissue masses. Earlier integration of these findings may reduce diagnostic delay and enable timely systemic evaluation and treatment.

Myeloid sarcoma may precede clinically recognized AML and can closely mimic benign soft-tissue lesions or lymphoid malignancies, creating substantial diagnostic difficulty in children. This case

underscores the importance of adequate biopsy, broad lineage-directed immunophenotyping, and early integration of radiologic, pathologic, and hematologic findings in persistent or recurrent soft-tissue masses. Recognition of the underlying myeloid lineage allowed appropriate AML-directed therapy, with the patient achieving remission and undetectable MRD after the first induction course, representing a favorable early treatment response.

Declarations

Ethics:

The requirement for ethical approval was waived by the Institutional Review Board of North Khorasan University of Medical Sciences. The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate:

Written informed consent to participate was obtained from the patient's parents.

Consent to publish:

Written informed consent for publication of the patient's clinical details and images was obtained from the patient's parents.

Patient Perspective

The patient's parents expressed gratitude for the multidisciplinary care and immense relief regarding their child's rapid clinical improvement and favorable response to the chemotherapy regimen.

AI Use Declaration

ChatGPT (OpenAI) was used only for language editing and improving clarity. All content was reviewed and approved by the authors.

Competing interests:

The authors declare no competing financial or non-financial interests, including any relevant business or family relationships, in relation to the work described.

Funding:

No funding was received for this study.

Author Contribution

S.S. led the patient's clinical hematologic management, conceptualized the case report, and provided medical supervision. M.R. conducted the comprehensive literature review, drafted the primary manuscript text, and prepared the final manuscript for submission. A.A. performed the critical histopathological evaluations, interpreted the immunohistochemical panels, and provided the diagnostic pathology findings. K.Y.H. contributed to the patient's clinical care and assisted in the collection of clinical data. All authors critically reviewed the manuscript for important intellectual content and approved the final submitted version.

Data availability:

The datasets generated and/or analysed during the current study are not publicly available due to patient privacy and confidentiality but are available from the corresponding author on reasonable request.

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Figures



Figure 1

Clinical photograph showing recurrent swelling and discoloration at the previous operative site on the left forearm.



Figure 2

Clinical photograph showing multiple petechial and purpuric lesions over the trunk at presentation.

Supplementary Files

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