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CASE REPORT

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Rare presentation of Pre-B acute lymphoblastic leukemia with severe eosinophilia, bicytopenia, and cardiac mass in a 4-year-old boy: a case report

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Abstract

Introduction Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy and most often presents with an increase in the number of blasts in the peripheral blood and bone marrow. Although ALL typically presents with circulating blasts, atypical findings such as hypereosinophilia may obscure diagnosis and delay appropriate management. Severe eosinophilia in patients with ALL is a very rare phenomenon and is usually associated with specific genetic abnormalities or myeloid malignancies. The combination of severe eosinophilia, bicytopenia, and cardiac mass is unusual and challenging in diagnosis and treatment.

Case presentation A 4-year-old male patient, with no significant past or family history, presented to the emergency department with persistent fever. On initial examination, hepatosplenomegaly was evident. Blood tests showed WBC = 125,000cell per microliter, Hb = 8.7 g/dL, Plt = 77,000 per microliter, and severe eosinophilia (73.4%) absolute eosinophil count 91,250. A peripheral blood smear showed abundant mature eosinophils without blasts. Chest imaging showed bilateral pulmonary involvement, and ultrasonography showed bilateral pleural effusion. Echocardiography revealed a mass in the right ventricle suggestive of thrombus formation or infiltration, along with some degree of heart failure. Molecular tests for BCR-ABL, PDGFRα, PDGFRβ, FGFR1, and t (5:14) were negative, and bone marrow flow cytometry was also negative. Bone marrow biopsy with immunohistochemistry confirmed the diagnosis of Pre-B acute lymphoblastic leukemia with positive CD20 and TdT. The patient underwent protocol treatment and the MRD at the end of induction was reported to be 0.0011% and the biopsy was negative. The cardiac mass was also resolved during chemotherapy treatment.

Conclusion This case emphasizes the importance of noting unusual eosinophilia with bicytopenia, even in the absence of peripheral blasts, and the need for bone marrow biopsy and immunohistochemical examination for accurate diagnosis.

Keywords Acute lymphoblastic leukemia, Eosinophilia, Bicytopenia, Cardiac mass, Children, Case report

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Introduction

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, accounting for approximately 25% of all cancers in this age group [1]. This disease is caused by the uncontrolled proliferation of immature lymphoblasts in the bone marrow, which leads to the replacement of normal hematopoietic tissue and the development of symptoms such as anemia, bleeding, fever, and organomegaly [2]. In most cases, the white blood cell count is elevated and blasts are clearly identifiable in the peripheral blood and bone marrow. However, in some patients, the initial presentation may be atypical, which may delay the diagnosis process [3].

Eosinophilia, as an abnormal increase in eosinophils in the peripheral blood, is often caused by allergic diseases, parasites or certain inflammatory disorders. The occurrence of severe eosinophilia (> 5,000/μL) in the setting of lymphoid malignancies, especially ALL, is a rare phenomenon and is estimated to account for less than 1% of ALL cases [4, 5]. In reported cases, this phenomenon is usually associated with specific genetic rearrangements such as FIP1L1–PDGFRα, PDGFRβ, FGFR1, or BCR-ABL [6, 7].

Possible mechanisms of eosinophilia in ALL include overproduction of eosinophil growth-stimulating cytokines, such as IL-3, IL-5, and GM-CSF, by leukemic cells or reactive immune cells [8].

On the other hand, cardiac thrombosis is very rare in children with hematological malignancies. Several factors, including cancer-related hypercoagulable state, endothelial damage, and side effects of chemotherapy treatments, can contribute to this phenomenon [9, 10]. The simultaneous reports of severe eosinophilia, bicytopenia, and cardiac mass in a patient with ALL are very limited in the scientific literature, and reporting such rare presentations enhances clinical vigilance and broadens understanding of atypical manifestations of ALL.

Case presentation

The patient, a 4-year-old boy, with no history of underlying disease, genetic problems, or medication use, presented with persistent fever over the past few days. The family did not report any similar history of hematological diseases. On physical examination, he had respiratory distress and tachycardia and the liver and spleen were clearly palpable. No significant lymphadenopathy was observed.

Laboratory findings

*Laboratory evaluation showed marked leukocytosis (*WBC: 125000 cell per microliter), anemia (Hb: 8.7 g/dL), thrombocytopenia (Plt: 77000/microliter), Sever Eosinophilia: (73.4%)

Ast: 45 u/l, Alt: 28 u/l, Alk ph: 294 u/l, Urea: 27 mg/dl, Cr: 0/6 mg/d, uricacid: 4/1 mg/dl, ldh: 581, pt: 13, ptt: 30, INR: 1.

Peripheral blood smear: abundant mature eosinophils, no blasts observed (Fig. 1).

Imaging

CXR: Bilateral pulmonary infiltration (widespread consolidation in both lungs).

Abdominal ultrasound: bilateral pleural effusion and hepatosplenomegaly.

Echocardiography: Some degree of heart failure and of 40% and mass in the right ventricle, suspected thrombosis or infiltration.

Infection consult was done and his stool exam and investigating of parasite was negetive.

Due to the presence of bicytopenia with marked leukocytosis with predominant eosinophilia, bone marrow aspiration and biopsy were performed.

Additional investigations

Bone marrow aspiration: Hypercellular marrow with myeloid 73% erythroid 9% lymphoid 5% blast 13% with prominant eosinophilic precursers, few small sized

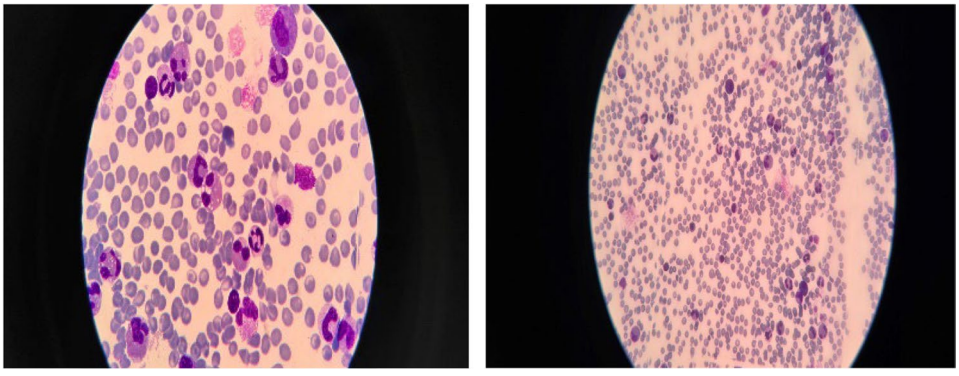


Fig. 1 Peripheral blood smear

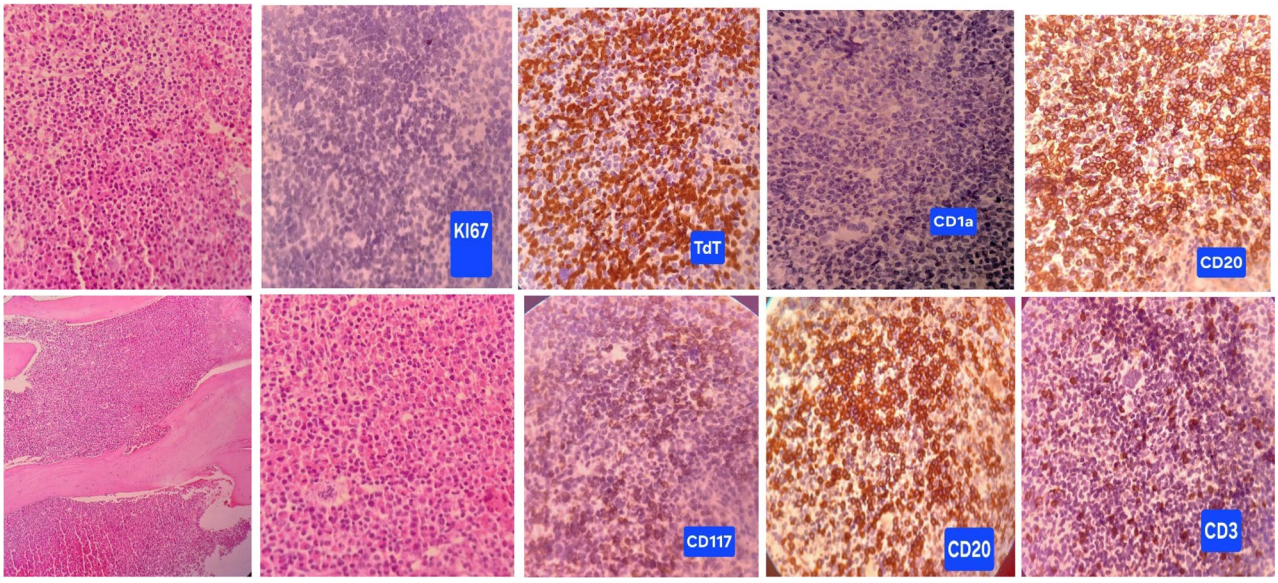


Fig. 2 Bone marrow biopsy (immunohistochemistry: positive expression of CD20 and TdT confirmed the diagnosis of Pre-B ALL)

lymphoid blastic cells with round hyperchromatic nuclei and scant cytoplasm are also noted.

Molecular tests (FISH analysis): BCR-ABL, PDGFRα, PDGFRβ, FGFR1 and t (5:14) not detected.

Bone marrow karyotype: normal.

Flow cytometry on bone marrow aspiration: Flow cytometry did not reveal a definitive leukemic blast population, prompting bone marrow biopsy for confirmation.

(Cd34 14%, cd117 2%, cd13 35%, cd33 37%, cd45 98%, cd38 70%, cd19 22%, cd10 8%, cd20 24%, cd3 32%, cd5 32%, cd4 43%, cd8 43%, cd56 4%).

Bone marrow biopsy: widespread invasion of immature lymphoid cells (showed 100% cellularity with increased eosinophilic precursors).

CD20: diffuse positive reaction in tumoral cells.
CD3: scattered positive reaction in marrow cells.
CD1a: negative reaction.
MPO: positive reaction in marrow cells.
TdT: diffuse positive reaction in tumoral cells.
CD117: scattered positive reaction in marrow cells.
Ki67: inconclusive.

Immunohistochemistry: as above mentioned Positive expression of CD20 and TdT confirmed the diagnosis of Pre-B ALL. Given the combination of bicytopenia and severe eosinophilia without circulating blasts, further evaluation was pursued with bone marrow biopsy (Fig. 2).

Treatment and follow-up process

Chemotherapy treatment was initiated according to the high-risk pediatric ALL COG protocol. In addition, due to the presence of a cardiac mass that was presumed thrombotic vs. infiltrative at first because of his unstable hemodynamic he recieved inotrope and diuretic. cardiac mass was infiltration due to hypereosinophilia as the cardiac assessment with MRI was not available and it was resolved with ALL chemotherapy treatment without anticoagulation and the cardiac drugs were tapered. The patient tolerated the treatment well, and clinical symptoms including fever and hepatosplenomegaly gradually resolved. Eosinophil counts had gradual decline and at the end of the induction phase his cell count was 3300 cell per microliter, follow-up biopsy showed remission. Follow-up echocardiography also showed that the cardiac mass completely regressed with chemotherapy, and the patient achieved hematologic remission (MRD 0.0011%).

Discussion

The present case demonstrates that severe eosinophilia can be the first manifestation of a lymphoid malignancy in children, even when blasts are not visible in the peripheral blood. This finding highlights the importance of performing a complete hematologic and bone marrow evaluation in patients with unexplained eosinophilia.

Previous studies have shown that eosinophilia associated with ALL is often associated with specific genetic disorders. For example, PDGFRβ and FGFR1 rearrangements have been reported in rare cases of ALL with eosinophilia [6]. However, in our patient, molecular investigations for BCR-ABL, PDGFR, FGFR1, and t(5:14) were all negative, making the case molecularly unique.

Pathophysiologically, the presence of eosinophils in ALL may be caused by excessive secretion of IL-5 and other eosinophil-stimulating cytokines from leukemic cells or

peripheral immune cells [8]. Leukemic blasts can produce eosinopoietic cytokines, mainly: IL-3, IL-5 (major eosinophil growth factor), GM-CSF. These cytokines stimulate eosinophil precursors in the bone marrow; leading to secondary eosinophilia. The altered stromal cells in leukemic marrow may favor eosinophil differentiation over other lineages. This contributes to persistently elevated eosinophil counts even without a direct clonal expansion. This condition can lead to a severe increase in eosinophils in the peripheral blood and tissues even in the absence of direct myeloid lineage involvement.

Another important challenge in this case was the negativity of flow cytometry, which is typically one of the main tools for diagnosing ALL [11]. This finding suggests that in some cases, the tumor burden may be low or the distribution of leukemic cells in the bone marrow may be heterogeneous and it is not obviouse in bone marrow aspiration, and therefore, biopsy and immunohistochemistry may be necessary for diagnosis.

In this patient, the presence of a cardiac mass added further diagnostic complexity. Cardiac infiltration and thrombosis is also a rare but potentially life-threatening manifestation in patients with hematological malignancies [9]. In ALL patients, this condition may occur as a result of a combination of activation of the coagulation system, endothelial damage, immobility, and the use of drugs such as asparaginase [12]. Prompt treatment with anticoagulants, along with control of the underlying disease, is vital to prevent severe cardiac complications and embolism.

Delays in diagnosing and starting treatment for diseases can lead to serious complications. Our patient was diagnosed at an early stage of the disease due to clinical suspicion and prompt biopsy, and had a very good treatment response with low MRD after induction, indicating a favorable prognosis.

Overall, this report highlights the importance of paying attention to the rare combination of severe eosinophilia and bicytopenia in children and the need to investigate hematologic malignancies even in the absence of peripheral blasts. Furthermore, the presence of a cardiac mass in these patients should be considered an emergency and managed with a multidisciplinary approach.

Conclusion

Severe eosinophilia in children should not be attributed solely secondary to common allergic or infectious causes, especially when accompanied by bicytopenia. Such eosinophilia may obscure leukemia and lead to delay diagnosis if marrow is not examined. In such circumstances, a complete bone marrow examination is necessary even in the absence of peripheral blasts. Cardiac mass synchrony in ALL patients requires prompt multidisciplinary intervention to reduce the risk of serious complications.

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Authors' contributions
All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

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

Competing interests
The authors declare no competing interests.

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