

The Implications of Musculoskeletal Manifestations in Acute Lymphoblastic Leukemia: A Decade's Experience from a Referral Center in Southern India

Original Article

Volume 62, Pages 489-494, July 2025

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Received: 3 February 2025 / Accepted: 12 March 2025 / Published online: 7 April 2025

<https://doi.org/10.1007/s13312-025-00064-y>

ABSTRACT

OBJECTIVES

Children with acute lymphoblastic leukemia (ALL) with musculoskeletal (MSK) manifestations may be misdiagnosed as juvenile idiopathic arthritis (JIA). The present study compared the baseline parameters and survival outcomes in patients with ALL with and without MSK symptoms.

METHODS

A retrospective chart review of children aged < 18 years diagnosed with ALL was performed. Based on contemporary parameters, the patients were stratified into standard-risk (SR), intermediate-risk (IR), and high-risk (HR) groups. Clinical and laboratory features and survival outcomes were compared between ALL patients with and without MSK symptoms.

RESULTS

Out of 255 participants, 67 (26%) had MSK manifestations; of these, 9 were pretreated for JIA with glucocorticoids/methotrexate. Patients with MSK manifestations had a longer median duration of symptoms before diagnosis (4 vs 2 weeks, $P < 0.001$), and a higher median platelet count ($53 \times 10^9 /L$ vs. $28 \times 10^9 /L$, $P = 0.002$). The 3-year event-free survival (EFS) for patients with MSK and without MSK manifestations were $84.4 \pm 5.2\%$ and $78.9 \pm 3.4\%$ ($P = 0.900$). All 9 pretreated patients received an IR/HR protocol (4 were SR if not for the pretreatment as JIA).

CONCLUSION

Patients with ALL with MSK manifestations have more preserved blood counts and a longer duration of symptoms before diagnosis. Pretreatment of children with ALL misdiagnosed as JIA with glucocorticoids/methotrexate can delay the diagnosis, confound the risk stratification, and upstage the risk group requiring administration of more toxic chemotherapy than necessary otherwise.

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Keywords: Malignant bone pain · Pediatric cancer · Risk stratification · Steroid pretreatment · Systemic onset juvenile idiopathic arthritis.

REFERENCES

1. Inaba H, Pui CH. Advances in the diagnosis and treatment of pediatric acute lymphoblastic leukemia. *J Clin Med*. 2021;10:1926.
2. Inaba H, Mullighan CG. Pediatric acute lymphoblastic leukemia. *Haematologica*. 2020;105:2524–39.
3. Kittivisut S, Sripornsawan P, Songthawee N, Chavananon S, McNeil EB, Chotsampancharoen T. Musculoskeletal involvement in childhood leukemia: characteristics and survival outcomes. *Pediatr Rheumatol Online J*. 2022;20:34.
4. Maman E, Steinberg DM, Stark B, Izraeli S, Wientroub S. Acute lymphoblastic leukemia in children: correlation of musculoskeletal manifestations and immunophenotypes. *J Child Orthop*. 2007;1:63–8.
5. Kang S, Im HJ, Bae K, Park SS. Influence of musculoskeletal manifestations as the only presenting symptom in B-cell acute lymphoblastic leukemia. *J Pediatr*. 2017;182:290–295.e1.
6. Bhatia P, Totadri S, Singh M, et al. PEST domain NOTCH mutations confer a poor relapse free survival in pediatric T-ALL: data from a tertiary care centre in India. *Blood Cells Mol Dis*. 2020;82:102419.
7. Sudhakar M, Kumar S. Juvenile idiopathic arthritis. *Indian J Pediatr*. 2024;91:949–58.
8. Gupta D, Singh S, Suri D, Ahluwalia J, Das R, Varma N. Arthritic presentation of acute leukemia in children: experience from a tertiary care centre in North India. *Rheumatol Int*. 2010;30:767–70.
9. Brix N, Rosthøj S, Glerup M, Hasle H, Herlin T. Identifying acute lymphoblastic leukemia mimicking juvenile idiopathic arthritis in children. *PLoS ONE*. 2020;15:e0237530.
10. Fonseca MB, Gomes FHR, Valera ET, et al. Signs and symptoms of rheumatic diseases as first manifestation of pediatric cancer: diagnosis and prognosis implications. *Rev Bras Reumatol Engl Ed*. 2017;57:330–7.
11. Kesarapu S, Vangala N, Uppin SG, Uppin MS, Paul TR, Rajasekhar L. Acute leukemia presenting with musculoskeletal manifestations: a case series. *Indian J Med Paediatr Oncol*. 2020;41:29–33.
12. Tannenbaum MF, Noda S, Cohen S, Rissmiller JG, Golja AM, Schwartz DM. Imaging musculoskeletal manifestations of pediatric hematologic malignancies. *AJR Am J Roentgenol*. 2020;214:455–64.
13. Brix N, Rosthøj S, Herlin T, Hasle H. Arthritis as presenting manifestation of acute lymphoblastic leukaemia in children. *Arch Dis Child*. 2015;100:821–5.
14. Trehan A, Bansal D, Varma N, Vora A. Improving outcome of acute lymphoblastic leukemia with a simplified protocol: report from a tertiary care center in north India. *Pediatr Blood Cancer*. 2017. <https://doi.org/10.1002/pbc.26281>.
24. Haynes BF, Fauci AS. The differential effect of in vivo hydrocortisone on the kinetics of subpopulations of human peripheral blood thymus-derived lymphocytes. *J Clin Invest*. 1978;61:703–7.