ISSN: 2692-5516

Case Report

Advances in Hematology and Oncology Research

Neonatal Leukemia: A Rare Hematologic Malignancy in Pediatrics: A Case Report

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Submitted: 2024, Oct 01; **Accepted:** 2024, Oct 22; **Published:** 2024, Oct 29

Citation: Gebrehana, A. W., Dereje, W. M., Kasawudeg, N. G., Abebe, B., Maru, G., et, al. (2024). Neonatal Leukemia: A Rare Hematologic Malignancy in Pediatrics: A Case Report. *Adv Hema Onco Res, 7*(2), 01-04.

Abstract

Background: *Even though Leukemia is one of the most common causes of childhood cancer its occurrence in the newborn period is very uncommon, especially when presenting with non-specific symptoms.*

Case Presentation: *A 10-day old female Ethiopian infant was referred from a public hospital to the Neonatal intensive care unit of Gondar University Comprehensive Specialized Hospital after they found a markedly elevated leukocyte count while working her up for early-onset neonatal sepsis as she was experiencing persistent vomiting since the first day of delivery. Physical examination was only notable for palpable spleen 3cm below the left costal margin. Further evaluation with peripheral morphology and bone marrow aspiration revealed numerous blast cells and a diagnosis of acute lymphoblastic leukemia.*

Conclusion: *Neonatal leukemia, a rare disease in newborns, may present with unusual symptoms. It should be considered among the differential diagnoses when accompanied by abnormalities in blood counts and other suggestive features.*

Keywords: Neonatal Leukemia, Congenital Leukemia, Leukemia, Acute Lymphoblastic Leukemia

Abbreviations

AML: Acute Myeloid Leukemia
ALL: Acute Lymphoblastic Leukemia
NL: Neonatal Leukemia
ANC: Antenatal Care
WBC: White Blood Counts
CBC: Complete Blood Counts
TAM: Transient Abnormal Myelopoiesis

1. Background

Leukemia presenting in the first 4 weeks of life is termed neonatal or congenital leukemia. This type of leukemia is rare with estimated incidence ranging from 1 to 5 per million live births [1]. Reports have shown that Acute Myeloid Leukemia (AML) is more common than Acute Lymphoblastic Leukemia (ALL) in neonatal leukemia [2,3]. The most common clinical signs are hepatomegaly, splenomegaly, and skin lesions (leukemic cutis). The most consistent hematologic abnormality is hyperleukocytosis which is usually associated with anemia and thrombocytopenia [4]. Aside from trisomy 21, the most frequently occurring chromosomal aberration in both neonatal AML and ALL is a translocation involving the KMT2A gene formerly known as Mixed Lineage Leukemia (MLL) gene, located on chromosomal band 11q23. The prognosis for NL is typically poor and it is usually associated with treatment-related mortality. Additionally, there is a high rate of relapse in NL compared to leukemia in older children [2].

2. Case Presentation

A 10-day-old female Ethiopian neonate was referred from a public hospital to Gondar University Comprehensive Specialized Hospital, Neonatal Intensive Care Unit after she was found to have markedly elevated leukocyte count while working her up for early onset neonatal sepsis. She was experiencing nonbilious vomiting of ingested matter occurring two to three times per day since the first day of life. Other than the vomiting the neonate had no failure to suck, fast breathing, fever, change in mentation, or abdominal

distention. She also has no sunken of eyes, decreased urine output, or weight loss. She was born to a 27-year-old para I mother at a gestational age of 40 weeks +2 days. The mother had regular ANC visits during her pregnancy. The mother has no history of radiation exposure or any chemotherapy drug intake. There was no family history of malignancy. The pregnancy was uneventful. The labor started spontaneously lasting 12 hours and the mode of delivery was a spontaneous vaginal delivery and the birth weight was 2600 grams.

Initially, the mother took her to a nearby health center on the 3rd day of life, where she was wrongfully reassured it was likely a physiologic regurgitation. Over the following days, the vomiting did not subside and the mother took her to a tertiary hospital on the 10th day of birth where a complete blood count was done as part of the evaluation for neonatal sepsis. The White Blood Cell Count (WBC) was markedly elevated (248,000/mm3) which prompted the team for a peripheral morphology examination which revealed numerous atypical lymphocytes and blast cells. Finally, she was referred to our center for further evaluation of possible leukemia. At admission at our hospital, the neonate was alert and her vitals were within normal range. She had no dysmorphic features. The only notable finding on physical examination was a palpable spleen 3 centimeters below the left costal margin. CBC results showed WBC ($273*10^3/mm^3$), Hemoglobin(14.3g/dl), Hematocrit (42 %) and Platelet count (56*103/mm3). Blood culture and CRP were not indicative of a possible sepsis. Her uric acid, Lactate dehydrogenase, serum electrolytes, and serum Creatinine levels were within normal range. Bone marrow aspiration revealed ALL (Figure).

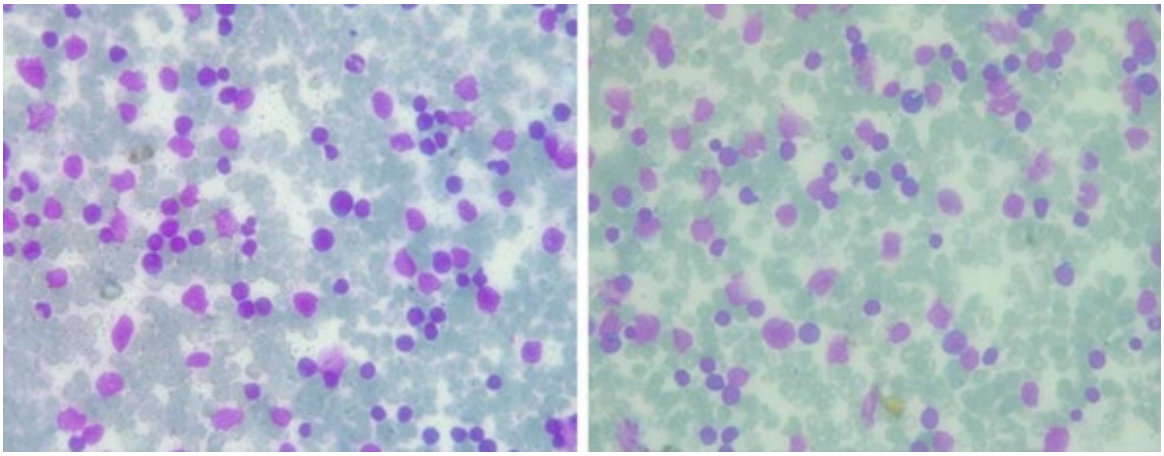

Figure: Bone Marrow Is Bussy with The Proliferation of Small to Intermediate-Sized Lymphoid Cells Having a Scant to Moderate Amount of Deep Blue Finely Vacuolated Cytoplasm, Round to Indented to Irregular Nuclei Some with Multiple Conspicuous to Prominent Nuclei, and Numerous Smudged Cells-No Auer Rods Seen

Because of in-availability other standard diagnostic tests like flow cytometry for immunophenotyping, karyotype, and fluorescence in situ hybridization were not done. The patient was started on antibiotics and IV hydration. After a discussion with the parents about the treatment options available and their possible benefits and toxicities, the parents decided not to start chemotherapy and the patient was discharged as she had no complications needing supportive care. Contact with the parents was maintained via telephone and the newborn developed fast breathing and became pale and was taken to a local health center and later died at the age of 55 days at the health center.

3. Discussion and Conclusion

Neonatal leukemia accounts for less than 1% of all childhood leukemia (5). NL is the third-most prevalent malignancy in infants after teratoma and neuroblastoma [6]. AML is more common than ALL in NL and out of the reported ALL cases, nearly all are of B- lineage with fewer than 5% T- lineage [7]. Based on cytogenetic and molecular characteristics a high proportion of NL patients have a KMT2A/11q23.3 rearrangement which is found in 70-80% of patients with ALL and 50% of those with AML [8,9]. Trisomy 21 is also associated with a preleukemic disorder which usually resolves spontaneously known as TAM (Transient Abnormal Myelopoiesis). Although infrequent, TAM may later develop into AML. The most common clinical manifestations in NL include hepatomegaly, splenomegaly, and leukemic cutis. Lymphadenopathy is less common in NL compared to leukemias in older children. CNS infiltration occurs in approximately 50% of cases and usually presents with bulging fontanelle, reduced level of consciousness and Papilledema [10]. Cutaneous involvements are especially seen in neonatal AML and can occur without peripheral blood and bone marrow involvement [11,12].

Criteria used for the diagnosis of NL include:

• Diagnosis within 28d of birth

• Specific number or proportion (usually 20%) of primitive or immature cells in the bone marrow aspirate, and significantly high peripheral blood leukocyte counts (> 25 × 109/L)

• Spread of primitive cells to areas beyond the blood and bone marrow and

• No evidence of other disorder that might cause infiltration of non-hematopoietic tissues [13].

The differential diagnosis of NL includes leukemoid reactions secondary to infections, Severe hemolytic disease of the newborn, particularly Rh incompatibility, TAM associated with Down syndrome, and advanced stages of neuroblastoma among others. The newborn's unique susceptibility to complications and toxicities has proven to be a challenge in the treatment of NL. Even though chemotherapy for Neonatal Leukemia (NL) can be curative, it usually has a poorer prognosis compared to leukemia in older children [14,15]. Studies have shown that the Prognosis for ALL is worse than that of AML [16]. The 4-year Event-Free Survival (EFS) in Interfant-99, the largest trial of infant ALL to date, was 47% [17]. Different clinical trials use a hybrid chemotherapy which combines the standard ALL regimen mixed with some elements of AML treatments. Certain characteristics in NL have been identified as high risk which pertain to poorer prognosis. These include the presence of KMT2A rearrangement, younger infants, and those with higher WBC count. [18].

Interestingly in some patients with NL spontaneous remission has occurred [19]. Its unclear which patients are likely to have spontaneous remission and can avoid chemotherapy but a case series has shown 7 neonatal cases all with t(8;16) have shown spontaneous remission, out of the 7 some eventually relapsed [20]. In conclusion, our case shows that NL may present with unusual symptoms and a high index suspicion is important to reveal the diagnosis, especially when accompanied by abnormalities in blood counts.

Acknowledgments

The authors gratefully acknowledge that all team members dedicate their best efforts to care for our patient. We would also like to thank the parents of our patient for maintaining continuous contact with us via telephone despite facing difficulties related to their infant's illness.

Author Contributions

AWG was a major contributor in conceptualizing and writing this manuscript and was also involved in the diagnosis of the patient and counseling of parents. WMD and NGK were involved with the diagnosis of the patient and also maintaining contact with the parents after discharge. BA, GM, and EA were involved with preparing and reviewing the Bone marrow aspiration and peripheral smears of the patient.

Availability of Data and Materials

Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics Approval and Consent to Participate

This study was conducted by the fundamental principles of the Declaration of Helsinki.

Consent for Publication

Written informed consent was obtained from the patient's mother for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the corresponding author.

References

1. Bader, J. L., & Miller, R. W. (1979). US cancer incidence and mortality in the first year of life. *American Journal of Diseases of Children, 133*(2), 157-159.
2. Bresters, D., Reus, A. C., Veerman, A. J., Van Wering, E. R., Van Der Does-van den Berg, A., & Kaspers, G. J. (2002). Congenital leukaemia: the Dutch experience and review of the literature. *British journal of haematology, 117*(3), 513-524.
3. Isaacs, H. (2003). Fetal and neonatal leukemia. *Journal of pediatric hematology/oncology, 25*(5), 348-361.
4. Heikinheimo, M., Pakkala, S., Juvonen, E., & Saarinen, U. M. (1994). Immuno-and cytochemical characterization of congenital leukemia: A case report. *Medical and pediatric oncology, 22*(4), 279-282.
5. Tsujimoto, H., Kounami, S., Mitani, Y., Watanabe, T., & Takifuji, K. (2015). Neonatal acute megakaryoblastic leukemia presenting with leukemia cutis and multiple intracranial lesions successfully treated with unrelated cord blood transplantation. *Case Reports in Hematology, 2015*(1), 610581.
6. Orbach, D., Sarnacki, S., Brisse, H. J., Gauthier-Villars, M., Jarreau, P. H., Tsatsaris, V., ... & Doz, F. (2013). Neonatal cancer. *The Lancet Oncology, 14*(13), e609-e620.
7. Brown, P. A. (2021). Neonatal leukemia. *Clinics in Perinatology, 48*(1), 15-33.
8. Pieters, R., De Lorenzo, P., Ancliffe, P., Aversa, L. A., Brethon, B., Biondi, A., ... & Valsecchi, M. G. (2019). Outcome of infants younger than 1 year with acute lymphoblastic leukemia treated with the interfant-06 protocol: results from an international phase III randomized study. *Journal of clinical oncology, 37*(25), 2246-2256.
9. Harrison, C. J., Hills, R. K., Moorman, A. V., Grimwade, D. J., Hann, I., Webb, D. K., ... & Gibson, B. E. (2010). Cytogenetics of childhood acute myeloid leukemia: United Kingdom Medical Research Council Treatment trials AML 10 and 12. *Journal of clinical oncology, 28*(16), 2674-2681.
10. Roberts, I., Fordham, N. J., Rao, A., & Bain, B. J. (2018). Neonatal leukaemia. *British Journal of Haematology, 182*(2), 170-184.
11. Zhang, I. H., Zane, L. T., Braun, B. S., Maize Jr, J., Zoger, S., & Loh, M. L. (2006). Congenital leukemia cutis with subsequent development of leukemia. *Journal of the American Academy of Dermatology, 54*(2), S22-S27.
12. Lee, E. G., Kim, T. H., Yoon, M. S., & Lee, H. J. (2013). Congenital leukemia cutis preceding acute myeloid leukemia with t (9; 11)(p22; q23), MLL-MLLT 3. *The Journal of Dermatology, 40*(7), 570-571.
13. Green, K., Tandon, S., Ahmed, M., Toscano, W., O'Connor, D., Ancliff, P., ... & Rao, A. (2021). Congenital acute myeloid leukemia: challenges and lessons. A 15-year experience from the UK. *Leukemia & Lymphoma, 62*(3), 688-695.

14. van der Linden, M. H., Valsecchi, M. G., De Lorenzo, P., Moericke, A., Janka, G., Leblanc, T. M., ... & Pieters, R. (2009). Outcome of congenital acute lymphoblastic leukemia treated on the Interfant-99 protocol. *Blood, The Journal of the American Society of Hematology, 114*(18), 3764-3768.
15. Creutzig, U., Zimmermann, M., Bourquin, J. P., Dworzak, M. N., Kremens, B., Lehrnbecher, T., ... & Reinhardt, D. (2012). Favorable outcome in infants with AML after intensive first- and second-line treatment: an AML-BFM study group report. *Leukemia, 26*(4), 654-661.
16. Bresters, D., Reus, A. C., Veerman, A. J., Van Wering, E. R., Van Der Does-van den Berg, A., & Kaspers, G. J. (2002). Congenital leukaemia: the Dutch experience and review of the literature. *British journal of haematology, 117*(3), 513-524.
17. Pieters, R., De Lorenzo, P., Ancliffe, P., Aversa, L. A., Brethon, B., Biondi, A., ... & Valsecchi, M. G. (2019). Outcome of infants younger than 1 year with acute lymphoblastic leukemia treated with the interfant-06 protocol: results from an international phase III randomized study. *Journal of clinical oncology, 37*(25), 2246-2256.
18. Sande, J. E., Arceci, R. J., & Lampkin, B. C. (1999, August). Congenital and neonatal leukemia. In *Seminars in perinatology* (Vol. 23, No. 4, pp. 274-285). WB Saunders.
19. Rossoff, J., Akpan, I., & Platanias, L. C. (2018). Spontaneous remission in congenital leukemia. *Leukemia & Lymphoma, 59*(10), 2271-2272.
20. Coenen, E. A., Zwaan, C. M., Reinhardt, D., Harrison, C. J., Haas, O. A., de Haas, V., ... & van den Heuvel-Eibrink, M. M. (2013). Pediatric acute myeloid leukemia with t (8; 16)(p11; p13), a distinct clinical and biological entity: a collaborative study by the International-Berlin-Frankfurt-Münster AML-study group. *Blood, The Journal of the American Society of Hematology, 122*(15), 2704-2713.