

Case Report-V

Congenital Leukemia – A Diagnostic Dilemma

KP PRAKASH, ATK RAU, ST BHAT AND AR RAU

ABSTRACT

A 6 day old newborn presented with fever, lethargy, poor suck and mild hepatosplenomegaly, features suggestive of sepsis. Septic work up was negative. Peripheral smear revealed hyperleukocytosis, thrombocytopenia and presence of atypical cells. Bone marrow examination revealed increased myeloblasts. Other causes of leukemoid reaction were ruled out and a final diagnosis of congenital leukaemia was made.

INTRODUCTION

Congenital Leukemia (CL) is an exceedingly uncommon disease in the newborn and is usually diagnosed at birth or within one month of life.¹ It presents a diagnostic dilemma as clinical manifestations are similar to sepsis. Most CL are myeloid in origin unlike pediatric leukemias which are usually lymphoid. Prognosis is uniformly poor. We report a newborn who presented with clinical features of sepsis and was subsequently diagnosed as CL.

CASE : A 6 day old male neonate was transferred to us with history of fever, increasing lethargy and poor suck not responding to IV antibiotics (started 48 hours earlier at the referring hospital). He was a term neonate (birth weight 3.0kg) born by normal vaginal delivery and third

in birth order to non-consanguineous parents. The mother had regular prenatal care with no history of antenatal medical illness.

On examination, the baby was lethargic and febrile. He had pallor, but no dysmorphic facies suggestive of Down's syndrome. He was tachypneic (respiratory rate - 76/min) and heart rate of 186/min. The anterior fontanelle was at level. The abdomen was mildly distended and liver and spleen were palpable 2cm and 1cm below the costal margins. No skin lesions were present. Other systems were clinically normal.

The baby was evaluated for early neonatal sepsis, which revealed a Hb of 16g/dL, TLC $121 \times 10^3/\mu\text{L}$ and platelet count of $37 \times 10^3/\mu\text{L}$. The peripheral smear showed 11% neutrophils, 5% lymphocytes, 4% monocytes, 10% bands and metamyelocytes and 70% atypical cells (fig 1).

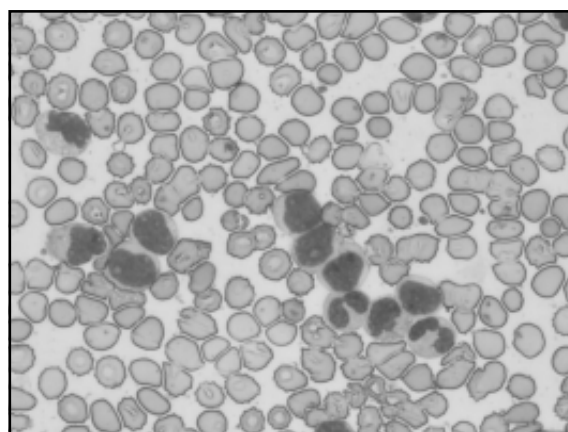


Fig 1: peripheral smear showing blasts and neutrophils (leishman x 400).

Department of Paediatrics (Prakash KP), Paediatric Haematology (Rau ATK) and Pathology (Bhat ST and Rau AR) Kasturba Medical College, Mangalore Karnataka 575001

Correspondence to: ATK RAU
E-mail: atkrau@gmail.com

There were no nucleated RBCs in the smear. CRP positive (86.6mg/l), blood group A positive. IgM levels for congenital TORCH infections were negative and blood culture was sterile after 48hrs. The mother's blood group A positive, VDRL negative. The neonate was given supportive treatment in the form of IV fluids, alkaline diuresis, IV antibiotics and platelet transfusions.

Bone marrow aspiration (fig 2) 47% myeloblasts (morphologically M0), negative for MPO, Sudan black and PAS. Immunophenotyping revealed the blasts to be positive for CD 45, CD13, CD33, CD117, CD34, HLA -DR and negative for B and T lymphoid markers. Karyotyping was done which showed normal 46 XY pattern. The final diagnosis was acute myeloid leukemia (AML - M0).

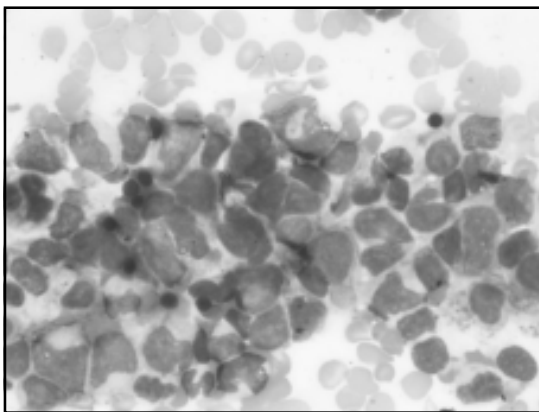


Fig 2: Bone marrow aspirate smear showing presence of numerous blasts (leishman x 400)

DISCUSSION

Congenital leukemia (CL) is a term applied to leukaemia diagnosed at birth or within the first month of life.¹ It is a rare entity, with reported incidence between 4.3 and 8.6 per million livebirths.² The criteria for diagnosis of CL are a) Disease presentation at or shortly after birth (<30days), b) Proliferation of immature white cells, c) Infiltration of the cells into extra hematopoietic tissues d) Absence of any other condition that mimics congenital leukemia.³ Etiological considerations in CL have included

chromosomal defects, intrauterine environmental insults, viral infections and exposure to radiation in pregnancy. CL has also been reported in association with Down's syndrome, Turner syndrome, Klippel-Feil syndrome and Ellis-van Crevald syndrome.⁴

Clinical signs of leukemia may be evident at birth with hepatosplenomegaly, petechiae and ecchymosis. Twenty five to thirty percent of infants with CL have specific cutaneous infiltrates (leukemia cutis) which usually appear as firm blue or red nodules ('Blueberry Muffin').^{5,6} In a study of 6 cases of CL, all of which were AML, autopsy showed leukemic infiltrates in the lungs and other organs.⁷

A large proportion of CL are of myeloid lineage, in contrast to pediatric leukemias in general, which are usually lymphoid in origin.^{1,3,10} About half of congenital AML is of M4 or M5 morphology and there is translocation of MLL gene at band 11q23 and CD14 reactivity in these cases. The t (9;11) translocation is the next common genetic abnormality found followed by the t (11;19) translocation.⁸

The differential diagnosis of CL includes sepsis and intra uterine infections (TORCH). Other possibilities include-hemolytic disease of the newborn (HDN) and transient myeloproliferative disease (TMD).^{1,3} Infections are ruled out by serology and culture as was done in the present case, while in HDN numerous erythrocyte precursors are seen in the peripheral smear, which was absent in this case. TMD of the newborn is seen usually in association with Downs syndrome. They often have associated transient polycythemia and or thrombocytosis, which were not seen in this case. Spontaneous resolution of all blood and bone marrow abnormalities occurs within 3 months of onset.⁹

The prognosis for CL is poor, with only 23% surviving at 24 months.^{10,11} However, rare cases of CL with spontaneous remission have been described, most of which were associated with Downs' Syndrome or mosaicism for trisomy

21⁸ and also Noonan's syndrome.¹² However there is one unique case of CL reported to be surviving beyond 14 years.⁴

In summary, we present a 6 day old neonate with CL and suggest that leukemia be kept in mind in a newborn with clinical features of sepsis and leukocytosis.

REFERENCES:

1. Perkins SL. Hematopoietic system. In: Gilbert-Barness E (ed). *Potter's pathology of the fetus, infant and child*. 2nd ed. Elsevier 2007, Philadelphia, 1453-1514.
2. Bajwa RP, Skinner R, Windebank KP, Reid MM. Demographic study of leukaemia presenting within the first three months of life in the northern health region of England. *J Clin Pathol* 2004;57:186-188.
3. McCoy JP Jr, Overton WR. Immunophenotyping of Congenital leukemia. *Cytometry* 1995;22:85-88.
4. Warriar RP, Emami A, Ravindranath Y, Inoue S, Kaplan J. Perinatal Leukemia: The surface antigens, cytochemistry and cytogenetic features. *Indian Pediatr* 1983;20:325-333.
5. Pui CH, Kalwinsky DK, Schell MJ, Mason CA, Mirro J, Dahl GV. Acute nonlymphoblastic leukemia in infants: clinical presentation and outcome. *J Clin Oncol* 1988;6:1008-1013.
6. Resnick KS, Brod BB. Leukemia Cutis in Congenital leukemia: Analysis and review of the world literature with report of an additional case. *Arch Dermatol* 1993;129:1301-1306.
7. Badhe PB, Sane SY. Congenital leukemia - Organ involvement in six autopsy cases. *J Postgrad Med* 1992;38:127.
8. Felix CA, Lange BJ. Leukemia in infants. *Oncologist* 1999;4:225-240.
9. Zipursky A. Transient leukaemia-a benign form of leukaemia in newborn infants with trisomy 21. *Br J Hematol* 2003;120:930-938.
10. Bresters D, Reus AC, Veerman AJ et al. Congenital leukaemia-the Dutch experience and review of the literature. *Br J Hematol* 2002;117:513-524.
11. Isaacs H Jr. Fetal and neonatal leukemia. *J Pediatr Hematol Oncol* 2003;25:348-361.
12. Bader-Meunier B, Tchernia G, Mielot F et al. Occurrence of myeloproliferative disorder in patients with Noonan syndrome. *J Pediatr* 1997;130:885-889.

