Congenital Leukemia : A Case Report

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Abstract

A 5 week-old infant presented with fever and pallor for two weeks, reluctant to feed for one week and passage of bloody stool one time two days back. Child was found less active and severly anaemic with hepato-splenomegaly. Peripheral blood film showed marked leukocytosis with many immature cells which are mostly blast cell resembling lymphoblast containing one-two nucleoli. Bone marrow aspiration revealed findings suggestive of acute lymphoblastic leukemia. Other possibilities like neonatal sepsis and TORCH infection were ruled out and a final diagnosis of congenital leukaemia was made.

CBMJ 2015 July: Vol. 04 No. 02 P: 55-57

Key words: Acute lymphoblastic leukemia, Congenital.

Introduction

Congenital leukemia is a rare condition that is diagnosed from birth to 6 weeks of life[1] Only a few cases of congenital leukemia have been reported so far. It occurs at the rate of 1 per 5 million births. Reaman et al[2] reported that only 2 of the 115 cases entered on children cancer group had congenital leukemia. Furthermore they observed that 18% of all children of acute nonlymphocytic leukemia and 3% of all children with acute lymphoblastic leukemia were below 1 year of age. Most of neonatal cases reported so far have acute non-lymphocytic leukemia, in contrast to the predominance of acute lymphoblastic leukemia found in children. Instances of familial neonatal leukemia are also extremely rare[3].

Congenital leukemia is characterized by non-specific symptoms requiring a high index of suspicion for further investigations and diagnosis. We report here a rare case of congenital lymphoblastic leukemia in a five-week-old infant.

Case report

A 5 week-old infant of low socioeconomic status presented with fever for 2 weeks, which was high grade, continuous in nature not associated with convulsion, and pallor of his whole body for same duration, which was gradually increasing day by day and also complaints of reluctant to feed for 1 week and passage of bloody stool 1 time 2 days back.

There was no history of jaundice or serosanguinous discharge from the nose. Special emphasis was given to elicit the history of maternal fever, premature rupture of membrane, rash or lymphadenopathy in the mother in the first trimester to rule out the TORCH (T=toxoplasma, O=others, likevaricella, hepatitis-B, malaria etc., R=rubella, C=cytomegalovirus, H=herpes

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simplex virus) infections and other bacterial infection. There was no history of abortion or still birth and no history suggestive of syphilis in the parents. The baby was born full term, with average birth weight, not yet vaccinated.

Child was severely pale,febrile, tachypneic, and manifested with hepato-splenomegaly. Liver was palpable 4 cm below costal margin, firm in consistency. Spleen was also palpable 2.5 cm from the left costal margin. There was no micro-cephaly, cataract, jaundice, lymphadeno-pathy, skin bleeds, moist lesions in the mucocutaneous areas of mouth, anus and external genitalia or pseudo paralysis, Fundoscopy was essentially normal with no evidence of chorioretinites.

Laboratory investigations on admission revealed hemoglobin of 6.4 g/dl and total leukocyte count of 44,000/mm^3 with 65% lymphoblasts, 5% neutrophils and 30% lymphocytes. The platelet count was 60,000/mm^3. Peripheral blood film showed marked leukocytosis with many immature cells which are mostly blast cell resembling lymphoblast, platelets were reduced. Septic screening and blood culture both was negative.IgM of TORCH was also negative. Bone marrow aspiration revealed findings suggestive of acute lymphoblastic leukemia. The smear was hypercellular with diffuse infiltration of immature cells of lymphoid series (lymphoblasts). These cells were big rounded with moderate cytoplasm and 1 or 2 prominent nucleoli. Myeloid and erythroid series of cells were reduced in number. Erythropoiesis was normoblastic.and reduced. Megakaryocytes were also reduced.

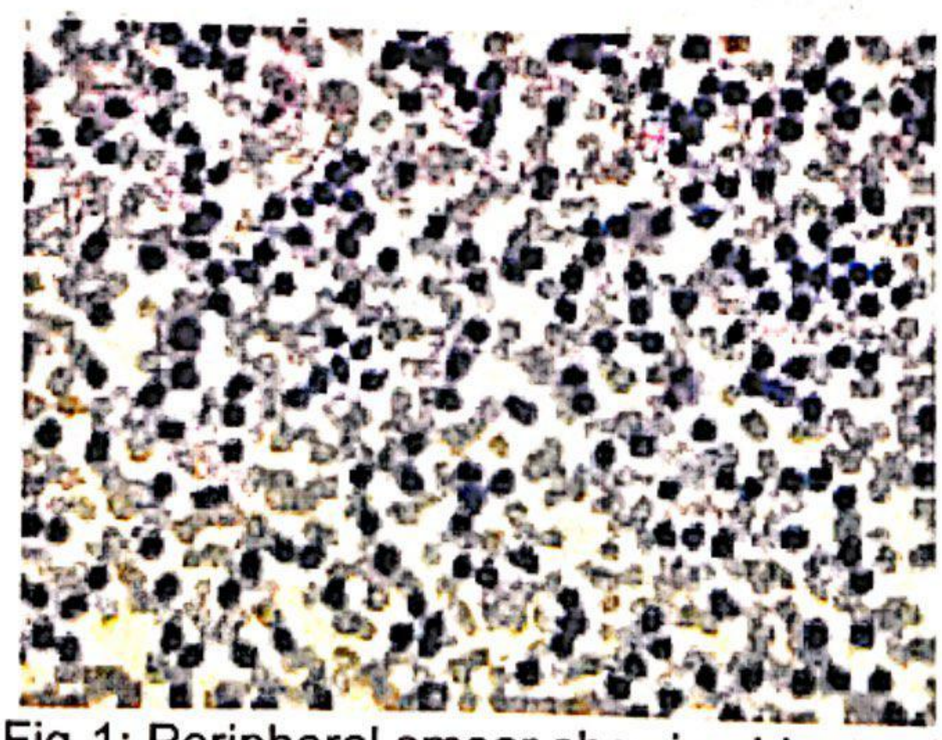

Fig-1: Peripheral smear showing blast cell.

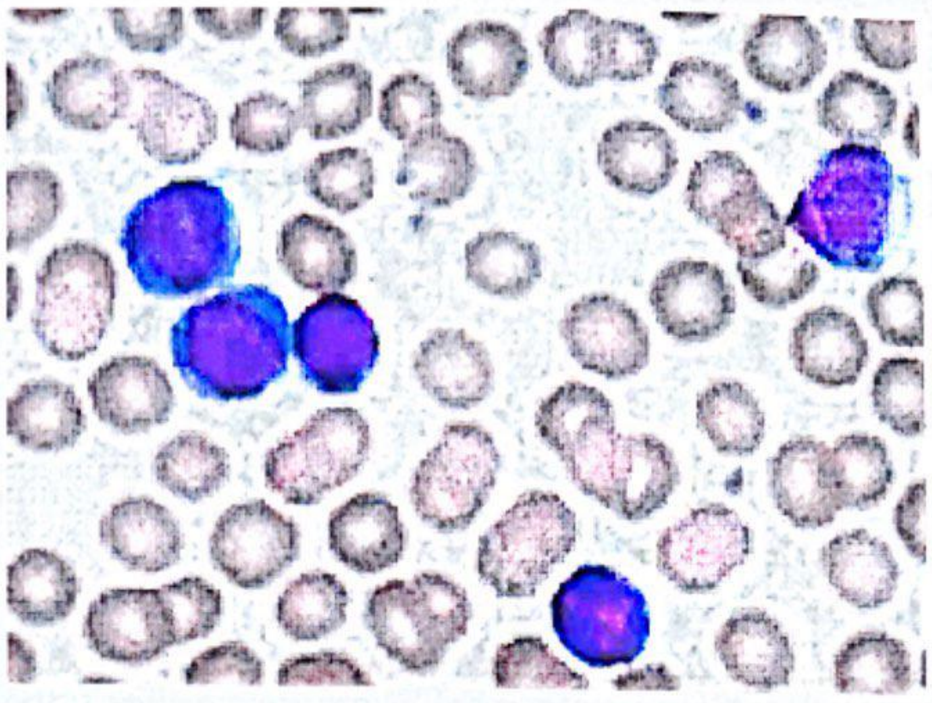

Fig-2: Bone Marrow aspirate showing Blasts and Neutrophils.

Cerebrospinal fluid cytopathology revealed infiltration by few rounded cells (72 cells/cu mm) showing dark nucleus and prominent nucleoli suggestive of leukemic infiltration. Specific tests to rule out congenital infections, namely TORCH, WR(Wassermann reaction), and VDRL(venereal disease research laboratory) were within normal limits. Urine culture and sensitivity was normal. X-ray skull did not reveal any calcification.Malaria and Kala-azar were ruled out by immunochromatographic tests.

Discussion

Congenital leukemia is a very rare disorder [2]. Only 200 reports of congenital leukemia are published in literature[4]. The majority are Non-Lymphocytic type (80%), while acute lymphoblastic leukemia (ALL) comprises only < 20%. Familial neonatal leukemia is extremely rare and no child born to a mother with leukemia has been found to have the disease during the neonatal period[3]. Congenital leukemia is occasionally associated with number of congenital anomalies and with chromosomal disorders such as Down's syndrome, Edward's and Patau's syndrome and a number of nonspecific chromosomal abnormalities. Subtle cytogenetic abnormalities may occur more commonly in the affected infants and their parents, when studied with newer cytogenetic techniques[5].

The clinical signs of leukemia may be evident at birth with hepatosplenomegaly, petechiae and ecchymosis. Leukemic cell infiltration into the skin (leukemia cutis) is commonly found[5]. In infants in whom the disease develops within the first month (not at birth), the symptoms are ill defined with low-grade fever, diarrhea, hepatomegaly and failure to gain weight. Leukemia cutis is less common[5].

Clinically, it is important to differentiate congenital leukemia from other leukoerythroblastic conditions, which are seen in response to bacterial infection, hypoxemia and severe hemolysis in the neonate[6]. Other differential diagnosis includes congenital syphilis, intrauterine viral disease, neuroblastoma and the transient myeloproliferation syndrome associated with Down's syndrome[7, 8, 9].

Cellular morphology, immunophenotype and chromosomal studies differentiate acute lymphoblastic from acute non lymphoblastic leukemia found in newborns[6]. FAB classification based on cell morphology reveals that the most common subtype in infantile and neonatal acute nonlymphocytic leukemia is the monocytic variety[10, 11]. The most common locus involved in translocation in infantile acute lymphoblastic leukemia is at 11q 23 – this is involved in at least 50% of infant leukemias and in many neonatal cases[12].

The course of congenital leukemia is one of rapid deterioration and death from hemorrhage and infection. Specifically, it is a more aggressive disease with increased incidence of leukocytosis, massive hepatosplenomegaly, CNS involvement, thrombocytopenia, hypo-gammaglobenimia, disseminated intravascular coagulopathy and less frequent remission induction by 14 days[13]. The current improved success of remission induction with treatment of acute non-lymphocytic leukemia in infants younger than 1 year is similar to that in older children using combination chemotherapy. However, the experience with newborns is limited, but between 1984 to 1989, 5 of 12 newborns with acute non-lymphocytic leukemia sustained complete remission with chemotherapy, and all were in the myelomonocytic or monocytic category[10, 12]. However, in acute lymphoblastic leukemia, the treatment outcome is significantly poorer in infants younger than 1 year at diagnosis (23% disease-free survival compared with 70% for older children) and may be even lower in newborns. Only 10 to 20% survival for infants younger than 6 months of age at diagnosis has been reported as compared to 40% for those, older than 6 months[13, 14]. Fewer than 15% of newborns with acute lymphoblastic leukemia have remission lasting more than few months.

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