Congenital Leukemia: A Case Report

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Introduction

Leukemia is rare during the first month of life. The majority of reported cases have acute nonlymphoblastic leukemia. Congenital leukemia is occasionally associated with a number of congenital anomalies and chromosomal disorders. The course of congenital leukemia usually results in rapid deterioration and death from hemorrhage or infection.

Here, we report a case of congenital acute lymphoblastic leukemia (ALL) in a one-day-old boy with trisomy 21 mosaicism and spontaneous complete remission.

Case Report

A newborn boy was admitted with respiratory distress and grunting begun since a few moments after birth. He was born full-term, by cesarian section due to breech position, from a 32-year-old healthy mother with no significant finding in her past medical history. Parents were unrelated, and there was no history of cancer within their family. Physical examination revealed a normal-looking boy, without any apparent anomalies, with normal weight, height, and head circumference of 3.57 Kg, 51 cm, and 35.5 cm, respectively. He had tachypnea and rales in the chest. Sepsis workup was done and appropriate antibiotics were given. Laboratory investigations on the first day of admission revealed total leukocyte count of 77200/mm^3 with 63% lymphoblasts, 12% neutrophils, and 24% lymphocytes, hemoglobin 10.7 g/dl, and platelet count of 106000/mm^3. On the third day of admission, respiratory distress became better but a generalized maculopapular rash was developed which eventually disappeared at the end of the tenth day. On the fifth day his liver and spleen began to enlarge and both reached the maximum size of about 4 cm below costal margins. Due to a further drop in hemoglobin level, packed red cell transfusion was given. TORCH study was performed with negative results. Blood culture was negative. Bone marrow aspiration was done and it was hypercellular with a marked predominance of immature cells of lymphoid series. According to French–American-British classification (FAB), ALL L2 was diagnosed. Marrow specimen was sent for immunophenotyping and chromosomal studies. Immunophenotyping revealed CD10:40.9%, CD19:44.8%, CD20:38%, and HLA-DR: 55.9%. Bone marrow immunophenotyping was consistent with Pre-B ALL. In chromosomal analysis, 22 metaphase spreads were studied on the basis of GTG technique at 350-400 band resolution. In 10 spreads, 47 chromosomes with an additional chromosome 21 was detected. The remaining 12 spreads revealed normal 46XY pattern. Hence the mosaicism of 47XY,+21/46,XY existed.

After confirmation of the diagnosis of ALL, as there was some improvement in patient situation and the parents were unwilling to start chemother-

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apy, we decided to wait and watch. Fortunately, his hepatosplenomegaly gradually regressed without any treatment, leukocytosis diminished, percentage of lymphoblasts decreased, and hemoglobin levels and platelet count gradually increased. At four months of age the child became normal in every aspect. He is now an 18-month-old completely normal child.

Discussion

Congenital leukemia is a rare malignancy (fewer than 5 cases per 1 million live births) diagnosed during the 1st month of life. Most of the reported neonatal cases had acute nonlymphoblastic leukemia, while acute lymphoblastic leukemia (ALL) constitutes 20% of cases,[1] in contrast to predominance of ALL found in later childhood. Congenital leukemia is occasionally associated with a number of congenital anomalies (heart defects, gastrointestinal tract anomalies, mental delays) and chromosomal disorders such as Down syndrome (DS), trisomies D and E, and a number of nonspecific chromosomal abnormalities. Clinical signs of leukemia may be evident at birth with hepatosplenomegaly, petechiae, ecchymosis, and leukemic cell infiltration into the skin (leukemic cutis) which results in nodular fibroma-like masses with blue or gray discoloration of the overlying skin. At birth, many patints have respiratory distress due to either leukemic infiltration in lungs or atelectasis. In those infants in whom signs of disease develop within the first month, symptoms are often ill-defined including low -grade fever, diarrhea, hepatosplenomegaly, and failure to gain weight. Severe leukemoid reaction, infections such as congenital HIV, syphilis, cytomegalovirus, toxoplasmosis, bacterial septicemia, severe erythroblastosis fetalis and congenital neuroblastoma can be confused with congenital leukemia.

Chromosomal abnormalities in leukemic cells have gained increased importance in subclassification and prognosis. A number of chromosomal translocations and deletions have been found to carry an unfavorable prognosis, such as t(4;11). In infantile leukemia, rearrangements of the MLL gene on chromosome 11q23 are the most common genetic abnormalities in both ALL and AML occurring in 70-80% and approximately 60% of patients, respectively.[2] Rare congenital forms of lymphoid or myeloid leukemia manifested at birth or during the first month of life carry a dismal prognosis especially when an MLL/11q23 rearrangement is present. Such cases should be carefully distinguished by chromosomal/molecular analysis and cell culture techniques from transient myeloproliferative disorders which require only supportive care and closed follow-up for subsequent development of leukemia.[2]

Transient myeloproliferative disorder (TMD) is an uncommon syndrome strongly associated with abnormalities of chromosome 21 occurring in 10% of infants with Down syndrome. These infants may later develop acute megakaryocytic leukemia.[3] Transient blast proliferation occurs most frequently at neonatal age and usually resolves spontaneously in two or three months.[4] TMD has some clinical and laboratory features that make it unique and distinguishable from true congenital leukemia with which it may be initially mistaken. It usually has a benign course followed by a favorable outcome. As trisomy 21 mosaicism may not have overt phenotypic stigmata, many patients of TMD may have a silent, non-detected course in these children.[4] Due to the difficulties in the differential diagnosis of TMD and true AML, it is recommended to delay specific cytostatic therapy in neonates with Down's syndrome until definite progression of the leukemic process is observed or cytogenetic analysis suggesting true AML is available.[5]

However, there is a distinction between congenital +21 (Down syndrome) and acquired +21. Acquired +21 is the most frequent aneuploidy observed in both adult and childhood ALL. Its overall incidence is about 15%. As the sole clonal abnormality (except DS patients), +21 accounts for 2% of pediatric and less than 1% of adult ALL cases. In childhood ALL, the incidence of +21 in 47-50 chromosomes and in more than 50 chromosomes ploidy groups is approximately 40% and 80%, respectively. If +21 is the only abnormality found in the patient, it has a favorable prognosis.[6]

In this report, we described a rare case of trisomy 21 mosaicism with congenital ALL –L2, Pre –B immunophenotyping whose disease resolved spontaneously.

In conclusion, patients with congenital leukemia are quite different in the way they present, their clinical behavior, chromosomal abnormalities, and the immunophenotyping characteristics. Further studies are needed to clarify the nature of this very

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rare form of leukemia.

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