# Ectrodactyly with Infant Acute Lymphoblastic Leukemia Associated With Very Rare translocation of t (5; 15) (p15; q11.2) : A case report

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**Abstract**

Infant leukemias are rare in childhood leukemias and have poor prognostic features. Most infant leukemias are presented with MLL rearrangement at diagnosis. t (5; 15) has been reported very rarely in infant leukemias. In addition, the relationship between congenital anomalies and leukemia is controversial. Here we report a case with t (5; 15) (p15; q11.2) infant leukemia and ectrodactyly.

## Introduction

Infants account for 2-5% and 6-14% of childhood acute lymphoblastic leukemias and acute myeloid leukemias, respectively (1). Patients in this group are characterized by hyperleukocytosis, hepatosplenomegaly, absence of CD 10 expression in the blasts, MLL rearrangement, and central nerve system involvement. The findings of extramedullary invasion may be the first symptom without any abnormality in peripheral blood. These features are associated with poor prognosis and treatment success is low despite intensive chemotherapy (2-4). MLL (11q23) rearrangement is present in 66% of infant acute lymphoblastic leukemia (ALL)s and 35% of acute myeloid leukemia (AML)s . Among infant leukemias with t(4; 11) event-free survival of ALL are lower than that of AMLs (5). Besides, clinical features change according to the opposite chromosome where MLL is translocated. Since it is the most common genetic feature, studies on infant leukemia focus on MLL rearrangements. Rare translocations are also seen in infant leukemias. t (5; 15) which is very rare has been reported in 7 infant ALL cases (4,6). In addition, various anomalies have been reported in infant leukemias. However, the relationship of these anomalies with leukemia is uncertain (7). Here we report a case with t (5; 15) (p15; q11.2) infant leukemia and ectrodactyly.

## Case Report

A 5.5-month-old girl admitted to our hospital with swelling on the cheek. Her physical examination revealed that she had ectrodactyly on right hand (Figure 1). She was tachypneic. She had splenomegaly (2 cm bellow coastal margin) and umbilical hernia with abdominal distention. Routine blood test results revealed anemic hemoglobin level of 5.9 g/dl, increased leukocyte count 26 570 /mm3 and platelet count of 104 000/mm3 with peripheral blasts. In addition LDH level increaesed to 1126 U/L, liver function and renal funtion tests were in normal range. Echocardiographic and chest radiography findings were normal. Right forearm radiography showed 2-4th phalangial bone aplasia (Figure 1). Abdominal sonography revealed two fold enlarged kidney.

Bone marrow examination revealed 52 % L1 type lymphoblasts, which had high positivity for CD 19, CD22, CD38, cyM, cy TDT, cy 79a ve HLA DR. Only 12% of blasts were dim and other blasts were negative for CD10. She hadn't central nervous system infiltration. Chemotherapy was started according to BFM İnterfant -2006. She had a good prednisolon response and minimal residual disease at day 15 of induction therapy showed low risk. Bone marrow aspiration at the end of the induction therapy complete remission was achieved with no blast. At the same time her kidney dimensions at sonography revert to normal. She has continued to consolidiation therapy according to the BFM interfant 2006 protocol.

**Chromosome, Fluorescence In Situ Hybridization and Molecular Analysis**

Bone marrow samples was obtained for routine cytogenetic and molecular analysis. Commercially avaliable routine reverse transcriptase polymerase chain reaction (RT-PCR) and flourescence in situ hybridiziation (FISH) panels were used prognostic classification. Reccurent genetic abnormalities for acute leukemia including t (4:11), t (9:22) and t (12:21) were negative. Convantional cytogenetic analysis was performed from over night colchisine exposed cell cultures. 46,XX, t(5;15)(p15;q11.2)[3]/46,XX[17] karyotype was found in the analysis (Figure 2). After that results, chromosome analysis was performed from peripheral blood samples to exclude constitutional changes. The result was normal. The bone marrow cytogenetic result revealed as a rare and somatic abberation.

**Discussion**

Because of genetic features and clinical characteristics infant leukemias are different from other childhood leukemias. Median duration of event free survival is 11 months(4). It is well known that hyperleukocytosis and MLL rearrangement in infant leukemia are associated with poor prognosis (1). Unlike these features of infant leukemias this patient didn't presented with hyperleukoctosis and she hadn't MLL rearrangement. In this case who had a good prednisolone response, t (5; 15) (p15;q11.2) was detected in cytogenetic analysis.

t(5; 15) was first reported in three infant ALL in 1987 (4,8). Seven infant ALL and only two childhood ALL patients with t (5; 15) (p15; q11-13) was reported until 2014 (6,9,10). On the basis of these data it was speculated that this chromosomal abnormality was characteristics of infant ALL and related with good prognosis(6).

Although CD10 weak positivity (6) is noteworthy in cases with t(5; 15) complete remission was achieved with induction therapy. Also event free survival of cases with t (5; 15) was better than those with MLL rearrangement (9). On the other hand 45-month-old girl reported by Kwon et al. had a good prednisolon response and achieved complete remission with induction therapy (10).

The 21-month-old boy reported by Lee et al. achieved remission 3 months after start of chemotherapy. However, Lee et al. reported that t (5; 15) was detected in cytogenetic analysis during relapse and they stated that it would be find positive at diagnosis if cytogenetic analysis was performed (9). If it can be detected before morphological relapse, it will be useful for the follow-up of patients. However infant leukemias with t(5; 15) and their clinical outcomes need to be reported.

On the other hand while hyperleukocytosis was detected in two of the cases, other two cases were not known. The remaining patients with t(5; 15) did not have hyperleukocytosis reported so far (6,9,10), like our patient. Extramedullary infiltration was reported only one of these patients. We thought that renal enlargement was related with extramedullary infiltration because her kidney shrunk in normal size with induction therapy.

Translocations such as t(9:22), t(1; 19), t(12; 21) known to be associated with leukemias and can be detected using RT-PCR and FISH. But cytogentic analysis still significant at the time of leukemia diagnosis. If we didn't perform cytogenetic analysis on bone marrow sample at diagnosis we couldn't catch t(5;15) in this case. On the other hand cytogenetic analysis not always available. For instance Heerema and et al who reported first three infant ALL cases with t(5;15) could obtain 39 cytogenetic analyses of 100 infant ALL in their study (4).

In addition, our patient had an ectrodactyly on her right hand (Figure 1). Split-hand / split-foot malforma-

tion (SHFM) defined ectrodactyly is seen once in 90,000 live births. Although it shows autosomal dominant inheritance autosomal recessive inheritenace has been reported. It is generally sporadic but it may be familial. There are syndactyly and aplasia in the phalanges with midline cleft in hand. There was no ectrodactyly in our patient's family member. SHFM is a heterogeneous condition caused by genetic abnormalities. Thus classified according to genetic defect and association with cleft palate-lip anomaly, hearing loss and fallot tetralogy (12-14). Our patient had 'isolated' ectrodactyly. Besides, ALL cases with t(5; 15) with ectrodactyly have not been reported yet.

Among the childhood malignancies, congenital anomalies are most common in leukemias. These anomalies include cleft palate, spina bifida, rib anomalies and birthmarks(15). It is suggested that rib anomalies may be associated with childhood leukemias (16). However the relationship between a specific congenital anomaly and leukemias is not known except Down Syndrome. Those with congenital anomalies were reported to have more cancer diagnoses in infancy than those without(17).

In conclusion, the case of infant leukemia reported here is the first case who had ectrodactyly with t (5:15). We consider that the clinical features, response to treatment and concomitant congenital anomaly of this case contribute to knowledge about infant leukemias.

Authors have no conflict of interest to declare.

ETHICS STATEMENT: Parents of patient have permitted with signature to publish their children's photos.

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**Figure 1. A.B**. Photos and **C** radiograph of patient showing ectrodactyly on right hand.

**Figure 2.** Patient's karyotype analysis of bone marrow at diagnosis: 46,XX, t(5;15)(p15;q11.2)[3]/46,XX[17]

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