A childhood acute lymphoblastic leukemia (ALL) case with t(3;17)(q23;p13),t(5;12)(q31;p13),inv(11)(p15q12)

t(3;17)(q23;p13),t(5;12)(q31;p13),inv(11)(p15q12) 'li bir çocukluk çağı akut lenfoblastik lösemi (ALL) olgusu

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Abstract

It is known that clonal chromosomal changes in childhood ALL are nonrandom and important markers for diagnosis, prognosis and relaps. In this report we present 4 year-old boy with ALL-L1 who has complex chromosomal rearrangements. Chromosome analysis was performed on bone marrow aspiration sample in relaps after one year from diagnosis and induction chemotherapy. The karyotype was; 46,XY,t(3;17)(q23;p13),t(5;12)(q31;p13),inv(11)(p15q12) [11]/46,XY[8]

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Özet

Çocukluk çağında görülen ALL'de, klonal kromozom değişimlerinin rasgele olmadığı ve tanı, prognoz ve nüks için önemli belirteçler olduğu bilinmektedir. Bu bildiride, kompleks kromozom anomalileri gözlenen ALL-L1'li 4 yaşında bir erkek olgu sunulmaktadır. Kromozom analizi, tanıdan ve indüksiyon kemoterapisinden bir yıl sonra meydana gelen nüks evresinde gerçekleştirilmiş ve 46,XY,t(3;17)(q23;p13),t(5;12)(q31;p13),inv(11)(p15q12) [11]/46,XY[8] karyotipi bulunmuştur.

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Anahtar kelimeler: ALL, kromozom anomalileri, sitogenetik, translokasyon.

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Introduction

Clonal chromosome abnormalities are frequently seen in childhood ALL cases and supply important data about the origin and progression of the disease. Although these chromosomal abnormalities are highly variable, they are not random.

We report a 4 year old ALL-L1 relaps case with a complex karyotype.

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Materials and Methods

Case

Four-year-old male patient (A.I.) was referred to our hospital complaining of fatigue, and fever. On arrival he was found to have the same history for one-month, for which he was only followed up and referred to our hospital as he did not get any better in time. His past medical history was non-revealing otherwise. Physical examination was within normal limits except for the massive lymphadenopathy and massive hepatosplenomegaly. His complete blood count on arrival revealed hemoglobin 9.4 gr/dL, white blood cell count (WBC) 214 900 cell/mm^3 and platelets 108 000/mm^3, with a peripheral smear showing 90% blasts. A diagnosis of T-cell acute lymphoblastic lymphoma (ALL) was made on bone marrow aspiration based on morphology and cytochemistry and flow cytometry. Cerebrospinal fluid (CSF) cytology was also found positive for blasts. As he had high WBC on arrival, he was put on Children's Cancer Group 1961 Poor Prognosis ALL chemotherapy protocol. He responded well to induction chemotherapy. But on the first year in his chemotherapy, he was found to have medullary relapse (T cell ALL) in the routine bone marrow examination after the late intensification block. The relaps had the same morphological, immunhistochemical and flow cytometry features as the initial diagnosis. A relapsed bone marrow specimen was sent to the cytogenetic laboratory for cytogenetic analysis. The patient was put on Children's Cancer Group 1961 Relapse ALL chemotherapy protocol. The patient was put on te 2nd induction phase, as he was found to have 20% of blasts in the bone marrow and no blasts in CSF after the first one. A week after the 2nd induction phase the patient was admitted with a resistant status epilepticus. The aetiology of status epilepticus was thought to be due to chemotherapy toxicity, as all investigations remained unrevealing. Although the convulsions were under control with anesthesia, the patient expired as a result of adult respiratory distress syndrome on his 9th respirator day.

Cytogenetics

ONC (Overnight Cochicine) and 24h. culture technique were applied to the bone marrow aspiration specimen in the relaps stage. 20 metaphases were examined with GTL (G-bands by trypsin using Leshmann) banding technique. Chromosome abnormalities were designated and described according to the ISCN (An International System for Human Cytogenetic Nomenclature) 2005 [1].

Results

Twenty metaphases were examined. There was a near-tetraploid metaphase. Karyotype derived from 19 cells is:46,XY,t(3;17)(q23;p13),t(5;12)(q31;p13),inv(11)(p15q12)[11]/46,XY[8] (Figure 1).

Discussion

In our search of literature, we found some t(3;17) findings that have different breakpoints than in our case [2, 3]. It's been known that p53 tumor suppressor gene had been localized in 17p13 which is one of the breakpoints of the t(3;17)(q23;p13) finding of our case [4, 5]. t(5;12)(q31-33;p12-13) anomalies are nonrandom chromosome abnormalities in myeloproliferative disorders (MPD) [5-9].

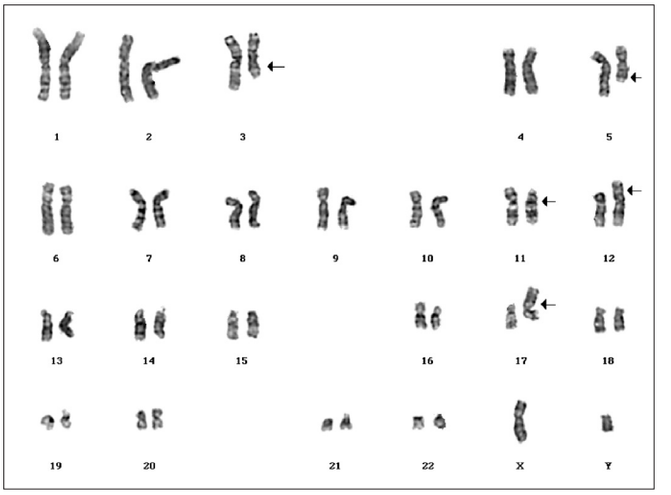

Figure 1. An exemplary karyotype of the case. Abnormal chromosomes are indicated by arrows.

ETV6 (TEL) gene is a transcription factor gene which lies on 12p13 and frequently involved in rearrangements with different chromosomes in ACS2 hematological malignancies. Yagasaki et al reported that a long fatty acyl CoA synthetase 2 gene, located in 5q31, was an ETV6 (TEL) fusion partner gene in a recurrent t(5;12)(q31;p13) in a myelodysplatic syndrome (MDS) and two acute myelogenous leukemia (AML) patients [10]. ETV6 (TEL) gene is also fused with PDGFbR on 5q33 in MDS and MPD [7, 11-12].

It has been reported that the t(5;12)(q31;p13) had been observed with IL3 and ETV6 involvements in an ALL cell line. IL3 gene, which was localized on 5q31, is a multipotent haemopoietic growth factor gene [5, 13].

Apart from chromosome 5, ETV6 has also been found to fuse with other genes in different chromosomes like AML1 in acute lymphoblastic leukemia (ALL), with ABL or JAK2 in early pre-B-cell ALL, with MN1 in MPD, with MDS1/EVI1 in MPD, and with STL in a B-cell ALL cell line [7].

Although ETV6 (TEL) is very frequently involved in rearrangements in hematological malignancies, it is not the only gene that goes into the chromosomal abnormalities in this region. Sato et al reported that ETV6 (TEL) is involved only one half of the balanced rearrangements with band 12p13 in hematological malignancies [11].

So far, t(5;12)(q31;p13) has been observed mostly in MPDs [10, 14]. In only one ALL cell line this finding has been reported [5]. As far as we know, ours is the first case that t(5;12)(q31;p13) found in bone marrow.

Although we could not find the inv 11 (p15q12) in hematological malignancies in our search of literature, a number of recurring aberrations involving different breakpoints of chromosome 11 in hematological malignancies had been reported [4, 5, 15]. The inv(11) (p15q22) is a recurrent chromosomal abnormality associated with de novo and therapy-related myeloid malignancies [16, 17] which shares the

11p15 breakpoint with our case. The NUP98 gene, which is located in 11p15, fuses with a number of genes from different chromosomes in usually acute leukemias [5, 16]. And there is a gene named RELA that its rearrangements were seen in lymphoid tumors, at 11q12-13.

Since the bone marrow sample for cytogenetic examination had been taken in relaps stage of the diseases, we were unable to understand if this complex karyotype was present in the time of the diagnosis or if these abnormalities were primary or secondary changes.

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