A Special Chromosome Imbalance "Jumping translocation of 1q" in Burkitt Lymphoma

Bir Burkitt Lenfoma Olgusunda Kromozom 1q'nun "Jumping Translokasyonu"

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ABSTRACT

Chromosome 1q gain that confers clonal expansion advantage to tumor cells has been reported in many solid tissue and hematological cancers, in many different forms; sometimes as a derivative chromosome, as isochromosome, or less frequently, due to an imbalance created by a jumping translocation. Although it is known that chromosome 1q gain provide the advantage of clonal expansion to the tumor cells and is relatively common in Burkitt lymphoma/leukemia, its detection in the form of jumping translocation is extraordinarily rare and results of JT containing 1q are controversial. Bone marrow cytogenetic examination performed on a case diagnosed with stage 4 Burkitt lymphoma/leukemia resulted in 46,XY,dup(1)(q21q42),t(8;14)(q24;q32)[5]/46,XY,der(6)t(1;6)(q21;q27),t(8;14)(q24;q32)[4]/46,XY,t(8;14)(q24;q32), der(11)t(1;11)(q21;q23)[2]/46,XY[3]. We present the clinical features of the case that was found to have 1q gain in the jumping translocation form to contribute to the literature.

Key words: Burkitt's Leukemia, Burkitt's Lymphoma, Bone Marrow, Cytogenetic Abnormalities, Translocation, Chromosomal

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ÖZET

Kromozom 1'in q kolunu içeren artışlar, birçok solid doku ve hematolojik kanserde; derivatif kromozom, izokromozom veya nadiren jumping translokasyon gibi farklı formlarda rapor edilmiştir. Kromozom 1q artışının tümör hücrelerine klonal genişleme avantajı sağladığı ve Burkitt lenfoma/lösemide görece sık olduğu bilinmesine rağmen jumping translokasyon formunda saptanması son derece nadirdir ve klinik sonuçları tartışmalıdır. Merkezimizde evre 4 Burkitt lenfoma/lösemi tanısı alan bir olguya yapılan kemik iliği sitogenetik çalışması 46,XY,dup(1)(q21q42),t(8;14)(q24;q32)[5]/46,XY,der(6)t(1;6)(q21;q27),t(8;14)(q24;q32)[4]/46,XY,t(8;14)(q24;q32),der(11)t(1;11)(q21;q23)[2]/46,XY[3] şeklinde sonuçlanmıştır. Jumping translokasyon formunda 1q kazancına sahip olduğu anlaşılan olgumuzun klinik özelliklerini literatüre katkı sağlaması amacıyla sunuyoruz.

Anahtar Sözcükler Burkitt Lösemisi, Burkitt'in Lenfoması, Kemik iliği, Sitogenetik anormallikler, Translokasyon, Kromozomal

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INTRODUCTION

Chromosome 1q gain has been reported in many solid tissue and hematological cancers, in many different forms; sometimes as a derivative chromosome, as isochromosome, or less frequently, due to an imbalance created by a jumping translocation (JT) (1,2). JT; defines a cytogenetic anomaly in which a donor chromosome segment is transferred to more than one different receptor chromosomes (3). 1q gain is observed in 25% of Burkitt lymphoma/leukemia (BL/L) but detection in JT form is extraordinarily rare and it's predictive value is unclear in BL/L (4,5). In this report, underlying mechanisms and clinical features of jumping 1q translocation are investigated in a case of central nervous system-negative advanced-stage BL/L.

CASE REPORT

An 11-year-old male patient was referred due to weakness, molar teeth mobility and subfebrile fever for a week. Physical examination revealed a gingival hypertrophy and right testicular swelling. The white blood cell(WBC) count was 11180/L, platelets count was 118000/L. Uric acid(12 mg/dl) and lactate dehydrogenase (>1800 IU) levels were high. Left shift and blast cells (4%) were seen in the peripheral smear. Bone marrow (BM) aspirate and biopsy sections were hypercellular and infiltrated with 55% of blasts having vacuolated basophilic cytoplasm, and nucleus with 3–4 nucleoli (L3 cytomorphology).Blast immunophenotype was compatible with mature B cell (CD10, CD19, CD20, CD22, CD45, CD79A and cy-IgM antigen expression). Imaging showed hepatosplenomegaly, tumoral infiltration in the mandible and bilateral testicles. Tumor cells taken from bone marrow were evaluated by G-banding and fluorescence in situ hybridization (FISH). Cytogenetic analysis showed three different clones consisting of chromosome 1q partial duplication and unbalanced translocations between 1q and chromosomes 6 and 11 (Figure 1 and 2). Cytogenetic result was: 46,XY,dup(1)(q21q42),t(8;14)(q24;q32)[5]/46,XY,der(6)t(1;6)(q21;q27),t(8;14)(q24;q32)[4]/46,XY,t(8;14)(q24; q32),der(11)t(1;11)(q21;q23)[2]/46,XY[3]. JT comprising chromosome 1q was confirmed with FISH analysis using the whole chromosome staining probe (Figure 3). Additionally, t(8;14)(q24;q32) was defined in all clones and confirmed by two fusion signals in 15% of 200 interphase cells analyzed with IGH/MYC translocation, dual fusion probe. Using the St. Jude staging system, stage 4 BL/L diagnosis was made. The patient was treated with the Non-Hodgkin lymphoma (NHL)-Berlin-Frankfurt-Munster (BFM) 2012 based therapy protocol and achieved a hematologic and cytogenetic remission. During two-year follow-up, there was no relapse.

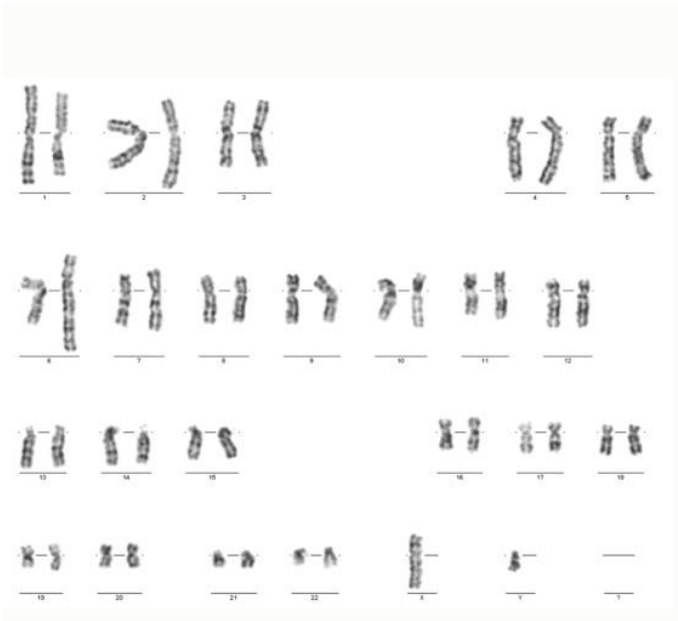

Figure 1: Karyotype analysis reveals the presence of 46,XY, der(6)t(1;6)(q21;q27), t(8;14))(q24;q32)

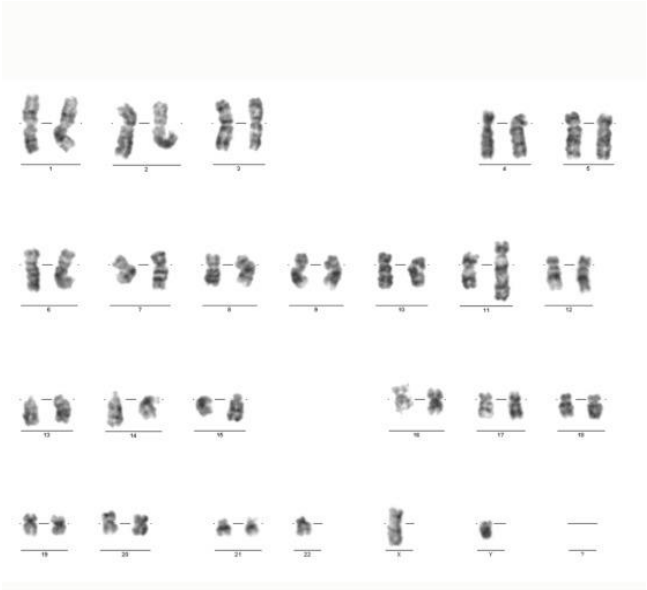

Figure 2: Karyotype analysis reveals the presence of 46,XY,t(8;14)(q24;q32),der(11)t(1;11)(q21;q23)

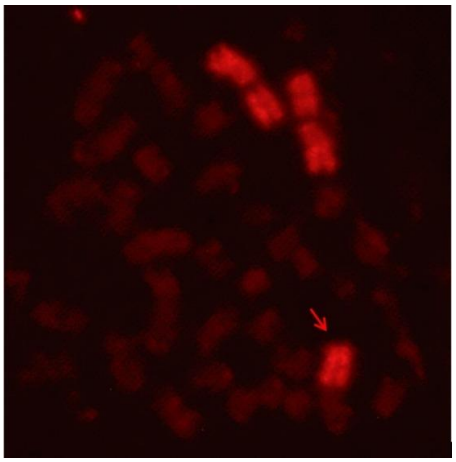

Figure 3: FISH analysis using Whole Chromosome 1 Painting probe (CytoCell). Arrow indicate 1q gain in 100x magnification.

DISCUSSION

In BL/L 1q gains are relatively frequent but occur in JT form as in our case is unusual and clinical consequences of jumping 1q still not well understood (5). Another point, the patient has higher percentage of t(8;14)(q24;q32) in the cytogenetic study than FISH. Due to proliferation of malignant cell line during 72 hours of culture, chromosomal abnormalities may be more in slides prepared with cytogenetic methodologies compared to uncultured interphase cells (6).

Researchers have shown that 1q gains provide the advantage of clonal expansion to the tumor cells (7). Altough controversial in BL/L, JT in myeloid neoplasms has been associated with treatment resistance and poor prognosis (4, 8). It has been suggested that the initiating event of JT of 1q is pericentromeric heterochromatin (PCH) decondensation induced by hypomethylation (2). PCH organization is crucial to centromere function and preservation of genome integrity (9). Hypomethylation induced in the centromeric and juxtacentromeric satellite DNA sequences of chromosome 1 by the effect of various oncogenic factors (ionizing radiation,cytotoxic drugs,viruses, immunodeficieny) causes decondensation in the pericentric heterochromatin region. This situation creates an possibility for rearrangements to occur in the donor chromosome and subsequent triradial configurations (2). Furthermore, the observation of telomere shortness in the receptor chromosomes suggests that telomeric function loss is also an effective factor in JT formation (3). Even tough certain chromosomal abnormalities, BM involvement and high LDH levels at diagnosis are poor prognostic biomarkers, many studies have shown that BL/L treated with convenient chemotherapy regimens confer good clinical outcome as in our patient. Poor prognosis has been claimed to be associated with progressive loss of interstitial telomere sequences in acquired JTs occuring in hematological malignancies (10). The good prognosis of our patient suggests the presence of interstitial telomeric sequences which is uncommon in acquired JTs.

CONCLUSION

On the basis of these findings, our work propose that JT might be a progression biomarker in Burkitt lymphoma/leukemia. More studies should be done to expand information about impact of jumping 1q translocation on survival.

Conflict of interest

No conflict of interest was declared by the authors.

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