

## A novel chromosomal abnormality t (9;14)(p24;q13) in B-acute lymphoblastic leukemia

Sureshkumar Raveendran, Santhi Sarojam, Geetha Narayanan<sup>1</sup>, Hariharan Sreedharan

Division of Cancer Research, <sup>1</sup>Division of Medical Oncology, Regional Cancer Centre, Medical College, Trivandrum, Kerala, India

Acute lymphoblastic leukemia is a malignant disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow. We describe the clinical, morphologic, immunophenotypic and cytogenetic findings in the case of a 26-year-old man with B-lymphoblastic leukemia. Surface marker analysis revealed that they are positive for CD markers CD10, CD19, CD13, CD34, CD45 and HLA-DR, but negative for CD20, CD33, CD117 and CD11C markers. Cytogenetic analysis established a novel translocation, t (9;14)(p24;q13). Apart from this, spectral karyotyping revealed an additional translocation, t (6p; 14q). This is the first documented case of B-lymphoblastic leukemia with concurrent occurrence of both abnormalities. Further studies are needed to understand the role of this abnormality in carcinogenesis.

**Key words:** B-acute lymphoblastic leukemia, conventional cytogenetics, Janus kinase 2, spectral karyotyping

a heterogeneous disease at the clinical, morphologic, immunophenotypic and cytogenetic level.<sup>[2]</sup> Cytogenetic analysis and molecular cytogenetics studies reveal recurring chromosomal abnormalities B-lymphoblastic leukemia. Individual chromosomal abnormalities in B-lymphoblastic leukemia are strong independent indicators of outcome of patients. Chromosome rearrangement including chromosome band 14q13 are frequently observed in B-lymphoblastic leukemia, however, translocations involving chromosome band 14q13 and chromosome 9 are very rare.<sup>[3,4]</sup> However, the chromosome bands involving 14q13 and 9p24 region has not yet reported. Here, we report a case of B-lymphoblastic leukemia with novel chromosomal translocation t (9;14)(p24;q13).

### Introduction

Chromosomal abnormalities recurrently associated with hematological malignancies, alter the structure and function of genes controlling cell proliferation and differentiations through multiple and complex pathways and different abnormalities are associated with a different outcome.<sup>[1]</sup> B-lymphoblastic leukemia (a.k.a. precursor B-cell acute lymphoblastic leukemia [ALL]) is

### Case Report

This was a case report of a 26-year-old boy who was presented to us in June 2011 with fever and body pain. On examination, he had pallor, cervical lymph nodes and splenomegaly. His hemogram showed a hemoglobin of 9.4 g%, total white blood cells count of 218,000/cmm with 97% abnormal cells, platelet count of 74,000/cmm and 2301 u/L serum lactate dehydrogenase. Peripheral smear showed 75% blasts with scanty blue cytoplasm and round to oval nuclei with immature chromatin. Immunophenotyping showed the blasts cells to be CD10+, CD19+, CD20-, CD13+, CD33-, CD117-, CD11C-, CD34+, CD45+, HLA-DR+. A diagnosis of B-lymphoblastic leukemia with CD13 co-expression was made. Bone marrow examination showed 60% blasts with scanty blue cytoplasm and round to oval nucleus

Access this article online	
Quick Response Code:	Website: www.ijhg.com
	DOI: 10.4103/0971-6866.132763

**Address for correspondence:** Dr. Sreedharan Hariharan, Division of Cancer Research, Regional Cancer Centre, Medical College, Trivandrum - 695 011, Kerala, India. E-mail: drshariharan@gmail.com

with immature chromatin, diagnostic of B-lymphoblastic leukemia. He was started on BFM-95 protocol. Post-induction bone marrow was in remission. This patient was under treatment with high dose methotrexate as consolidation.

Bone marrow aspirate withdrawn at the time of disease diagnosis was used for classical cytogenetic analysis after short-term culture after receiving official institutional approval. Harvesting and GTG banding were performed as per the standard procedure.<sup>[5]</sup> Karyotypes were described according to ISCN 2009.<sup>[6]</sup> 30 metaphases were karyotyped using Cytovision Software (Cytovision, USA). Cytogenetic investigation of bone marrow cells revealed the presence of a novel chromosomal translocation 46, XY, t (9;14)(p24;q13) in 50% of the leukemic cells analyzed. Microscopic evaluation disclosed the translocation between the short arm of chromosome 9p24 and the long arm of chromosome 14q13 [Figure 1]. Spectral karyotyping (SKY) was performed to confirm the chromosomal translocation. A 22 mm × 22 mm region of the metaphase preparation on one of the GTG slides was hybridized with applied spectral imaging-SKY paint probe mixture (Applied Spectral Imaging, Migdal Ha'Emek, Israel). The result was analyzed using the SKY system according to the manufactures instructions. SKY confirmed der (9) t (9p;14q) [Figure 2]. Unexpectedly, SKY analysis also revealed another translocation involving chromosome 6 and 14; der (6)(6p;14q), in 1/30 metaphase analyzed [Figure 3]. However, in cytogenetic analysis we couldn't detect this abnormality.

## Discussion

Cytogenetic analysis and molecular cytogenetic studies reveal recurring chromosome abnormalities in approximately 80% of ALL, including numerical and structural changes, such as translocations, inversions, or deletions.<sup>[7]</sup> Here we have identified a novel balanced translocation der (9) t (9;14)(p24;q13) in B-lymphoblastic leukaemia. SKY revealed additional translocation, t (6p; 14q). To the best of our knowledge der (9) t (9;14) (p24;q13) and der (6) t (6p;14q) in the same patient has not been previously described in the literature.<sup>[8]</sup>

Until date, t (9;14) involving 9p24 band region has

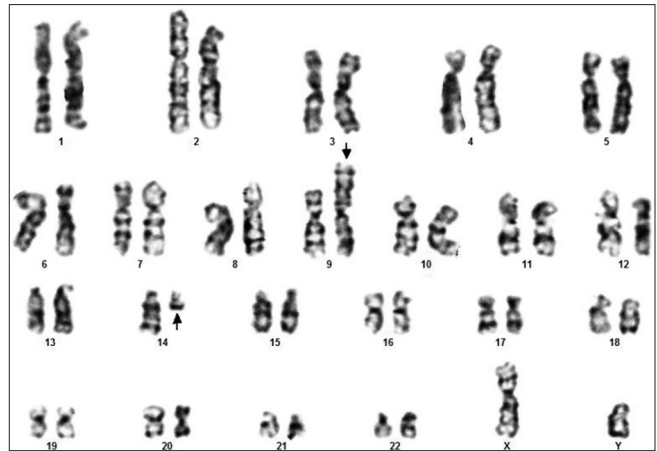


Figure 1: G-banded karyotype of the bone marrow cells showing t(9;14)(p24;q13)



Figure 2: Spectral karyotyping of the metaphase spread after spectrum based classification. The karyotype was confirmed as der (9)t(9p;14q)

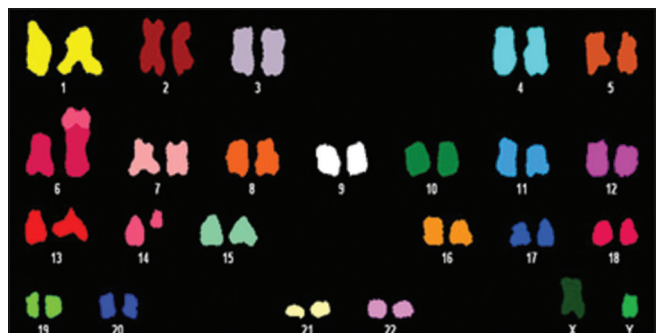


Figure 3: Spectral karyotyping of the metaphase spread showing der (6)t(6p;14q)

not been reported in B-ALL, although there have been two cases which had t (9;14) concerning 9p24 band in extranodal marginal zone B-cell lymphoma.<sup>[9]</sup> Chromosome band 9p24 harbors several genes that play an important role in carcinogenesis, such as dedicator of cytokinesis 8 at 9p24.3, Janus kinase 2 (JAK2) at 9p24, programmed cell death 1 ligand 2 at 9p24.2, interleukin 33 at 9p24.1 and tumor protein D52-like 3

at 9p24.1. Among these genes, JAK2 reported to be directly involved in leukemogenesis.<sup>[10]</sup> Constitutive activation of the JAK and signal transducer and activator of transcription pathway occurs in several hematopoietic malignant diseases.<sup>[11]</sup> In this case, expressional variation of JAK2, owing to the t (9;14) might be the reason for leukemogenesis.

Structural abnormalities of the long arm of the chromosome 14 are very frequently found in B-lymphoblastic leukemia. In B-ALL, the recurrent chromosomal aberrations are mainly concentrated in the band position 14q32, with the most reported translocation being t (8;14)(q24;q32), which leads to the formation of oncogenic IGH-c-MYC fusion protein. So far, the band involving 14q13 with chromosome 9 was reported only once with the reported translocation t (9;14)(p21;q13).<sup>[4]</sup> Band 14q13 is known to carry several oncogenes. Among them, the gene encoding nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha is mutated in some Hodgkin's lymphoma cells.

Apart from the above mentioned novel translocation, an additional chromosomal translocation involving chromosome 6 and 14 was also identified by SKY analysis, der (6)(6p;14q) in the same patient. However, we failed to identify this same translocation by conventional cytogenetic technique. Taken together, the identification of novel translocations der (9) t (9;14)(p24;q13) and der (6) t (6p;14q) in a single B-lymphoblastic leukemia patient suggests that new rearrangements of genes leading to fusion transcripts may be involved in the malignant progression. However, it is unclear as to what role, if any, these breakpoints has played in leukemogenesis. Moreover, why both these translocations occurred together and how this functions, remains unclear. In future, molecular characterization of these types of cytogenetic abnormalities would provide insights into the heterogeneity of genomic rearrangement which further leads to tumorigenesis.

## Acknowledgments

We thank Dr. Jayarama S. Kadandale, Centre for Human Genetics, Bangalore for SKY analysis. The first author is a recipient of Senior Research Fellowship from ICMR, Government of India.

## References

1. Rowley JD. The role of chromosome translocations in leukemogenesis. *Semin Hematol* 1999;36 4 Suppl 7:59-72.
2. Reichard KK, Kang H, Robinett S. Pediatric B-lymphoblastic leukemia with RUNX1 amplification: Clinicopathologic study of eight cases. *Mod Pathol* 2011;24:1606-11.
3. Gmidène A, Sennana H, Elghezal H, Ziraoui S, Youssef YB, Elloumi M, *et al.* Cytogenetic analysis of 298 newly diagnosed cases of acute lymphoblastic leukaemia in Tunisia. *Hematol Oncol* 2008;26:91-7.
4. Strefford JC, Worley H, Barber K, Wright S, Stewart AR, Robinson HM, *et al.* Genome complexity in acute lymphoblastic leukemia is revealed by array-based comparative genomic hybridization. *Oncogene* 2007;26:4306-18.
5. Henegariu O, Heerema NA, Lowe Wright L, Bray-Ward P, Ward DC, Vance GH. Improvements in cytogenetic slide preparation: Controlled chromosome spreading, chemical aging and gradual denaturing. *Cytometry* 2001;43:101-9.
6. Shaffer LG, Slovak ML, Campell LJ, editors. ISCN 2009: an International System for Human Cytogenetic Nomenclature. Basel: Karger; 2009.
7. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukaemia. *Lancet* 2008;371:1030-43.
8. Mitelman F, Johansson B, Mertens F. Mitelman database of chromosome aberrations and gene fusions in cancer, 2011. Available from: <http://www.cgap.nci.nih.gov/Chromosomes/Mitelman>. [Last updated on 2013 May 15; last accessed on 2013 Aug 20].
9. Vinatzer U, Gollinger M, Müllauer L, Raderer M, Chott A, Streubel B. Mucosa-associated lymphoid tissue lymphoma: Novel translocations including rearrangements of ODZ2, JMJD2C, and CNN3. *Clin Cancer Res* 2008;14:6426-31.
10. Ho K, Valdez F, Garcia R, Tirado CA. JAK2 translocations in hematological malignancies: Review of the literature. *J Assoc Genet Technol* 2010;36:107-9.
11. Bercovich D, Ganmore I, Scott LM, Wainreb G, Birger Y, Elimelech A, *et al.* Mutations of JAK2 in acute lymphoblastic leukaemias associated with Down's syndrome. *Lancet* 2008;372:1484-92.

**Cite this article as:** Raveendran S, Sarojam S, Narayanan G, Sreedharan H. A novel chromosomal abnormality t (9;14)(p24;q13) in B-acute lymphoblastic leukemia. *Indian J Hum Genet* 2014;20:79-81.

**Source of Support:** Nil, **Conflict of Interest:** None declared.