

A RARE CASE OF A COMPLEX VARIANT PHILADELPHIA CHROMOSOME TRANSLOCATION IN CHRONIC MYELOID LEUKEMIA

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INTRODUCTION

- The Philadelphia chromosome (Ph chromosome) results from a balanced translocation between the long arms of chromosome 9 and 22, denoted as t(9;22)(q34;q11.2).
- This rearrangement results in a fusion gene BCR-ABL1, encoding a fusion protein with enhanced tyrosine kinase activity.
- The Ph chromosome is observed in >95% of patients with chronic myeloid leukemia (CML), 15-20% of patients with adult acute lymphoid leukemia (ALL), and 1-2% of patients with acute myeloid leukemia (AML).
- In most CML patients, the Ph chromosome results from a standard reciprocal translocation, the t(9;22).
- Approximately 4-8% of Ph chromosome-positive patients have complex variant translocations involving three or more chromosomes.
- We present cytogenetic and FISH data from a patient with CML with a complex variant translocation involving four chromosomes, chromosomes 6, 7, 9 and 22.

MATERIALS & METHODS

- A bone marrow aspirate from a 69 year old female patient with leukocytosis
- Conventional cytogenetic and fluorescence in situ hybridization (FISH) studies were performed.

Cytogenetic Studies:

- 2 cultures
 - Culture treated overnight with Colcemid
 - 24 hour culture treated with Ethidium bromide during harvest
- 20 GTG banded metaphase cells were analyzed (10 from each culture)

For FISH:

- Interphase FISH was performed with a tricolor, dual fusion BCR/ABL1 probe set (Abbott Molecular, Des Plaines, IL).
- At least 200 interphase nuclei were scored

RESULTS

Cytogenetic Result:

- The G-banded chromosomes revealed an apparently balanced reciprocal four-way translocation involving 6p23, 7p15, 9q34, and 22q11.2 in all 20 cells analyzed (Figures 1 and 2).
- ISCN: t(6;9;22;7)(p23;q34;q11.2;p15)[20]

FISH Result:

- Both double fusion (2R2G2F2A) and single fusion (2R2G1F2A) patterns were observed indicating BCR/ABL1 fusion (Figures 3a, 3b, 4a and 4b).
- ISCN: nuc ish(AS11x2), (ABL1x3), (BCRx3), (ABL1 con BCRx1) [97/200] / nuc ish(AS11x2), (ABL1x4), (BCRx4), (ABL1 con BCRx2) [11/200]

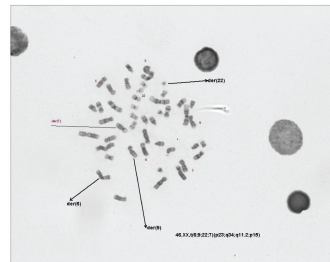


Figure 1: metaphase showed the abnormal chromosomes: 6,7,9 and 22

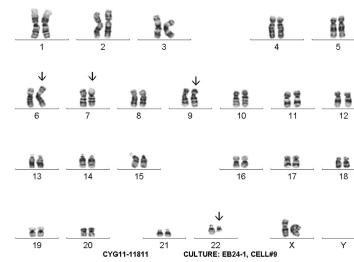


Figure 2: Karyotype image of the metaphase in the figure 1

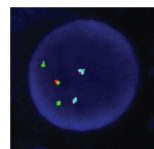


Figure 3a: 2R2G1F2A

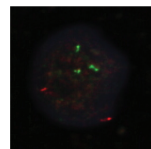


Figure 3b: 2R2G1F2A

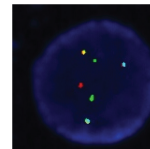


Figure 4a: 2R2G2F2A

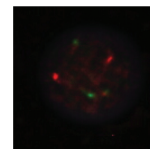


Figure 4b: 2R2G2F2A

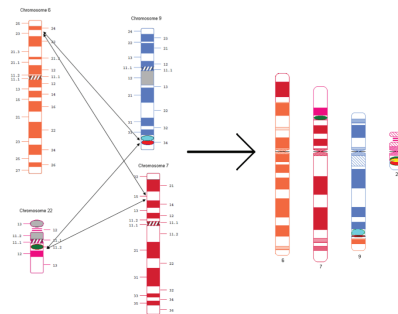


Figure 5: Model of our 4-way Ph translocation

DISCUSSION

With the dual fusion FISH probe for the t(9;22), in the traditional t(9;22), the two fusion signals are located one on the derivative 9 and the other on the derivative 22 (the Philadelphia chromosome). In the case described in this poster, because the derivative 9 does not have the BCR material from chromosome 22, the clone with the single fusion represents the primary clone. The clone with two fusion signals likely represents a clone with two copies of the Philadelphia chromosome – an observation associated with the blast phase of CML. This clone was not identified by conventional cytogenetic studies (most probably due to the small numbers of cells in which it is present, 5.5% as indicated by FISH data).

With a dual fusion probe, one fusion signal pattern indicates the presence of a complex rearrangement involving more than the chromosomes 9 and 22.

When two clones, one with a single fusion pattern and the other with two fusion patterns coexist, it indicates most likely, clonal evolution with the presence of two Philadelphia chromosomes.

CONCLUSIONS

This case illustrates the importance of

- Understanding the characteristics of the probe while interpreting FISH data and
- Performing cytogenetic studies in conjunction with FISH studies.

BIBLIOGRAPHY

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- 2) McKeithan, T., Warshawsky, L., Espinosa, R., and LeBeau M. "Molecular cloning of the breakpoints of a complex Philadelphia chromosome translocation: Identification of a repeated region on chromosome 17". (1992) *Proc. Natl. Acad. Sci.* 89, 4923-4927