Cell, Gene and Therapy

CASE REPORT Open Access

Chromosome Translocation reports in Myeloid Leukemia

Z. Sasaninezhad[1], N. Mansouri[2*], N. Safavi Naeini[2], M. Ghadiani[3], M. Rezaei Tavirani[4], H. Allahmoradi[5]

[1]Department of Genetic, Faculty of Advnced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

[2]Department of Medical Genetics, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[3]Department of Internal Medicine/Oncology, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[4]Proteomics Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[5] General Practitioner, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Background: According to the literature, there are a number of chronic and acute myeloid leukemias with unique, complex chromosome translocations. This study aims to conduct a brief review of the incidence of complex chromosome translocations in myeloid leukemia and reports a case of myeloid leukemia with complex chromosome translocations.

Methods: We conducted a web-based search for all peer review articles published on the subject of complex chromosome tranlsocations in chronic and acute myeloid leukemia in MEDLINE, PubMed and Mitelman (http://cgapanci.nih.gov/chromosomes/Mitelman) databases in addition to other pertinent web references. In addition, we performed conventional cytogenetic studies of 24- to 72-h cultures on bone marrow/peripheral blood cells obtained from the current case. Cells were finally treated by the giemsa-trypsin-giemsa banding technique.

Results: The result of this case revealed an abnormal karyotype that had a novel complex translocation which involved chromosomes 2, 5, 9, and 22. We performed karyotyping after the initiation of chemotherapy. Karyotyping results showed a complex karyotype 46,XX, t(2;5;9;22).

Conclusion: This study discusses a case of chronic myeloid leukemia with complex chromosome translocations and may provide novel information regarding these translocations in leukemias. **Cell, Gene and Therapy, Vol.2, Number 4, Winter 1st, 2021; 131- 135**

Keywords: Complex, Chromosome, Translocation, CML, Leukemia

Introduction

Based on a review of the literature, we located data from patients diagnosed with chronic myeloid (CML) and acute myeloid (AML) leukemias with unique complex chromosome translocations. All human chromosomes with the exception of the Y chromosome are involved in complex chromosome translocation.[1] Complexity is defined as the presence of three or more different chromosome abnormalities in the malignant clone and/or variant. In other words, changes from cell to cell despite the presence of a clonal origin.

The majority of myeloid leukemia patients have three-way complex translocations involving another chromosome in addition to primary or nonrandom changes such as t(1;8;21),[2] t(8;21;14),[3] t(9;22;11),[4] and t(8;21;8),[5]. Few reports have shown the occurrence of four-way

*** Corresponding Author: Department of Medical Genetics**
Email: zaharasasanianezhad@yahoo.com

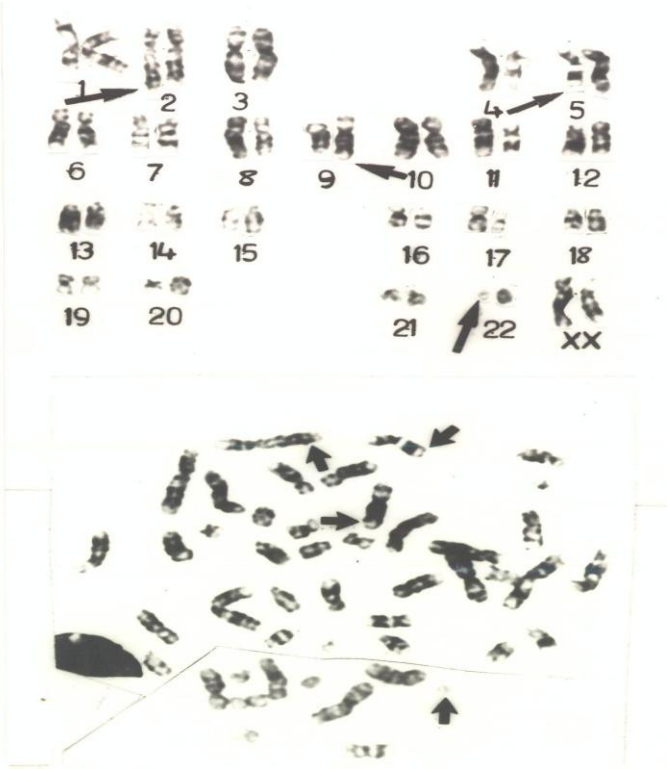

Figure 1. Karyotype of bone marrow cell showing 46,XX,t(9;22;2;5).

t(8;17;15;21) rearrangements in AML such as (M2),[6] t(8;11;16;21),[7] and t(5;17;15;20)[8]. Recently t(9;22;7;1), a very rare rearrangement in myeloid malignancies, has been reported in the literature.[9] In addition, a novel five-way translocation t(7;11;9;22;9) (q22;q13;q34; q11.2;q34) involving the Ph chromosome in a patient diagnosed with CML was reported by Yokota and coworkers in 2012.[10] Here we presented a case of myeloid leukemia associated with complex chromosome translocations.

Materials and Methods

Cytogenetic analysis

During the past twelve years, chromosome banding studies were performed on 187 unselected consecutive adults with an initial diagnosis of de novo CML and AML[11,12] who were admitted to the major referral hospitals affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran.

We performed conventional cytogenetic studies of 24- to 72-h cultures on bone marrow/peripheral blood cells by standard methods. Cultures were evaluated by giemsa-trypsin-giemsa banding according to the ISCN.[13] A minimum of 80 metaphases were analyzed. Approximately 0.5 ml of bone marrow/peripheral blood was obtained from each participant. Briefly, the heparinized sample was immediately mixed with 4 ml RPMI – 1640 (Gibco BRL, USA) cell culture medium supplemented with 15%-20% heat inactivated fetal bovine serum (Gibco BRL, USA) and incubated for 24-72 h at 37ºĊ and 5% CO_2. Next, the cultured cells were harvested by 75 ml colcemid (10µg/ml; Gibco BRL, USA) and incubated at 37ºĊ for 30 min. The contents of the tube were then centrifuged for

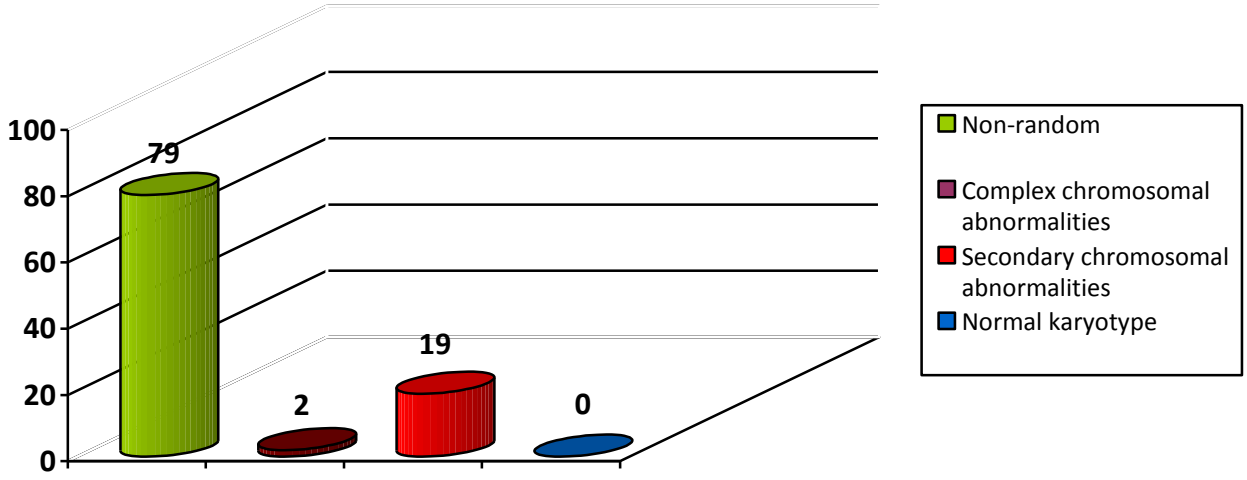

Figure 2. Distribution of chromosomal damages in myeloid leukemia.

10 min at 1000 rpm and suspended in 10 ml of 75 mM KCl (0.56%; Sigma) that had been prewarmed to 37ºĊ, for 20 min. At this stage 1 ml of 20□ Carnoy's Fixative (3:1 methanol:acetic acid; Fisher Scientific) was added to halt additional cell swelling. This stage was repeated four times. Then, cells were placed on clean slides and cultured for three days at 60□ on a slide warmer. Slides were banded for 10 sec with 0.2 X trypsin (Difco, USA) and stained for 3 min with giemsa (Harleco).[14] Slides were examined with a Nikon light microscope. We analyzed 80, well-spread G-banded metaphases.

Results

Cytogenetic analysis of the bone marrow cells revealed an abnormal karyotype with a novel complex translocation that involved chromosomes 2, 5, 9, and 22 in our CML patient, a 24-year-old female. Cytogenetic study was indicative of a clonal abnormality that involved a complex Ph translocation, 46,XX,t(9;22;2;5) in 25 cells (Figure 1). Although this case had complex chromosomal abnormalities, there was no history of previous malignant diseases, occupational or therapeutic exposures. We recorded the percentage of all abnormal cytogenetic cells to be between 25%.

We have previously reported the distribution of total chromosomal changes in CML and AML patients from our institute,[11,12,20] as summarized in Figure 2.

Discussion

According to the literature, the numbers of myeloid leukemia with unique complex chromosome translocations were detected.[15-23] The present work confirmed our findings that most cases of CML and AML have additional specific chromosome changes.[11,12,20] Additionally, 46,XX,t(9;22) and 46,XX, t(9;22;2;5) were noted in the current case, which was compatible with the results reported by others.[2-10] The present report described a case of CML that had an unusual translocation involving chromosomes 2, 5, 9, and 22 with various break points.

According to some studies, chemical exposure may modify patterns of chromosomal changes in myeloid leukemias in humans.[24,25] However, the data of our case had no history of any previous malignant diseases, occupational or therapeutic

exposure. The general results of this study agreed with previously reported findings of complex chromosomal abnormalities in CML patients.

Conclusion

In CML, translocation other than the standard reciprocal such as 9;22 occur in a few cases. Although it is generally accepted that in CML a complex translocation does not influence the course of the disease. Hence the significant of these translocations in evolution of the disease is unclear, owing to the limited number of cases that have undergone long term clinical follow up. Therefore the present report may provide novel knowledge and data for complex chromosomal translocations in leukemias.

Acknowledgement

The authors would like to express their appreciation to Miss Niloofar Safavi for her excellent technical assistance and material collection. The authors declare they have no conflicts of interest. This article is part of a thesis.

References

1. Heiem S. Variant Ph translocations in chronic myeloid leukemia. *Cancer Genet Cytogenet* 1985;18:215-7.
2. Ahmad F, Kokate P, Chheda P, Dalvi R, Das BR, Mandava S. Molecular cytogenetic findings in a three-way novel variant of t(1;8;21)(p35;q22;q22): A unique relocation of the AML1/ETO fusion gene 1p35 in AML-M2. *Cancer Genet Cytogenet* 2008;180(2):153-7.
3. Ishida F, Ueno M, Tanaka H, Makishima H, Suzawa K, Hosaka S, et al. t(8;21;14) (q22;q22;q24) is a novel variant of t(8;21) with chimeric transcripts of AML1-ETO in acute myelogenous leukemia. *Cancer Genet Cytogenet* 2002;132(2):133-5.
4. Belli C, Alu MF, Alfonso G. Novel variant Ph translocation t(9;22;11) (q34;q11.2;p15)inv(9) (p13q34) in chronic myeloid leukemia involving a one-step mechanism. *Cytogenet Genome Res* 2011;132:304-8.
5. Xue Y, Xu L, Chen S, Fu J, Guo Y, Li J. t(8;21;8)(p23;q22;q22): A new variant form of t(8;21) translocation in acute myeloblastic leukemia with maturation. *Leuk Lymphoma* 2001;42:533–337.
6 Vieira L, Oliveira V, Ambró sio AP, Marques B, Pereira AM, Hagemeijer A, Boavida MG. Translocation (8;17;15;21) (q22;q23;q15;q22) in acute myeloid leukemia (M2): A four-way variant of t(8;21). *Cancer Genet Cytogenet* 2001;128:104e7.
7. Albano F, Specchia G, Anelli L, Liso A, Zagaria A, Santoro A, et al. Submicroscopic deletions in an acute myeloid leukemia case with a four-way t(8;11;16;21). *Leuk Res* 2005;29(7):855-8.
8. Yamanouchi J, Hato T, Niiya T, Miyoshi K, Azuma T, Sakai I, et al. A new four-way variant t(5;17;15;20) (q33;q12;q22;q11.2) in acute promyelocytic leukemia from Japan. *Int J Hematol* 2011;94(4):395-8.
9. Adriana Z, Al Bahar S. Novel four-way Ph translocation t(9;22;7;1) (q34;q11;q22;p13) in a chronic myeloid leukemia patient receiving tyrosine kinase inhibitor therapy. *Int J Hematol* 2012;95(3):315-9.
10. Yokota S, Nakamura Y, Bessho M. A novel five-way translocation t(7;11;9;22;9)(q22;q13;q34;q11.2;q34) involving Ph chromosome in a patient of chronic myeloid leukemia: A case report. *Mol Cytogenet* 2012;5:20.
11. Movafagh A, Hajifathali, Esfahani F, Attarian, Ghadiani M, Rezvani H, et al. Geographic heterogeneity of cytogenetic characteristics of AML in the early detection: A comparative study of Iranian and Indian adult patients. *IJCP* 2009;2:85-9.

12. Movafagh A, Hajifathali A, Zamani M. Secondary chromosomal abnormalities of de novo AML. A first report from the Middle East. *APJCP* 201;12:2991-4.
13. Shaffer LG, Slovak ML, Campbell LJ, editors. An international system for human cytogenetic nomenclature. Basel: S. Karger, 2009.
14. Misawa S, Horiike S, Taniwaki M. Detection of karyotypic abnormalities in most patients with APL by adding ethidium bromide to short term culture. *Leuk Res* 1988;12(9):719-9.
15. Gupta M, Ashok Kumar J, Sitaram U, Neeraj S, Nancy A, Balasubramanian P, et al. The t(6;9) (p22;q34) in myeloid neoplasms: A retrospective study of 16 cases. *Cancer Genet Cytogenet* 2010;203(2):297-302.
16. Zhu Y, Xu W, Liu Q, Pan J, Qiu H, Wang R, et al. Abnormalities of chromosome 17 in myeloid malignancies with complex chromosomal abnormalities. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi* 2008;25(5):579-82.
17. Albano F, Specchia G, Anelli L, Liso A, Zagaria A, Santoro A, et al. Submicroscopic deletions in an acute myeloid leukemia case with a four-way t(8;11;16;21). *Leuk Res* 2005;29(7):855-8.
18. Ishida F, Ueno M, Tanaka H, Makishima H, Suzawa K, Hosaka S. t(8;21;14) (q22;q22; q24) is a novel variant of t(8;21) with chimeric transcripts of AML1-ETO in acute myelogenous leukemia. *Cancer Genet Cytogenet* 2002;132(2):133-5.
19. Shinagawa A, Komatsu T, Ninomiya H. Complex translocation (6;21;8), a variant of t(8;21), with trisomy 4 in a patient with acute myelogenous leukemia (M2). *Cancer Genet Cytogenet* 1999;109:72-5.
20. Movafagh A, Varma N, Varma S. Co-expression of two FAB-specific chromosome changes, t(15;17) and t(8;21), in a case of acute promyelocytic leukemia. *A J Hematol* 1996;72:375-7.
21 . Ayraud N, Raynaud S, Bayle J, Dujardin P. Variant translocation t(8;21;15) in an acute myeloblastic leukemia with phenotypic differential evolution. *Cancer Genet Cytogenet* 1985;15:191-7.
22. Selypes A, László A. A new translocation t(1;4;11) in congenital acute nonlymphocytic leukemia (acute myeloblastic leukemia). *Hum Genet* 1987;76(1):106-8.
23. Yamamoto K, Nagata K, Morita Y, Inagaki K, Hamaguchi H. New complex t(2;11;17)(p21;q23;q11), a variant form of t(2;11), associated with del(5)(q23q32) in myelodysplastic syndrome-derived acute myeloblastic leukemia. *Cancer Genet Cytogenet* 2002;137(2):119-23.
24. Weh HJ, Zschabcr R, Hossfeld DK. Double minute chromosome a frequency marker in leukemia patients with previous history of malignancy disease. *Cancer Genet Cytogenet* 1982;5:279-80.
25. Mitelman F, Brandt L, Nilsson PG. Relation among occupational exposure to potential mutagenic/carcinogenic agents, clinical findings, and bone marrow chromosomes in acute nonlymphocytic leukemia. *Blood* 1978;52:1229-37.