Case Report
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Unique Variant Complex Chromosome Translocation in Myeloid Leukemia: Report of a Case and Literature Review

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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(9;22;2;5).

Conclusion: This study discusses a case of chronic myeloid leukemia with complex chromosome translocations and may provide novel information regarding these translocations in leukemias.

Keywords: Complex, Chromosome, Translocation, CML, Leukemia

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Introduction

Based on the peer review literature, the data of CML and AML patients with a unique complex

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chromosome translocations were detected. All human chromosomes except the Y chromosome have been involved in complex chromosome translocation.[1] Complexity was defined as the presence of three or more different chromosome abnormalities in the malignant clone and/or variant i.e., changes from cell to cell despite the presence of a clonal origin.

The majority of myeloid leukemia patients shows 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] t(8;21;8),5 whereas few reports have shown the occurrence of four-way t(8;17;15;21) rearrangements in the case of acute myeloid leukemia (M2),[6] t(8;11;16;21),[7] recently t(5;17;15;20) report,[8] and more recently t(9;22;7;1) that is a very rare complex chromosome translocation in myeloid malignancies recorded in the current literature.[9] Also 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 reported by Yokota and coworkers in the year 2012.[10] Here we present a case with myeloid leukemia associated with complex chromosomes translocations.

Materials and Methods

Cytogenetic analysis

During the last twelve years, chromosome banding studies were performed on 187 unselected consecutive either adults sex patients of de novo CML and AML at initial diagnosis[11,12] in whom one interesting case of CML patient exhibited unique variant complex chromosome translocation and was the subject of present investigation. All patients were admitted to the major referral hospitals affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran.

We performed conventional cytogenetic studies of a 24- to 72-h culture were carried out on bone marrow/ peripheral blood cells by standard methods and 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, heparanized bone marrow/blood was immediately mixed with 4 ml RPMI – 1640 (Gibco BRL, USA) cell cultured medium supplement with 15-20% heat inactivated fetal bovine serum (Gibco BRL, USA). This tube cultured for 24-72 hours at 37ºĊ under the aeration of 5% Co2 in the incubator. After an incubation period, the cultured cell harvested by 75 ml colcemide 10µg/ml (Gibco BRL USA) and incubated at 37ºĊ for 30 minutes. The contents of the tube were then centrifuged for 10 min at 1000 rpm and resuspended in 10 ml of 75 mM Kcl 0.56% (Sigma, Co) prewarmed to 37ºĊ for 20 min. At this stage 1ml of Carnoys Fixative 3:1 methanol: acetic acid (Fisher Scientific) with 20ºĊ temperature was added in to the tube to stop further cell swelling. This fixation repeated four times. Then cells dropped on to clean slides, and cultured for 3 days at 60ºĊ temperature on the slide warmer. Slides then banded for 10 second with 0.2 X trypsin (Difco, Co USA) and stained for 3 min Giemsa (Harleco, Co).[14] Eighty well spread G-banded metaphases were selected. Slides were examined with Nikon automatic arranging software program.

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

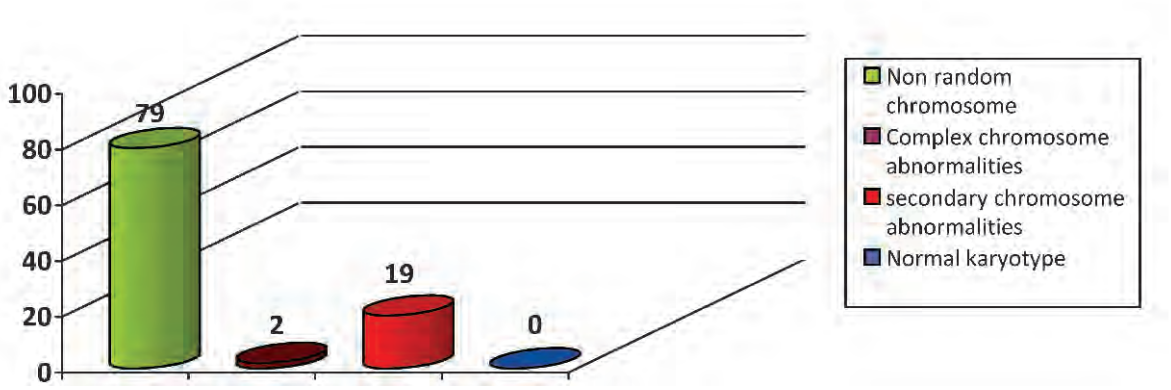

Figure 2. Distribution of chromosomal damages in myeloid leukemia.

Results

Cytogenetic analysis of bone marrow cells revealed an abnormal karyotype with a novel complex translocation involving chromosomes 2,5,9,22 in CML patient, a 24 years old female, cytogenetic study indicates clonal abnormality involving complex Ph translocation viz., 46,XX,t(9;22;2;5) in 25 cells (Figure.1). This case had complex chromosomal abnormalities without any history of previous malignant diseases or occupational or therapeutic exposure. The percentage of all abnormal cytogenetic cells was recorded to be approximately 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

The present work confirm and extends our finding that most cases of chronic and acute myeloid leukemia show the additional to specific chromosome changes.[11,12,20] In additional evidence is that 46, XX, t(9;22) and 46, XX, t(9;22;2;5) occurred in the case reported here and is compatible with the results reported by others.[2-10] The present report describes case of CML with a unusual translocation involving chromosomes 2,5,9,22 with the various break points.

According to some indications exist that chemical exposure may modify patterns of chromosomal changes in myeloid leukemia in human,[21-25] however, the data of our case recorded without any history of previous malignant diseases or occupational or therapeutic exposure. The general results of this study are in good agreement with previously reported findings in the series of complex chromosomal abnormalities in the series of chronic myeloid leukemia patients.

Conclusion

In CML, translocation other than the standard reciprocal such as 9;22 occur in the few cases, although it is generally accepted that in CML complex translocation have no influence in the course of disease, the significant of these translocation to the evolution of the disease is unclear, owing to the limited number of cases with long term clinical follow up. Hence, present report may provide novel knowledge and data of complex chromosome translocations in the wide field of leukemias.

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