



A Novel Case of Constitutional Robertsonian Translocation rob (14;21)(q10;q10) with Additional Cytogenetic Abnormality in Acute Myeloid Leukemia

Dharmesh M Patel; Pina J Trivedi*; Mahnaz M Kazi; Priya K Varma; Archana B Patel

Cytogenetic Laboratory, Department of Cancer Biology, Gujarat Cancer, and Research Institute, Asarwa - 380 016, Ahmedabad, Gujarat, India.

*Corresponding Author(s): Pina J Trivedi

Head & Senior Scientific Officer Cytogenetic Laboratory, Cancer Biology Department, The Gujarat Cancer & Research Institute, Asarwa, Ahmedabad Gujarat, India.
Email: pina.trivedi@gcriindia.org & pjt1410@rediffmail.com

Abstract

Robertsonian translocations between acrocentric chromosome are the most common type of constitutional chromosome rearrangement. Frequencies of rob(14;21) ranging between 14.8 and 19.6%. However, Robertsonian translocations are very rarely observed in neoplastic condition. The current study presents a case of 37 years old female with unusual constitutional Robertsonian translocation rob(14;21)(q10;q10) with t(10;22)(p13;q12) in acute myeloid leukemia with monocytic differentiation. The constitutional translocation might relate to a genetic uncertainty within the probability of somatic cytogenetic changes leading to haematological disorders and neoplasia. Thus, present case report therefore supports the hypothesis of such Changes in gene dosage are a major driver of cancer. However prognostic significance of constitutional cytogenetic abnormalities in leukemia has remained a matter of debate.

Received: Nov 30, 2022

Accepted: Dec 28, 2022

Published Online: Dec 30, 2022

Journal: Annals of Oncology Case Reports

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

Copyright: © Trivedi PJ (2022). *This Article is distributed under the terms of Creative Commons Attribution 4.0 International License*

Introduction

In the general population Robertsonian translocation is one of the most common, balanced structural rearrangements observed. One in 1,000 healthy individuals is thought to carry a Robertsonian translocation inherited from one of the parents with a normal phenotype [Choi BH;2013]. Robertsonian translocations are special types of chromosomal rearrangements which originate through centric fusion of the long arms of acrocentric chromosomes belonging to group D (13–15) and group G (21–22), [Li Y 2014, Ma SK 1997]. Even though Robertsonian translocations are one of the most common constitutional chromosomal changes observed in humans, an individual with “balanced” Robertsonian translocation have an estimated incidence [Schoemaker MJ;2019]. They are rarely found in human cancers. In the present study, we report a case of consti-

tutional Robertsonian translocation rob(14;21)(q10;q10) with additional cytogenetic abnormality t(10;22)(p13;q12) in acute myeloid leukemia. The constitutional translocation might relate to a genetic uncertainty within the probability of somatic cytogenetic changes leading to haematological disorders and neoplasia. Hence, the present case report supports the hypothesis of such changes in gene dosage are a major driver of cancer, engineered from a finite, but increasingly well explained, selection of mutational mechanisms increased susceptibility of carriers to leukemia. However, prognostic significance of constitutional cytogenetic abnormalities in leukemia has remained a matter of debate. On the based on reviewed the literature for this rare event in leukemia, we found that the prognostic significance of constitutional cytogenetic abnormalities in AML has remained a matter of debate.



Cite this article: Dharmesh M, Pina J, Mahnaz M, Priya K, Archana B. A Novel Case of Constitutional Robertsonian Translocation rob (14;21)(q10;q10) with Additional Cytogenetic Abnormality in Acute Myeloid Leukemia. *Ann Oncol Case Rep.* 2022; 1(1): 1007.

Case details

A 37-year-old female with Acute Myeloid Leukemia (AML) with monocytic differentiation who was registered at our institute due to high-grade fever. The peripheral blood examination showed haemoglobin levels 3.7gm/dL, white blood cell counts 69,770/ μ L and platelet count 76,000/ μ L. The investigations from bone marrow aspiration showed hypercellular bone marrow aspirate. Composed predominantly of blasts which are medium to large, have moderate amount of granular cytoplasm, opened nuclear chromatin and 0-3 prominent nucleoli. Erythroid, myeloid, and megakaryocytic lineages are markedly suppressed. Sudan Black-B staining was positive and Periodic acid Schiff (PAS) staining was negative, M: E ratio was altered. Diagnosis based on morphological findings was acute myeloid leukemia and suggested for immunophenotyping. In immunophenotyping blasts mainly expressed myeloid markers MPO, CD33, CD13, CD15 and CD117 along with HLADR and CD34. Final diagnosis based on immunophenotyping was acute myeloid leukemia with monocytic differentiation.

The patient received standard chemotherapy for AML. The patient was expired within 1 month of hospitalization.

Materials and methods

This study was approved by the Institutional Scientific Review Board and Ethics Committee. Prior consent was obtained from the patient.

Conventional cytogenetics study

Cytogenetic study at diagnosis was performed in direct bone marrow preparations and after short-term overnight cultures using standard cytogenetic protocol. Unstimulated culture of bone marrow aspirate was set up in RPMI-1640 medium supplemented with 20% newborn calf serum, L-glutamine, and antibiotics (penicillin and streptomycin). The cells were cultured in incubator at 37°C followed by overnight incubation in the presence of colcemid (10 μ L/8 ml of culture). The cultures were exposed to hypotonic solution (0.075 mol/L KCL) and fixed with methanol: acetic acid (3:1). The slides were prepared by air dry method and stained with Giemsa banding.

Subsequently at diagnosis and after achieved complete remission, the patient's constitutional karyotype was examined in Phytohaemagglutinin-M (PHA-M) stimulated culture of lymphocytes from peripheral blood. Mitogen-stimulated blood culture was set for 72 hours. Metaphase chromosomes were banded by GTG-banding technique [Verma RS;1995]. Detail of the karyotypes were reported according to the International System for Human Cytogenomic Nomenclature 2020 [McGowan-Jordan J;2020].

FISH assay

FISH was performed on metaphase cells following the manufacturer's guidelines (Abbott Molecular, Inc., Des Plaines, IL, USA). Whole Chromosome Painting for chromosome 14 (WCP 14) with spectrum Green (SG) and Whole Chromosome Painting for chromosome 21 (WCP 21) with spectrum Orange (SO) were used to reveal the Robertsonian translocation. FISH results revealed that there is Robertsonian translocation between chromosome 14 and 21. To confirm the part of 22 on chromosome 10p region, FISH was carried out using WCP 10 spectrum green and WCP 22 using spectrum orange. FISH results revealed that there was chromosome material from 22q was observed on p arm of chromosome 10. The analysis of both conventional cy-

togenetics and FISH was carried out using Zeiss Axiolmager.Z2 fluorescence microscope (Carl Zeiss, Germany) equipped with Metafer and CCD camera (MetaSystems, Germany).

Results

Conventional cytogenetics

Classical chromosome analysis detected an abnormal female chromosome complement. The karyotype results showed 45,XX,rob(14;21)(q22;q21),t(10;22)(p13;q12)[20]. It shows the presence of rob (14;21) in all cells of stimulated culture also (Figure 1).



Figure 1: Partial Giemsa-banded karyotype shows rob (14;21) (q10;q10) and t(10;22)(p13;q12).

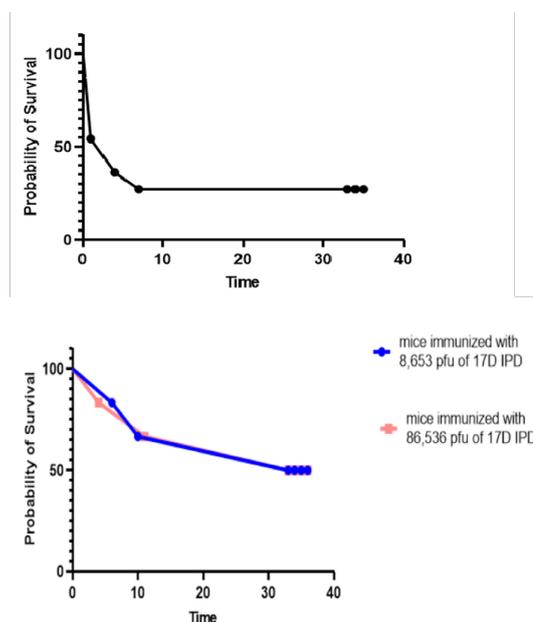


Figure 2: (a) Metaphase Fluorescent in Situ Hybridization results of whole chromosome paint probes. Spectrum Green for chromosome 14 and Spectrum Orange for chromosome 21. (b) Results of whole chromosome paint probes. Spectrum Green for chromosome 10 and Spectrum Orange for chromosome 22.

FISH

The metaphase FISH results of WCP 14 (SG) with WCP 21 (SO) and WCP 10 (SG) with WCP 22 (SO) revealed whole chromosome translocation between 14 and 21 and translocation of chromosome 10 and 22. The karyotype was 45,XX,rob(14;21)(p15q13),t(10;22)(q22;q21)[20] [Figure 2a, 2b].

Discussion

Chromosome abnormality is an important basis in diagnosing malignant hematological diseases. The occurrence of Robertsonian translocations has been repeatedly associated with an increased incidence of various blood dyscrasias, including preleukemia, leukemia and thrombocytopenia [Becher R, 1985]. Translocations are extremely common between chromosomes 13 and 14 (rob(13;14)) and 14 and 21 (rob(14;21)), with other combinations being rare [Zhao WW;2015]. Carriers of these translocations have 45 chromosomes, but the resulting loss of the short arms is presumed inconsequential because the short arms mainly contain repetitive ribosomal DNA [Page SL 1996]. However, mortality and site-specific cancer incidence have not been systematically investigated in carriers. A predisposition to hematological disorders in carriers of balanced Robertsonian translocations has been suggested [Pathak S. 1996]; evidence for this and for premalignant conditions is, however, derived from case reports [Welborn J. 2004]. Recently, carriers of rob(15;21) have been estimated to be at much higher risk of a rare form of Acute Lymphoblastic Leukemia (ALL). Risk of leukemia has, however, not been prospectively investigated in Robertsonian translocation carriers overall or according to subtype [Li Y, 2014].

We here report a 37-year-old female with Acute myeloid leukemia with rob(14;21)(q10;q10) and t(10;22)(p13;q12) chromosomal translocation. It has been hypothesized that constitutional chromosomal anomalies are associated with some degree of genetic instability [Nowell P;1984], which may then result in further structural and/or numerical chromosome abnormalities [Stratton MR;2009].

AML developed by the present patient might be the result of the genetic instability of her Robertsonian t(14;21). However, reports of patients with a balanced t(14;21) along with t(10;22) p13 are rare, and to our knowledge there are no other case reports of such carriers suffering from AML [Mitelman F;2022]. No final conclusions can be made at this time because patient also suffering from acquired cytogenetic abnormality t(10;22). Our current case report also in favour of our previous case report suggests that patients diagnosed with balanced Robertsonian translocations might be at increased risk of leukemia. These findings might be related to genetic factors as well as factors correlated with reasons for referral for cytogenetic test [Dharmesh Patel;2022]. To assess risks in individuals with balanced Robertsonian translocations, one needs a cohort design in which large numbers of carriers are followed over a long period of time for mortality and cancer risk. Obviously, no general conclusions can be drawn from this single case. But one can speculate that Robertsonian translocations, may be associated with blood dyscrasias. It would be of scientific interest, therefore, to observe known carriers of Robertsonian translocations in a prospective study regarding hematologic disorders.

References

- Schoemaker MJ, Jones ME, Higgins CD, Wright AF, United Kingdom Clinical Cytogenetics Group, Swerdlow AJ. Mortality and cancer incidence in carriers of balanced robertsonian translocations: a national cohort study. *American journal of epidemiology*. 2019; 188: 500-508.
- Verma RS. Tissue culture techniques and chromosome preparation. *Human chromosomes principles and techniques*. 1995.
- McGowan-Jordan J, Hastings RJ, Moore S, editors. *ISCN 2020: An International System for Human Cytogenomic Nomenclature (2020)*. Reprint Of: *Cytogenetic and Genome Research 2020*; 160: 7-8.
- Becher R, Mahmoud HK, Schaefer UW, Schmidt CG. Ph-positive CML in a family with a constitutional Robertsonian translocation 14; 15. *Cancer genetics and cytogenetics*. 1985 1; 18: 229-234.
- Zhao WW, Wu M, Chen F, Jiang S, Su H, et al. Robertsonian translocations: an overview of 872 Robertsonian translocations identified in a diagnostic laboratory in China. *PLoS One*. 2015; 10: e0122647.
- Page SL, Shin JC, Han JY, Andy Choo KH, Shaffer LG. Breakpoint diversity illustrates distinct mechanisms for Robertsonian translocation formation. *Human molecular genetics*. 1996 1; 5:1279-1288.
- Pathak S. Constitutional translocations and predisposition to T- and B-cell malignancies. *Cytogenet Cell Genet*. 1986; 43: 223-225.
- Welborn J. Constitutional chromosome aberrations as pathogenetic events in hematologic malignancies. *Cancer Genet Cytogenet*. 2004; 149: 137-153.
- Choi BH, Kim UH, Lee KS, Ko CW. Various endocrine disorders in children with t (13; 14)(q10; q10) Robertsonian translocation. *Annals of Pediatric Endocrinology & Metabolism*. 2013; 18: 111-115.
- Li Y, Schwab C, Ryan SL, Papaemmanuil E, Robinson HM, et al. Constitutional and somatic rearrangement of chromosome 21 in acute lymphoblastic leukaemia. *Nature*. 2014; 508: 98-102.
- Ma SK, Chow EY, Wan TS, Chan LC. Robertsonian translocation as an acquired karyotypic abnormality in leukaemia. *British journal of haematology*. 1997; 98: 213-215.
- Nowell P, Besa E, Emanuel B, Pathak S, Finan J. Two adult siblings with thrombocytopenia and a familial 13; 14 translocation. *Cancer genetics and cytogenetics*. 1984; 11: 169-174.
- Stratton MR, Campbell PJ, Futreal PA. The cancer genome. *Nature*. 2009; 458: 719-724.
- Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (2022). Mitelman F, Johansson B and Mertens F (Eds.).
- Dharmesh M Patel, Pina J Trivedi, Priya K Varma, Mahnaz M Kazi, Prabhudas S Patel. A Novel Case of Sole Constitutional Nonhomologous Robertsonian Translocation rob (14;15) (q10;q10) in B-Cell Acute Lymphoblastic Leukemia. *Journal of Clinical and Laboratory Research*. 2022; 5.