Case Report

Complex Chromosomal Rearrangement: A Case Report to Emphasize the Need for Parental Karyotyping and Genetic Counseling

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Abstract

Complex chromosomal rearrangements (CCRs) are rare structural rearrangements which involve at least three or more chromosomal breaks. The present report emphasizes the significance of parental karyotyping and the need of genetic counseling for couples with bad obstetric history (repeated abortions/miscarriages). The report includes the cytogenetic assessment of the proband and the mother, carried out at our accredited laboratory. The karyotype analysis of the proband revealed an apparently balanced translocation, identified to have been familially inherited from the mother having CCRs with double two-way translocations involving four chromosomes.

Keywords: *Bad obstetric history, genetic counseling, karyotyping, translocation*

Introduction

Complex chromosomal rearrangements (CCRs) are rare structural rearrangements, which involve at least three or more chromosomal break points. Various classifications have been proposed to categorize CCRs. Depending on their structure, they can be classified as three-way exchange, double two-way exchange, and exceptional CCRs. Depending on the mode of transmission, they can be either familial or *de novo* rearrangements. Depending on the number of chromosomal breaks involved in the rearrangement, they can be divided into two groups: those with four or fewer breaks and those with more than four breaks. CCRs can also be classified as balanced, with no loss or gain of chromosome material or unbalanced.[1,2] Balanced chromosomal rearrangements may or may not exhibit any phenotypic abnormalities and can go undetected for multiple generations.[2] Carriers of balanced CCRs are at risk of infertility, miscarriages, recurrent spontaneous abortions, and also birthing children with unbalanced CCRs. Carriers of unbalanced CCRs have high probability of multiple malformations, global developmental delay etc.[3]

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The proband involved an 8-year-old male child with clinical history of mental retardation and aphasia and was referred for cytogenetic analysis to our laboratory. Parents exhibited a history of two miscarriages and also the mother was deaf and mute.

Karyotype analysis was performed on phytohemagglutinin-stimulated peripheral blood lymphocytes, cultured in Roswell Park Memorial Institute 1640 medium. Twenty GTG-banded metaphases were analyzed using the Applied Spectral Imaging software, and results were outlined as per the latest International System for Human Cytogenomic Nomenclature 2016 and the College of American Pathologists guidelines.

The karyotype analysis of the proband revealed apparently balanced translocation involving short arm of one of the chromosome 2 and long arm of one of the chromosome 12, the breakpoints being p16 and q22, respectively [Figure 1]. To understand the origin of translocation (*de novo* or familial) detected in the

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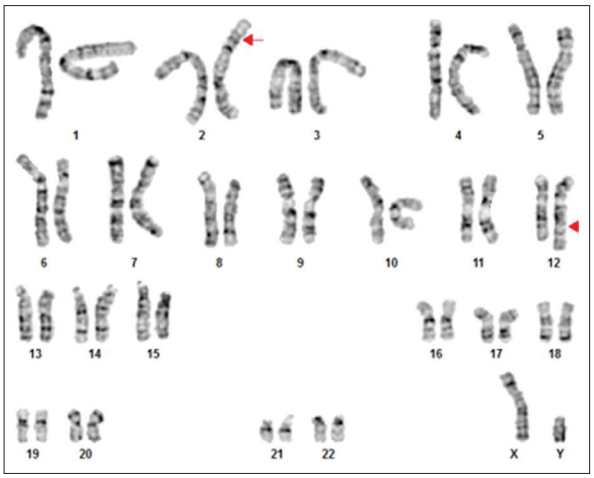

Figure 1: Proband with familial translocation inherited from the mother

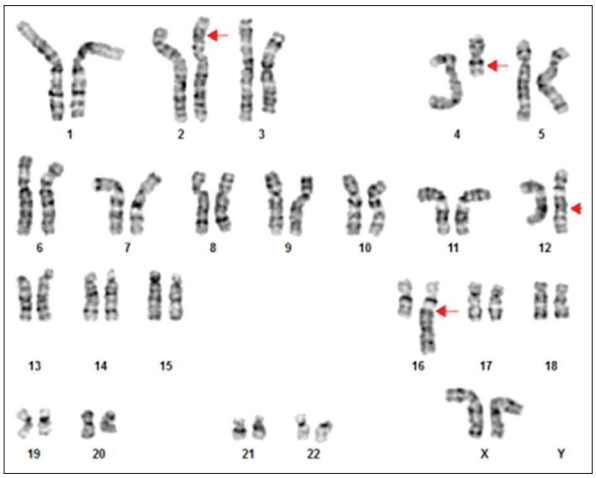

Figure 2: Double two-way translocation in the mother of proband

proband, samples from the parents were requested for karyotype analysis. The karyotype of the mother revealed a CCR (double two-way translocation). The first translocation involved short arm of chromosome 2 and long arm of chromosome 12 at break points p16 and q22, respectively, identical to the proband. The second translocation involved long arm of chromosome 4 and long arm of chromosome 16 [Figure 2].

Discussion

Majority of reported constitutional CCRs are *de novo* events that appear to have transpired during spermatogenesis. On the contrary, occasionally reported familial CCRs appear to be transmitted predominately through females, which possibly suggests chromosome rearrangements to be more readily tolerated in female meiosis than male meiosis.[4]

Double two-way exchange are the simplest form of CCRs consisting either simultaneous occurrence of two reciprocal translocations or a reciprocal translocation along with a Robertsonian translocation or an inversion.[1] Multiple, but simple, two-way translocations account for the most number of CCRs that have been reported.[5]

A particularly exasperating aspect of CCRs is the observation of patients carrying apparently balanced CCR at microscopic level, but clinically exhibiting subtle phenotypic abnormalities and/or physical deformities. Such features are observed in about 30%–40% of apparently balanced CCRs, suggesting the occurrence of genomic alterations in the proximity of breakpoints or elsewhere in the genome.[6,7] Similarly, the mother of the proband also revealed an apparently balanced CCR with phenotypic abnormality (deaf and mute).

As discussed by Karaman and Tos, children who inherit apparently balanced translocation from one of the parents have also the probability to exhibit mental retardation or congenital malformation. The attributable causes could be cryptic deletions, duplications, or the translocation break point leading to inactive genes, particularly unmasking a recessive allele inherited from the other parent.[8] Likewise, the proband inherited one of the apparently balanced translocations from the mother (translocation involving short arm of chromosome 2 and long arm of chromosome 12 at break points p16 and q22, respectively) and also showcased mental retardation and aphasia.

Advance molecular techniques such as whole chromosome painting (by fluorescent *in situ* hybridization), microarray, or comparative genome hybridization can play a significant role in the identification of exact amount of deviations from the normal pattern, especially in patients with phenotypic abnormalities, mental retardation having apparently balanced rearrangements.[6]

Chromosomal analysis was not conducted on the proband's mother up until this point in time despite being deaf and mute and experienced two miscarriages. She was only investigated to rule out origin of proband's apparently balanced karyotype. Karyotyping is an inexpensive technique, and hence, it should be the recommended preliminary investigation tool for patients with a history of children with mental retardation or developmental delay and also for couples with infertility and bad obstetric history like spontaneous abortions or repeated miscarriages.[7,9]

The genetic information obtained from chromosomal analysis and advanced molecular techniques can serve as good analysis tool, especially for balanced as well as unbalanced carriers of CCR's to understand the pregnancy outcome and for further counseling and management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Chen YJ, Zhang WW, Sun XM, Hu CJ. A rare complex chromosomal rearrangement in an oligospermic male: A case report and review of the Chinese literature. Asian J Androl 2014;16:325-6.
2. Iyer P, Vyas J, Ranjan P, Saranath D. A de novo complex chromosomal rearrangement of 46, XX, t (7;15;13)(p15;q21;q31) in a female with an adverse obstetric history. Int J Human Genet 2009;9:139-43.
3. Ngim CF, Keng WT, Ariffin R. Familial complex chromosomal rearrangement in a dysmorphic child with global developmental delay. Singapore Med J 2011;52:e206-9.
4. Gersen S, Keagle M. The Principles of Clinical Cytogenetics. New York, NY: Springer New York; 2013.
5. Zneimer S. Cytogenetic Abnormalities. 1st ed. New York, NY: John Wiley and Sons; 2014.
6. Pellestor F, Anahory T, Lefort G, Puechberty J, Liehr T, Hédon B, *et al*. Complex chromosomal rearrangements: Origin and meiotic behavior. Hum Reprod Update 2011;17:476-94.
7. Ranjan P, Desai K, Gada Saxena S. Derivative chromosome 11 in a child resulting from a complex rearrangement involving chromosomes 3, 6 and 11 in father: Significance of parental karyotyping. Indian J Hum Genet 2013;19:262-5.
8. Karaman A, Tos T. De novo three-way chromosome translocation [46, XX, t (1;20;4) (p32;q12;q32)] in a patient with developmental delay: A case report. Turk J Pediatr Dis 2013;7:7-10.
9. Bandopadhyay D. Chromosomal aberrations in mental retardation: A preliminary study. J Anat Soc India 2017;66:S23.