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CASE REPORT

Inherited Robertsonian translocation (13;14) in a child with Down Syndrome

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ABSTRACT

Background: Down's syndrome is a genetic disorder caused by abnormal cell division, resulting in extra genetic material from chromosome 21. Non-homologous Robertsonian translocation (RT) between chromosomes 13 and 14 is a common genetic abnormality seen in couples with reproductive failure. The present report highlights the co-occurrence of Down's syndrome with RT of chromosomes 13 and 14.

Case Presentation: A 6-month-old male child, born to second-degree consanguineous parents, was referred to our institute for the conventional karyotyping method. Peripheral blood cultures were set up following the standard protocol for karyotype analysis, which revealed Down's syndrome and non-homologous RT between chromosomes 13 and 14 in the child, inherited from his mother. A normal karyotype was found in the father.

Conclusion: The study highlights the importance of cytogenetic analysis in detecting additional chromosomal abnormalities in syndromic children.

Keywords: Developmental delay, Down's syndrome, karyotype, Robertsonian translocation.

Introduction

Down's syndrome is a chromosomal disorder caused by an error in cell division, resulting in the presence of an extra chromosome 21 or trisomy 21. It is the commonest autosomal chromosomal anomaly with an incidence of 1 in 600 to 1,000 live births in all races and economic groups. In this condition, the extra genetic material causes a delay in a child's physical and mental development. Although more than 90% of the cases show free trisomy 21, about 5%-6% are seen along with Robertsonian translocations (RTs) between D and G group chromosomes.

RTs are balanced structural chromosomal abnormalities caused by the fusion of two acrocentric chromosomes. Among 23 pairs of chromosomes, five pairs are acrocentric chromosomes placed in groups D and G of a karyotype. Translocations involving chromosomes 13, 14, and 14, 21 are the most frequently seen RTs in couples with reproductive failure (1). It has been estimated that 1/1,000 healthy persons may carry an RT. The latter are at a higher risk of producing unbalanced gametes due to chromosomes' non-disjunction during meiotic division, resulting in monosomic or trisomic fetuses. Balanced RT couples may have fertility problems and unfavorable pregnancy outcomes like miscarriages, stillbirths, offspring having mental disabilities, and uniparental disomy (2). RTs involving chromosome 21 may lead to translocation Down's syndrome. Here, we report a rare case of male Down's syndrome with co-occurrence of trisomy 21 and a maternally inherited non- homologous RT between chromosomes 13 and 14.

Case Presentation

The proband was a 6-month-old, only male child, born to second-degree consanguineous parents (uncle-niece once removed), who was referred to our institute. The proband's mother was 21-year old and the father was 22-year old at birth. The child's birth weight was 2.4 kg, presented with a normal cry, and a physiological jaundice history on the 4th day. The proband showed mild developmental delay by holding the head at 5 months of age and responding to a social smile at 6 months and facial dysmorphism. The clinical examination of the proband showed a weight of 5.6 kg, height of 60 cm, a head circumference of 42 cm, and an abdominal circumference of 44 cm, with mildly delayed milestones, depressed nasal bridge, hypotonia,

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small ears, protruding tongue, no simian crease, brachycephaly, and epicanthal folds.

Pedigree analysis

Three-generation pedigree of the proband was obtained and is shown in Figure 1.

According to Moorehead et al. (3), cytogenetic analysis of the child and parents' peripheral blood lymphocytes was carried out, and standard GTG banding was conducted. Twenty-five metaphases were screened using an Olympus BX53 microscope, and karyotype analysis was conducted using the ASI spectral imaging software; the results were interpreted as per ISCN 2016 nomenclature (4). The present study is in line with ICMR's ethical regulations approved by our Institutional Ethical Committee. Informed written consent was obtained from the proband's parents.

Karyotyping analysis of the proband revealed 46,XY, rob(13,14)(q10;q10)+21 chromosomal constitution in all the observed metaphases (Figure 2). As the proband showed a balanced translocation of rob(13;14)(q10;q10), along with the +21 (Trisomy 21) (46,XY, rob(13;14)(q10;q10)+21), parental karyotype was also analyzed for the possible inherited translocation. The chromosome analysis of the mother revealed a similar balanced RT with 45,XX, rob(13;14) (q10;q10) karyotype and father with a normal 46,XY karyotype (Figures 3 and 4).

Discussion

Down's syndrome is a chromosomal disorder characterized by the presence of an extra chromosome 21 or with the translocation of 21 with any acrocentric chromosome (13, 14, 15, and 22). Here, we discuss a rare case of Down's syndrome with a maternally inherited balanced RT between chromosomes 13 and 14. The mother was phenotypically normal and karyotypically showed balanced RT for chromosomes 13 and 14, which could be *de novo* as there was no family history of abortions or any other known bad obstetric history reported in the maternal side. Although carriers of rob (13;14) are phenotypically normal, there is a greater chance of infertility, aneuploid gametes formation, spontaneous abortions, and progenies with multiple congenital anomalies, mental retardation, and uniparental disomy-related complications (5).

Zhao et al. (6) carried out a study on the Chinese population in 872 cases of RTs, which revealed that 93% of the balanced translocations had problems of infertility, miscarriage, or offspring with known chromosomal abnormalities. Jaiswal et al. (7) reported a paternal transmission of rob(13;14) in a child with Down's syndrome with a soft sub-mucous cleft palate. The present study reports an inheritance of RT of chromosomes 13 and 14 from a carrier mother to a Down's syndrome child, a rare finding reported for the first time in Telangana. An

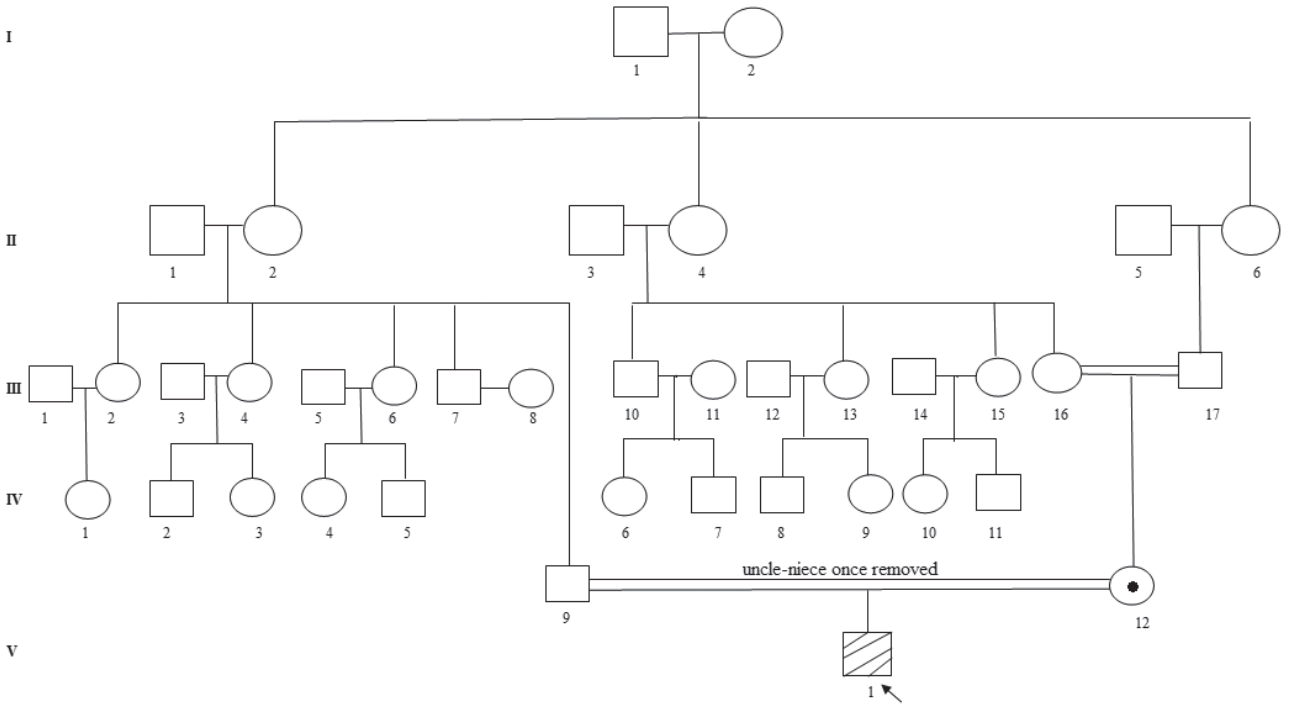

Figure 1. *Pedigree representing (IV-12) with 45,XX, rob(13;14)(q10;q10) karyotype in mother, (V-1) with 46,XY, rob(13,14)(q10;q10)+21 karyotype in proband (arrow), and (III-9) with normal karyotype of 46,XY chromosomal constitution in father.*

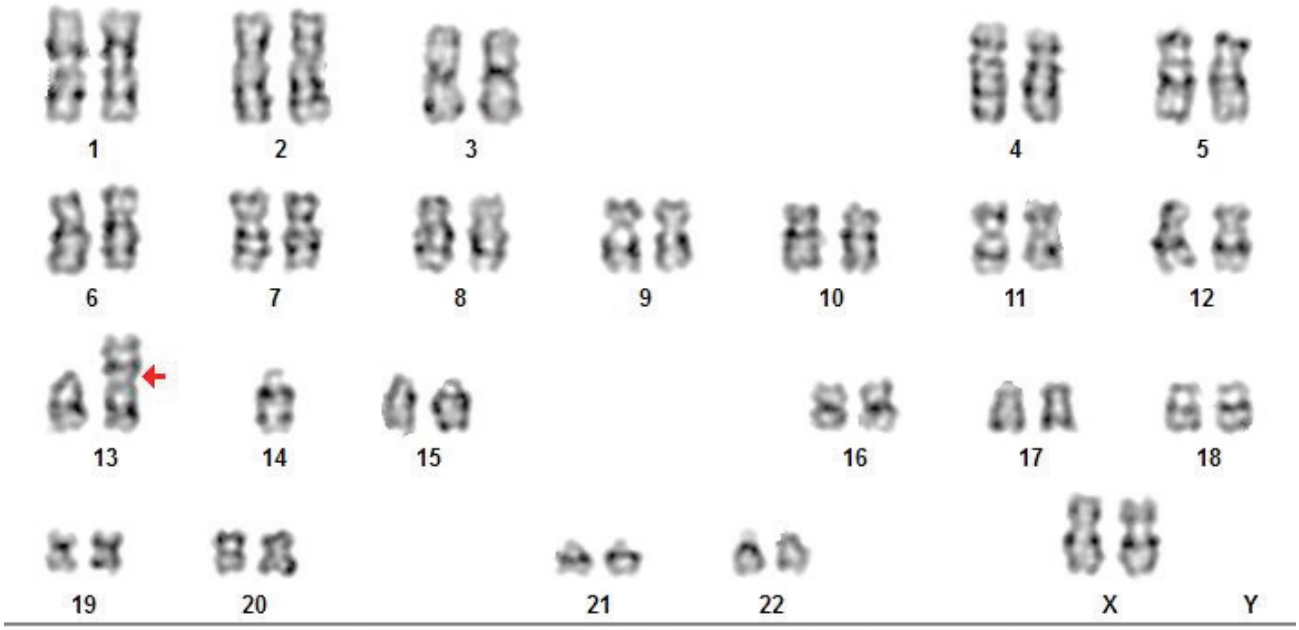

Figure 2. *Karyotype of the proband showing RT with trisomy 21 with 46,XY, rob(13;14)(q10;q10)+21 chromosomal constitution.*

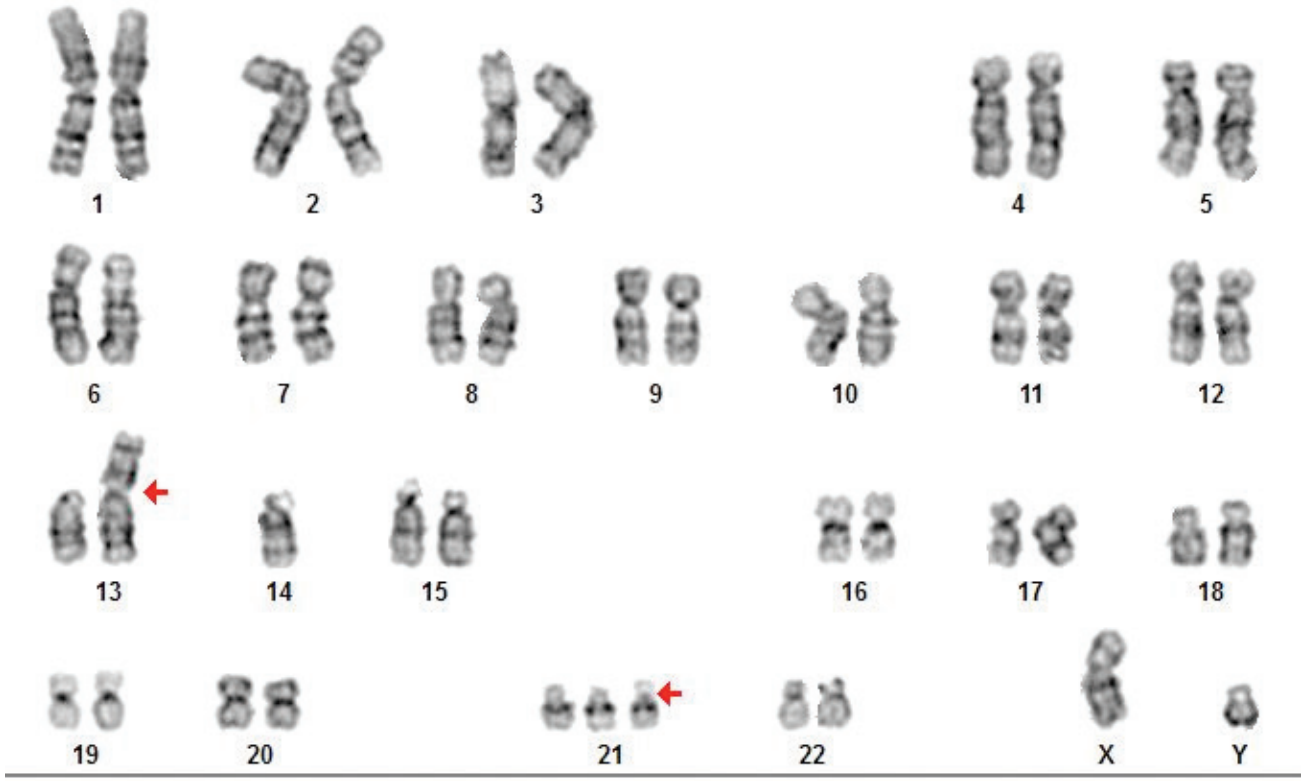

Figure 3. *Karyotype of the mother with RT and 45,XX, rob(13;14) (q10;q10) chromosomal constitution.*

increase or decrease in the diploid set of chromosomes in an offspring of rob t(13;14) carriers is due to an interchromosomal effect wherein a trivalent structure is formed by pairing of translocated chromosomes and two corresponding normal chromosomes during gamete formation at meiosis I, leading to both normal gametes and RT gametes (8). Gardner et al. (9) observed that, in carriers of such translocations, different modes of

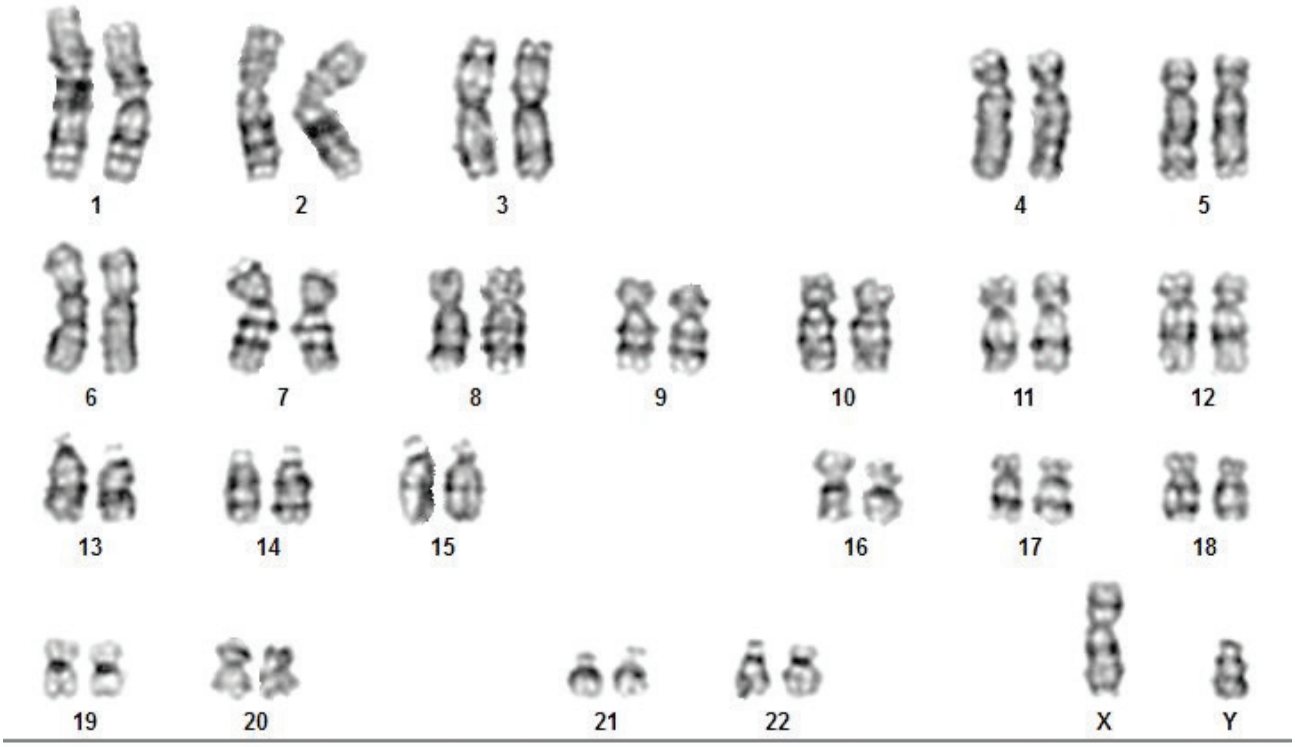

Figure 4. *Normal karyotype of the father with 46,XY chromosomal constitution.*

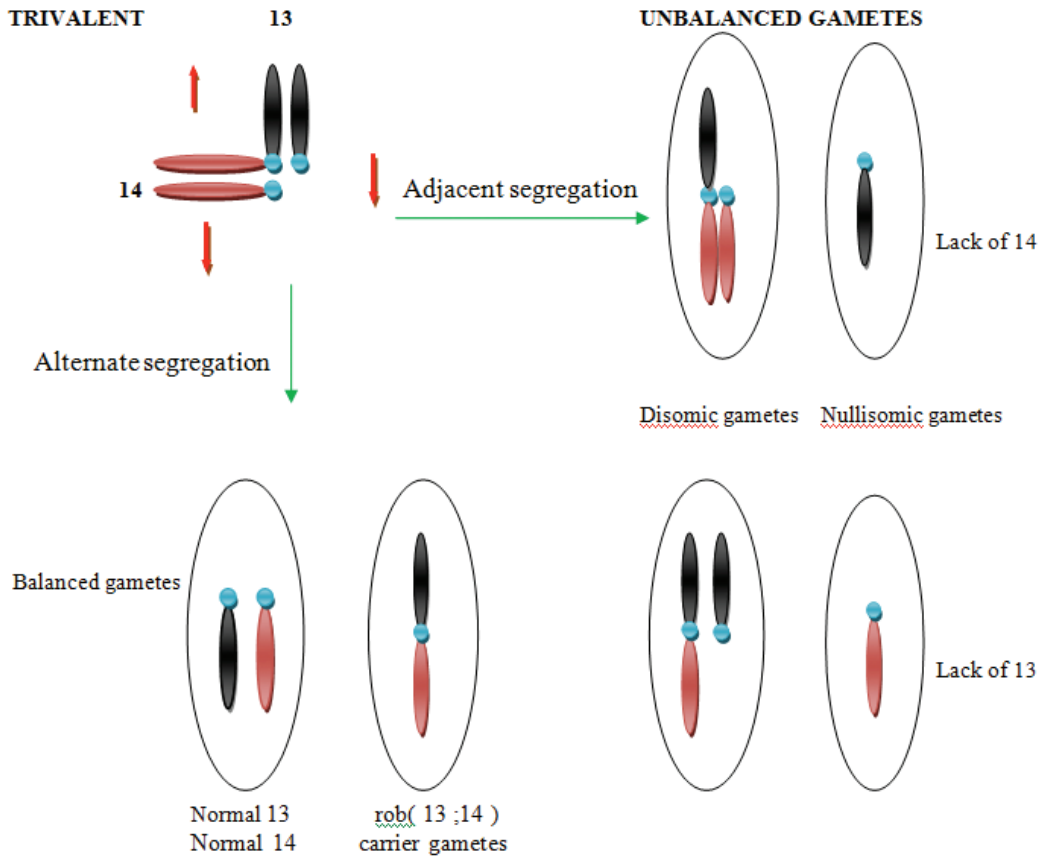

Figure 5. *Meiotic segregation of a female with rob(13q;14q) heterozygote.*

segregations are expected at the end of meiosis I for the translocated and non-translocated chromosomes, which would result in the formation of either balanced (alternate segregation mode) or unbalanced (adjacent 1, adjacent 2, and 3:1 segregation modes) gametes. Only products of alternate segregation have normal/balanced gametes.

The RT creates four different types of gametes (Figure 5). A normal and a carrier gamete are formed due to balanced translocations, whereas disomic and nullisomic are possible with unbalanced translocations (10). A study by Keymolen *et al.* (11) indicated an increased risk for chromosomal imbalance in RT carriers' pregnancies. The dysmorphic features observed in the proband could be due to the presence of trisomy 21 and a balanced RT between chromosomes 13 and 14.

Conclusion

In conclusion, this case report delineates a Down's syndrome child with the necessity of cytogenetic analysis of proband with inherited RT between chromosomes 13 and 14. Early detection of chromosomal aberrations by cytogenetic analysis helps the couple for appropriate genetic counseling. It allows them to make an informed reproductive decision on subsequent pregnancies, which enable them to prevent the distress of repeated abortions and implications on societal barriers.

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List of Abbreviations

ISCN	International System for Human Cytogenetic Nomenclature
RT	Robertsonian translocation

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Declaration of conflicting interests
The authors of this report have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Ethical approval
Ethical approval was obtained from Institutional Ethical Committee of Institute of Genetics and Hospital for Genetic Diseases, Osmania University, Begumpet, Hyderabad, India, Reference # 033/IEC/IOG/OU/14, dated: 18.06.2014.

Consent for publication
Informed consent was obtained from the patient's parents.

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