A Rare *De Novo* Robertsonian Translocation t(21q; 21q) in an Iranian Child With Down Syndrome: A Case Report

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Abstract- Down syndrome or trisomy 21 is the most common genetic disorder with a prevalence of 1 in 700 live-born infants. It is characterized by the intellectual disability of varying range, developmental delay, distinctive facial features and various physical abnormalities. The most frequent clinical features include hypotonia, short stature, short neck, upward slanting eyes, flat nasal bridge, bulging tongue, small ears and a single palmar crease of the hands. Mainly there are three cytogenetic forms of Down syndrome including free trisomy 21, mosaicism and Robertsonian translocation. We describe the case of a 1-year-old Iranian female child who presented to our genetic counseling center with intellectual and physical disabilities. The most common features of Down syndrome were present. The cytogenetic analysis confirmed the diagnosis, with detection of the Robertsonian translocation t(21q; 21q). The patient's parents were found to be both phenotypically and cytogenetically normal, so the identified Robertsonian translocation t(21q; 21q) probably have arisen *de novo*.

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Introduction

Down syndrome, also known as trisomy 21, is a genetic complex disorder and is due to a gene dosage effect of the whole or part of the third copy of chromosome 21. It is the most common and best known autosomal chromosome abnormality in humans which is usually caused by an error in cell division (1,2). The overall incidence of Down syndrome is 1 in 700 live births, but it varies in different populations. Advancing maternal age could increase the risk of Down syndrome (3).

Down syndrome is characterized by physical and mental retardation. Physical symptoms include low muscle tone, short stature, short neck, upward slanting eyes, flat nasal bridge, bulging tongue, small ears and a single crease across the palm of the hand. Patients have mild to moderate cognitive impairment. Language is delayed, and both short and long-term memory is affected. Down syndrome is also associated with a wide range of health challenges, including heart defects, endocrine problems, hearing loss, immunodeficiency, poor eyesight, gastrointestinal abnormalities, and a heightened risk of early-onset dementia (4). Here, we report an Iranian female patient with Down syndrome due to a rare *de novo* Robertsonian translocation t(21q; 21q).

Case Report

The proband is a 1-year-old Iranian girl, born at full term with a cesarean section (Figure 1). She was the first child of her apparently healthy, non-consanguineous and young parents (age at the child's birth: mother 21 yrs, father 24 yrs). Family history was unremarkable on both the maternal and paternal sides. The pregnancy was normal. Although the results of screening tests showed an increased risk for Down syndrome, amniocentesis was not done. On physical examination, the newborn's birth weight was 2,680 g (10^{th} centile) and the length was 50 cm (50^{th} centile). At the clinical assessment at the age of 1-year-old, we observed hypotonia, short

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neck, brachycephaly, short and broad hands and fingers, palmar simian crease and short statue. She had delayed developmental milestones. The parents noticed a delay in achieving neck control. Hearing and vision were normal. Also, the results of all biochemical tests were found to be normal. The face had dysmorphic features like flat face, short nose, low set ears, upward slanting palpebral fissures, flat nasal bridge, and a large tongue suggestive of Down syndrome.

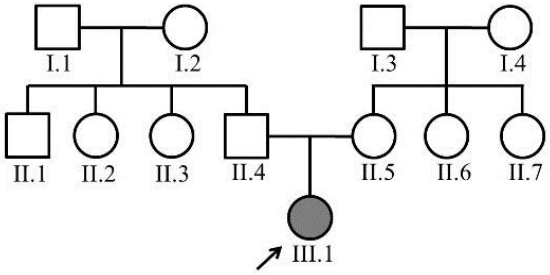

Figure 1. Family pedigree. Squares and circles represent males and females, respectively. An arrow indicates the proband. The filled symbol refers to the patient (III.1) and clear symbols represent normal individuals

Since the patient had phenotypic features of Down syndrome, karyotyping was ordered. The result came as 46, XX, der (21;21) (q10;q10),+21 (Figure 2), which confirmed the diagnosis of Down syndrome. The results were explained to parents during a genetic counseling session. To determine the origin of the translocation, chromosomal analysis of both parents was necessary. After obtaining written informed consent, parental blood samples were taken, and karyotype tests were performed. Karyotypes from both the parents were normal, so the identified Robertsonian translocation t(21q;21q) probably have arisen *de novo*.

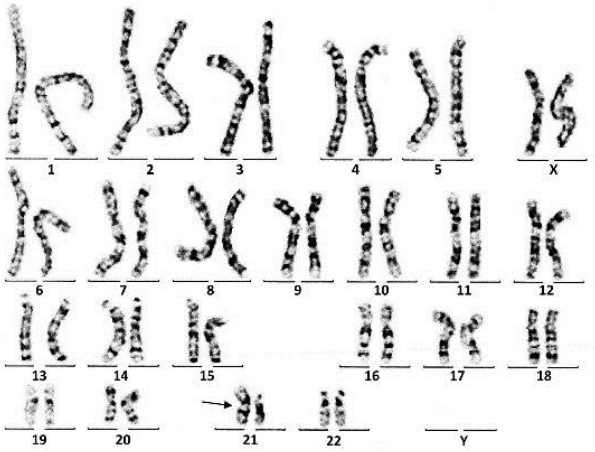

Figure 2. Karyotype of the patient showing 46, XX, der (21;21) (q10;q10),+21

Discussion

In the study described here, a 1-year-old Iranian Down syndrome patient with mental retardation, developmental delay and dysmorphic features were found to have a rare *de novo* Robertsonian translocation t(21q; 21q). The type of karyotypes in Down syndrome patients plays an important role in diagnosis and genetic counseling. In about 90% of the individuals, the chromosome consistency is an extra chromosome 21, whereas 6-7% of the Down syndrome cases show mosaic cell lines with different percentages of normal and trisomy cells. About 3% of the Down syndrome occurs due to Robertsonian translocation or rarely reciprocal translocation (5,6). Out of every 1,000 newborn babies, one has a Robertsonian translocation (7). Robertsonian translocations are an unusual type of chromosome rearrangement caused by two particular chromosomes joining together which mainly observed in group D acrocentric chromosomes including 13, 14, 15 and group G including 21 and 22 (8,9). Down syndrome due to Robertsonian translocation may either be *de novo* or inherited if one of the parents is the carrier (10).

The parental carrier status must be established to identify the origin of translocation and prevent the recurrence of the disease in the family. Balanced carriers of Robertsonian translocations are phenotypically normal, but they are at high risk of having chromosomally abnormal pregnancies. A carrier with t(21q;21q) Robertsonian translocation will always have a Down syndrome offspring (11).

Our patient's symptoms and presentation were typical of Down syndrome. Cytogenetic analysis of the patient revealed a karyotype of 46, XX, der (21;21) (q10;q10),+21. The peripheral blood karyotype of both parents was normal. Therefore, the Robertsonian translocation must have arisen either *de novo* or due to ovarian mosaicism. For *de novo* translocations, the recurrence risk to further offspring is minimal (overall 1%), which is similar to complete trisomy 21 (12). Genetic counseling could be done with assurance of little risk recurrence in the future but fetal karyotyping and well Down syndrome screening tests could be of great help in reducing recurrence (13).

In conclusion, we described the clinical and cytogenetic findings of a 1-year-old female Iranian child with Down syndrome due to a rare *de novo* Robertsonian translocation t(21q;21q), displaying mental retardation, developmental delay, and typical dysmorphic features. Both parents of the affected child had normal karyotypes, so the Robertsonian

translocation in this patient probably have arisen *de novo*.

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