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CASE REPORT

Down's Syndrome Presented with Transmission of Maternal Translocation of 2; 21 Chromosomes. A Case Report

Mohammad Moniruzzaman[1]*, Pallab Kumar Das[1], Mhabuba Akter[1], Jasmin Nur[1], Zeenat Farzana Rahman[1], Md. Sohrab Alam[1], Mansura Khan[1], M. Sawkat Hasan[2]

[1]Department of Immunology, BIRDEM General Hospital, Dhaka, Bangladesh, [2]Division of Laboratory Science, BIRDEM General Hospital, Dhaka, Bangladesh

Abstract

Background: Down's syndrome is a genetic condition marked by distinctive physical characteristics and some degree of cognitive impairment. Down's syndrome is mostly caused by trisomy of chromosome 21, while chromosome translocations are also frequent.

Objective: To evaluate a rare 2;21 translocation in the proband's family that was associated with Down syndrome.

Methods: Chromosomal analysis was carried out using the G-banding technique and traditional peripheral lymphocyte culture.

Case: The proband was a 9 months baby boy of non-consanguineous parents. The doctors clinically diagnosed him as having Down's syndrome with all typical features. The proband was found to have trisomy 21 associated with a 2;21 translocation inherited from his mother because his mother has the same type of translocation without any phenotypic features. Maternal age at the time of the study was 35 years and first pregnancy ended in stillbirth at 26th weeks of gestation, the proband was the second issue. His maternal aunt and cousin brother both had the same type of translocation. In chromosomal analysis, the proband's father and uncle had normal genotypic distribution. The current example was a Down's syndrome case with one normal 21 no chromosome and one Reciprocal translocation t (2;21).

Conclusion: The present case of Down's syndrome occurs due to reciprocal translocation (2;21) probably has arisen by familial transmission. Once an imbalanced translocation in the fetus/child has been found, the prenatal cytogenetic analysis is critical for the next pregnancies.

Keywords: Cytogenetics, Translocation, Down's syndrome, Karyogram.

Introduction

Down's syndrome is the most common chromosomal abnormality in humans, with distinct physical characteristics and some degree of cognitive handicap. Down's syndrome has been clinically recognized for around 150 years, and it is associated with trisomy 21, which was discovered 100 years later.[1] Down's syndrome represents the most common neurogenetic aneuploidy with three chromosomes 21 instead of two in the human leading to mental retardation.[2] Chromosome 21 is the smallest human autosomal chromosome, containing between 200 and 300 genes. The chromosome analysis found 127 recognized genes, 98 predicted genes, and 59 pseudogenes.[3] The genetic abnormality entails the creation of higher amounts of products from genes on chromosome 21 that have been over-expressed in Down's syndrome patient's cells and tissues, resulting in phenotypic abnormalities.[4] It affects around 9.8:10 000 live-born newborns in Europe and one in every 800 children is born with Down's syndrome.[5,6] The estimated prevalence of Down syndrome in the United States range from 12 per 10,000 and in 2002, 83400 children with DS aged 0–19 years lived in the United States.[7] There are two lac children with this syndrome in Bangladesh and incidence rises day by day. In DS patients, three kinds of cytogenetic trisomy 21 have been reported, with free trisomy 21 being the most prevalent, translocation trisomy 21 being the second most common, and mosaic trisomy 21 being the rarest.[8] The most prevalent are Robertsonian translocations 21q;21q, followed by 13q;21q, 14q;21q,

***Correspondence:** Mohammad Moniruzzaman, Assistant Professor, Department of Immunology, BIRDEM General Hospital, Dhaka, Bangladesh*

Email: drmonirbirdem@gmail.com

15q;21q, and Reciprocal translocations 8q;21q, which are also seen in some cases.[8] Trisomy 21 associated with translocation comes in two varieties: familial and de novo. In the familial form, a parent is a carrier of translocation and can transmit that translocation to the child in an unbalanced form, whereas in the de novo form, parents have a normal karyotype and the abnormal chromosome occurs as a spontaneous event in maternal meiosis I from a chromatid translocation.[9]

The case

A rare 2;21 translocations presented with Down's syndrome is reported in the Cytogenetics unit of the Immunology Department of BIRDEM General Hospital in 2022. The current proband, a 9-month-old boy from non-consanguineous parents, was referred to the Cytogenetics Unit of the Department of Immunology at BIRDEM General Hospital for cytogenetic testing. Proband's maternal and paternal ages at birth were 35 and 41 years, respectively. The child had a delayed developmental milestone and a history of repeated respiratory tract infections. We found a characteristic mongoloid face, a depressed nasal bridge, a low set ear, hypotonic motor activity, poor neck control, and simian crease in both hands (Figure-1).

Figure-1: Photograph of the proband showing Down's syndrome features. (Annexed 01: Consent form)

The child had no heart abnormalities in echocardiography and thyroid function abnormalities. Clinically proband was diagnosed as Down's baby and in the cytogenetic analysis we found 47, XY, +21,t(2;21) in this proband. He was the second baby in his family and the first issue was a male baby stillbirth at 26th weeks of gestation. The proband's mother, first cousin aunty (26 years), and cousin brother (5 months) on his maternal side all had the same sort of translocation. Here females were carriers with trisomy 21 associated with a 2;21 translocation and their male babies had the same type of translocation with Down's features which indicate a familial form of genetic transmission. In chromosomal analysis, the proband's father (43 years) and uncle (30 years) had normal genotypic distribution and they were originated from different families (Figure-2).

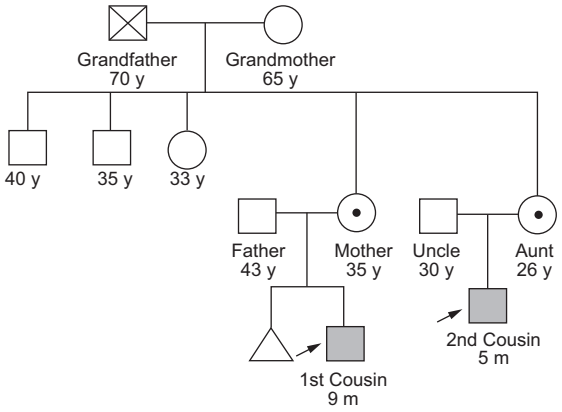
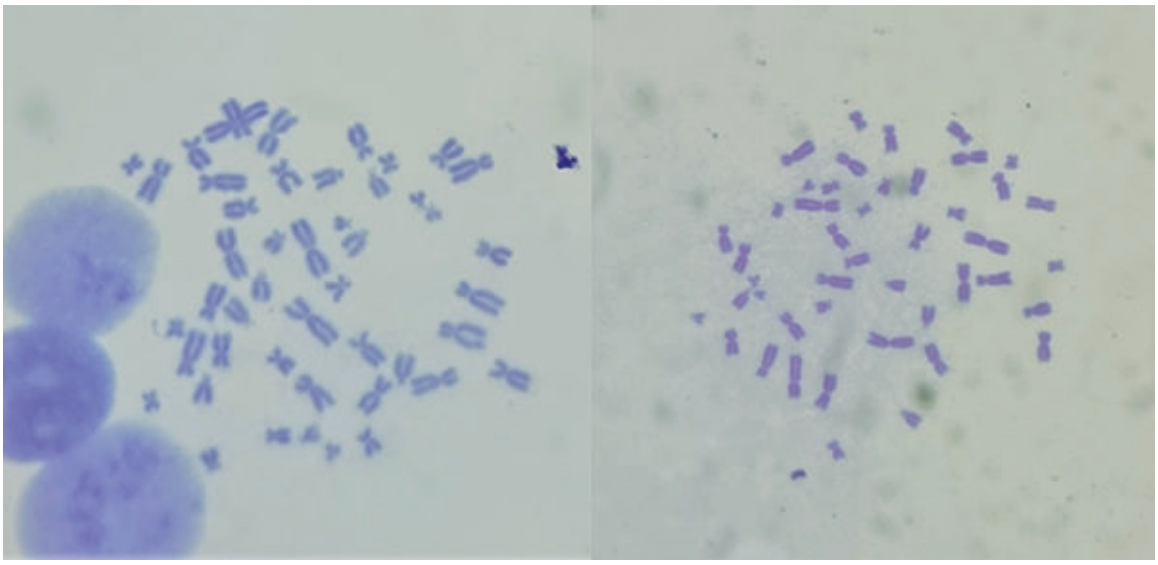


Figure-2: Pedigree chart of the patient's family.

For chromosomal analysis, conventional peripheral lymphocyte culture was done by the standard method using the G-banding technique. The protocol employed for karyotyping was as follows: about 2 ml of heparinized blood was collected in a syringe from the peripheral veins of the referred patient. Lymphocytes were grown in PB-MAX ™ karyotyping medium (Containing Optimized RPMI 1640 medium, supplemented with Fetal Bovine Serum, L-glutamine, and phytohemagglutinin) manufactured by Life Technologies Corporation, USA. The samples were incubated for 72 hours at 37°C in a 5% CO2 incubator (Forma Scientific, USA). The cells were arrested at the metaphase stage of the cell cycle with 0.1% colchicines after the incubation. Then after one hour of incubation (with colchicines) the cells were treated with KCL hypotonic solution. After that, the cells were fixed by three times wash with a fixative solution (3:1; methanol: glacial acetic acid). The slides were then stained with Giemsa and air dried. Chromosome analysis was done under 100X magnification and at least 70 metaphase spreads were screened. In the cytogenetic analysis we found 47, XY, +21,t(2;21) in this proband and his mother (Figure-3).



(a) (b)

Figure-3: Chromosomal distribution of the proband (a) and his mother (b).

After that we sent this proband blood sample to Dr. Lal PathLabs laboratory for an automated banding karyogram and they revealed 47,XY,+21,t(2;21)(p21;q22) an abnormal male chromosome complement in all cells examined with two normal copies of 21 and an additional copy of 21. Also, a balanced reciprocal translocation between the p arm of chromosome 2 and the q arm of chromosome 21 at breakpoints 2p21 and 21q22, respectively was observed (Figure-4).

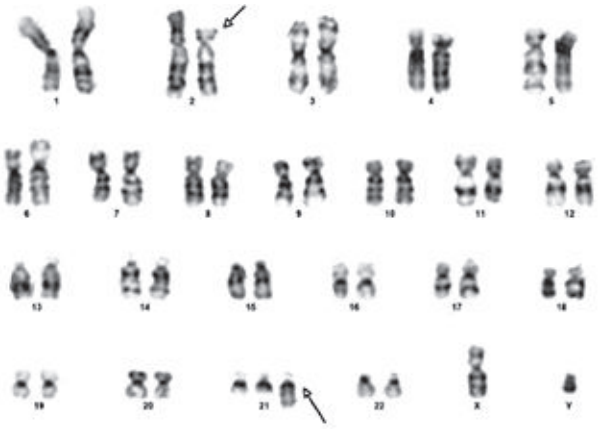


Figure-4: Karyogram of the proband showing 47,XY,+21,t(2;21)(p21;q22)

Discussion

In Down's syndrome, translocation frequently featured a Robertsonian translocation between chromosome 21 and other acrocentrics. Reciprocal translocation in Down's syndrome is relatively rare and results from the exchange of fragments between two chromosomes without any gain or loss of genetic information. It is a common type of chromosomal abnormality, occurring in approximately one in every 625 babies.[10] A reciprocal translocation, t(4;21)(q27;p11), is described that occurs in a balanced carrier mother and her Down syndrome child, 47,XX,t(4q-;21p+),+21.[11] Pazarbasi and his colleagues reported the inheritance of a translocation between chromosomes 3 and 21 in a family with one of two fetuses with Down's syndrome carrying the same translocation 47,XX,+21, t(3;21)(q21;q22) and the other also carrying the same translocation without the additional chromosome 21.[12] Autosomal reciprocal translocations have been proposed as the most common chromosomal abnormalities in couples, with the mother being the main carrier in the majority of cases. The most common abnormality (2.9%) among couples with recurrent pregnancy loss was autosomal balanced reciprocal translocations.[13] Carriers may be identified as a result of repeated miscarriages with or without healthy and/or affected children.[14] Kovaleva discovered that carriers of balanced reciprocal translocations are more likely to have trisomy 21 offspring.[15] In our situation, carrier mothers had a nearly normal phenotype, while their kids had trisomy 21 with Down's syndrome traits. Stillbirth was the initial issue in the first carrier, and proband was the second issue. This stillbirth could have been caused by an imbalanced

translocation; however, there was no prenatal diagnosis and investigations were undertaken. Once an imbalanced translocation in the fetus/child has been found, the prenatal cytogenetic analysis is critical for the next pregnancies.[13]

The cytogenetic analysis of amniotic fluid cells can successfully prevent the birth of infants with chromosomal disorders and lower the risk of congenital abnormality.[16]

Conclusion

The present case of Down's syndrome occurs due to reciprocal translocation (2;21) probably has arisen by familial transmission. If a couple has a known chromosomal rearrangement and is in a high-risk group, such as advanced maternal age, prenatal diagnosis is important. Cytogenetic studies on other members of the carrier family, as well as thorough genetic counseling, are recommended.

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Annexed 01: Consent form

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Ibrahim Memorial Diabetes Centre, 122, Kazi Nazrul Islam Avenue, Dhaka-1000, Bangladesh
Phone : 880 -2- 58616641-50, 9661551-60 Fax : 880-2-9667812, E-mail : dg-birdem@dab.bd.org