

Down Syndrome and Recurrent Abortions Resulting from Robertsonian Translocation 21q21q

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Robertsonian translocation 21q21q was found in a woman who had multiple pregnancies in which the outcome was either Down syndrome or abortion. Three live children had Down syndrome and there were five spontaneous abortions.

Down syndrome occurs in approximately one of 750 live births¹ and is associated with a variety of karyotypes. Approximately 92.5% have simple trisomy-21, while in about 4.8% the extra chromosome 21 material is present in the form of an unbalanced Robertsonian translocation or as an isochromosome of the long arm of chromosome 21. The remaining 2.7% are heterogenous and include mosaicism, double trisomies and reciprocal translocations.³

The short arms of an acrocentric chromosome are particularly prone to breakage and the production of structural abnormalities and most instances of translocation Down syndrome involve two acrocentric chromosomes. Most have been translocation of chromosome 21 to a D group chromosome or another G group chromosome.⁴ Rare instances have constituted the formation of an isochromosome. In the years prior to banding, it was not possible to know if the G group chromosome was a 21 or 22, so precise information is available in only a small number of families. Hecht² provided meiotic evidence that a 21/G translocation was 21/21, commenting that previous evidence was purely statistical. Banding has, of course, made the distinctions secure. A 21q21q may originate de novo through a recombination of two chromosomes at the region of the centromere. Two possible mechanisms for this include fusion of two chromosomes without loss of genetically active material or exchange between the long arms of sister chromatids. In either case, the loss of the centromere raises the possibility that break points may be situated such that there is some loss of chromosomal material. An error in the division at the centromere at the second meiotic division or the formation of an unstable

telocentric chromosome at the first division may result in an isochromosome.⁴ We observed t(21q21q) in a Saudi mother of three infants with Down syndrome who has a history of five spontaneous abortions.

Case Report

A 24-year-old Saudi female was referred to the Obstetric Department of King Faisal Specialist Hospital and Research Centre because of her pregnancy history. She had eight pregnancies, five of which ended in abortion (Figure 1). All three live born infants had Down syndrome. Of these, two died within the first year of life with complex congenital heart disease. In the most recent pregnancy, a karyotype was performed and the mother was found to have the t(21q21q). She delivered an infant with Down syndrome at term and this female infant had congenital heart disease. There was a complete atrioventricular canal, double outlet right ventricle, primary atrioseptal defect and ventricular septal defect. Surgical intervention was not possible. The family history was otherwise negative in both parents with regard to congenital malformation, recurrent abortion or mental retardation.

Chromosomal Analysis

Chromosomal preparations were made and banded using standard techniques for the mother and the infant. The karyotype of the mother was 45XX, t(21q21q) with a balanced translocation involving the homologues of

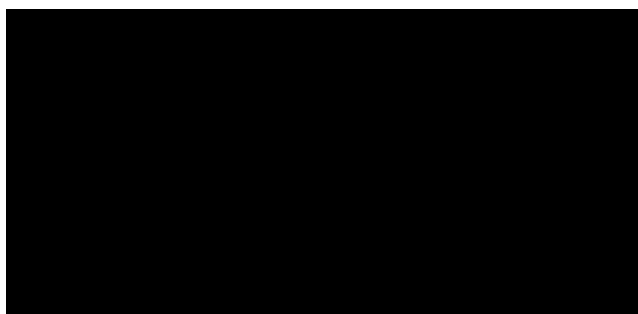


FIGURE 1. Pedigree of the family. The mother had a balanced duplication of chromosome 21. The spontaneous abortions are indicated by the small circles. All of the live-born infants had Down syndrome and all died.

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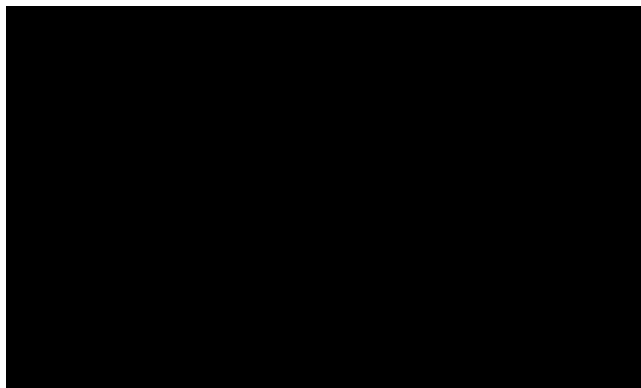


FIGURE 2. Karyotype of the mother indicating the Robertsonian translocation of chromosome 21.

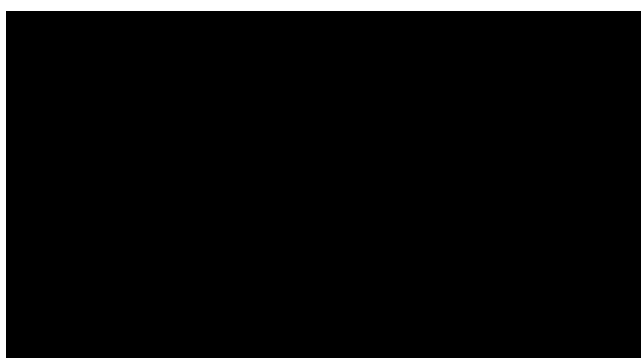


FIGURE 3. Karyotype of the infant who was trisomic for chromosome 21 because of the presence of the translocation chromosome and the paternal 21.

chromosome 21 (Figure 2). The karyotype of the infant was 46XX, -21, +(21q21q) (Figure 3). Chromosomal analyses had not been done on any of the aborted fetuses which had all occurred prior to the cytogenetic analysis of the mother.

Discussion

Balanced Robertsonian translocation between homologous chromosomes are rare.^{4,5} Carriers of this anomaly are phenotypically normal, as in our family, and have 45 chromosomes. Recent studies with molecular probe markers indicate that the duplicated allele studies were homozygous, indicating that the translocation was between sister chromatids of the same chromosome 21.⁵ Molecular identification of the break points indicated that there is a certain incidence of partial deletion in the formation of these fused chromosomes.^{5,6} Furthermore,

there was a significantly increased incidence of crossing over in meiosis in female translocation carrier parents.⁶

Carriers of duplications of chromosome 21 cannot produce normal children because their gametes are either nullisomic or disomic; the risk of abortion or an infant with Down syndrome is 100%. Abortions at an early gestational age have been attributed to monosomy and the fetuses are assumed to be nonviable.^{7,8} Transmission of (21q21q) to offspring is not always from the mother; there are reports of paternal transmission.^{8,9} The resulting pattern of Down syndrome and abortion would be the same as with transmission from the mother. Moreover, Sudha and Gopinath¹⁰ reported balanced Robertsonian translocation between two couples with a history of repeated abortions. The male partner of one couple and the female partner of another couple exhibited this anomaly. They found that the translocation (21q 21q) was transmitted to their live children with Down syndrome.

Genetic counseling in these situations is difficult because normal children from affected parents have not been reported. In these instances, couples may decide not to have children.

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