

Cumhur GÜNDÜZ¹
Ferda ÖZKINAY²
Özgür ÇOĞULU²
Gül SAPMAZ¹
Tufan ÇANKAYA²
Cihangir ÖZKINAY²

A Father Born to Consanguineous Parents Had Double Translocation 21;22 [44,XY, t(21q;22q), t(21q;22q)] Due to Familial Translocation in Four Generations

Departments of ¹Medical Biology, ²Pediatrics, Subdivision of Genetics and Teratology, Faculty of Medicine, Ege University, İzmir - TURKEY

Received: February 02, 2000

Key Words: Double translocation, Down Syndrome

Robertsonian translocations are the most common translocations found in humans (1). The breakpoints forming these rearrangements are at or near the centromers of both chromosomes involved. The carriers of Robertsonian translocations are usually normal in other respects. Such a translocation of chromosome 21 to the other chromosome 21 or to one of the other acrocentrics is frequently a cause of familial Down Syndrome (2-4).

Biparental inheritance of Robertsonian translocations, which involves the same chromosomes in both parents, has only been reported very rarely (5).

Here we present a phenotypically normal male with a unique karyotype of 44,XY,t(21q;22q),t(21q;22q). The parents of the presented case were first cousins who were considered to have inherited this translocation from common ancestry.

A 37-year-old woman and her husband were referred to the genetics subdivision in order to have genetic counseling because her fetus had a chromosome composition of 45,XX,t(21q;22q). This was the 6th pregnancy of the mother. She had given birth to 2 healthy children and she had undergone 3 abortions within the first trimester. Both parents were investigated for balanced translocation and the chromosome composition of 44,XY,t(21q;22q),t(21q;22q) was detected in the father (Fig. 1). The mother's karyotype



Figure 1. Karyotype of double translocation carrier male.

was normal. Pedigree analysis revealed that the parents of the father were first cousins (Fig. 2). The sister of this double translocation carrier father had had a daughter with Down Syndrome. Hospital records showed that she had the karyotype 46,XX,-22,t(21q;22q) (see pedigree, I-2). When the diagnosis had been established in this Down Syndrome child, the parents were investigated and the maternal inheritance of the translocation was shown. During genetic counseling with this family, other family members at risk of being translocation carriers were advised to undergo chromosomal analysis. Although the situation was explained in detail, the family members refused any cytogenetic study.

The male carrying the double translocation refused to bring his phenotypically normal children for cytogenetic study.

Balanced or unbalanced double translocation carriers have occasionally been reported (6-9). Most of these were double translocation heterozygotes and reciprocal translocations. Double translocation homozygosity is extremely rare. In a review of the literature, only one case was found to have two translocations involving the same acrocentric chromosome (5).

In the report of Rajangam et al. the index case was diagnosed as having Down Syndrome with the karyotype 45,XY,der (14;21) (p11.1;p11.1) pat,der (14;21) (p11.1;q11:1). The parents in this case were not consanguineous. The authors also confirmed nonconsanguinity using both cytogenetic and molecular genetic techniques (5). In a case of parental consanguinity, theoretically, double translocations involving the same chromosomes are expected to be more common. To date there have been no reported cases exhibiting pedigree and cytogenetic features similar to those found in our case.

Pedigree analysis of our case revealed a family member with translocation Down Syndrome (Fig. 2, I-2), which can be expected in such a family.

The cytogenetic analyses of the individual with DS (Fig. 2, I-2) and her parents had been done 6 years previously and it was shown that the translocation had been inherited from the mother. At that time, although the family members at risk of being translocation carriers were invited for genetic counseling, none of them in fact came for counseling.

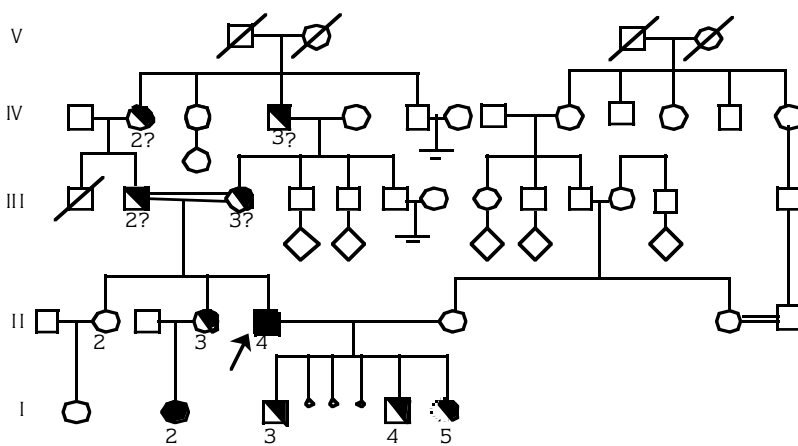


Figure 2. Pedigree.

- I2: 46,XX,t(21q;22q) I3: 45,XY,t(21q;22q)
- I4: 45,XY,t(21q;22q) I5: 45,XX,t(21q;22q)
- III3: 45,XX,t(21q;22q) II4: 44,XY,t(21q;22q),t(21q;22q)
- II2, III2,3 IV2,3: Could not be analyzed

Until chromosomal analysis was carried out on the fetus (Fig. 2, I-5) due to advanced maternal age, the double translocation carrier male presented here was unaware of his condition.

After his chromosomal constitution was identified, it was suggested that his two healthy children (Fig. 2, I-3, I-4) have cytogenetic analysis, but he refused to bring the children to the hospital. When taking into consideration the pedigree, we can say that these two children are obligate carriers and have a high risk of having a DS child. The father was warned of this possibility.

The family had also had three early pregnancy losses. There is no possibility of the father having offspring with only trisomy 21. Both trisomy 21 and 22 or both monosomy 21 and 22 may be present in his offspring and these might be responsible for the recurrent early miscarriages in this family.

Correspondence author:

*Cumhur Gündüz
Ege University, Faculty of Medicine,
Department of Medical Biology
Bornova İzmir 35100 TURKEY*

References

1. Motulsky V: Human Genetics, 3rd ed., Springer Co. London, 1996, 589.
2. Friedman JMI, Dill F, Haydan MR, Mc Gillivray BC: Genetics, Harwal Publishing Co, Malvern, Pennsylvania 1992, 36-7.
3. Erciş M, Balcı S. Can a parent with balanced Robertsonian translocation t(21q;21q) have a non-Down's offspring? Lancet 353 (9154): 751, 1999
4. Balcı S, Beksaç S, Altaş D. An unusual familial chromosomal translocation in both parents: mother 45,XX,t(14q;21q), father 46,XY,t(1:4)(p36.1;p14). Result of eleven pregnancies (the last child had 45,XX t(14q;21q)del(4)(p14) Wolf Hirschorn Syndrome) with clinical, cytogenetic and postmortem findings. Cytogenet Cell Genet 85: 575, 1999
5. Rajangam S, Michaelis RC, Velagaleti GVN, Lincol S, Hegde S, Lewin S, Tarkton J, Thomas IM. Down Syndrome with biparental inheritance of der(14q21q) and maternally derived Trisomy 21: Confirmation by FISH and microsatellite polymorphism analysis. Am J Med Genet 70: 43-47, 1997.
6. Bijlsma JB, de France HF, Bleeker-Wagemakers LM, Dijkstra PF. Double translocation t(7;12).t(2;6) heterozygosity in one family. A contribution to the trisomy 12p Syndrome. Hum Genet 40: 135-47, 1978.
7. Couzin DA, Watt JL, Auchterlonie IA. A complex double translocation involving four chromosomes and five breakpoints in a child with mild mental retardation. J Med Genet 20: 389-92, 1983.
8. Bourrouillou G, Rolland M, Colombies P. Secondary 18p2 due to a paternal double translocation. J Genet Hum 31: 243-9, 1983.
9. Siadeer I, Nivalon-Chevallier A, Mugneret F, Turc-Carel C. Double translocation 46,XX,t(2;5).t(2;8) with major reproduction problems. J Genet Hum 36: 89-92, 1988.