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Short Report

Volkan BALTACI[1]
Didem AKYOL[1]
Sedat KADANALI[2]

Risk Assessment and Prenatal Diagnosis in a Recent Pregnancy in a Family with a Child with Down Syndrome due to t (21q;21q)

[1]Dr. Zekai Tahir Burak Women's Hospital Ankara,
[2]Department of Obstetrics and Gynecology, Faculty of Medicine, Atatürk University Erzurum-Turkey

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Down syndrome, or trisomy 21, is by far the most common and best known chromosome disorder and is the single most common genetic cause of moderate mental retardation. About one child in 800 is born with Down syndrome, and the incidence is much higher among the live births or fetuses of mothers 35 years of age or older (1).

About three quarters of all Down syndrome conceptuses are lost through spontaneous abortion either in the first trimester or, less frequently, later in pregnancy, and many live-born children with the syndrome die in early postnatal life (1).

The clinical diagnosis of Down syndrome usually presents no particular difficulty. Nevertheless, karyotping is indicated for confirmation and to provide a basis for genetic counseling. Although the particular karyotpe responsible for Down syndrome has little if any effect on the phenotype of the patient, it is essential for determining the risk of recurrence (1).

We here present a family with a boy with 21q;21q-type translocation of Down syndrome. He was six years old. His clinical presentation included the classical findings of Down syndrome. We found 46,XY, -21, + t(21q;21q) chromosomal consitution in all metaphases obtained from peripheral blood cells of the child (Figure 1). Then we examined his parents. Both spouses were 32 years old. They were healthy people with no consanguinity between them. Following cytogenetic studies, it was determined that they were not carriers for 21q;21q translocation. Their chromosomal structures were normal. The boy's mother was admitted counseling for her most recent pregnancy; from her history we learned that the had gravidity 3, parity 1, and D&C 1. The second pregnancy was terminated by D&C at the 7th week of gestational age at the parents' wishes two years ago. This pregnancy was at the 15th week of gestational age. We performed amniocentesis during the 16th week of gestational age; fetal karyotype revealed 46,XX. This pregnancy resulted in the birth of a healthy female child. After delivery, cytogenetic tests were conducted on chord blood to confirm the amniotic results. The results of the tests were identical.

In about 95% of all patients, Down syndrome involves trisomy for chromosome 21, resulting from meiotic nondisjunction of the 21st chromosome pair (1). A 21q:21q translocation chromosome is a chromosme made up of two long arms of chromosome 21, seen occasionally in Down syndrome carriers or patients (1). It is thought to originate as an isochromosome rather than by Robertsonian translocation (an attachment of two different chromosome 21 homologues). Although this is a rare abnormality, it is particularly important because all gametes of a carrier of such a chromosome must eitherontain the 21q:21q chromosome with its double amount of chromosome 21 genetic material, or lack it and have no chromosome 21 representative at all. The potential progeny inevitably have either Down syndrome or monosomy 21, which is rarely viable (2, 3). An individual unfortunate enough to have this defect is unable to have normal children and will probably have only children with Down syndrome (1).

The recurrence risk for Down syndrome is about 1% in the case of a previous offspring with trisomy 21 and minimal in case of de novo 21q:21q translocation (4). For this reason we performed amniocentesis during the 16th week of gestational age; thus we also eliminated the chance of Down syndrome which might have originated from paternal or maternal gonadal mosacism. Although

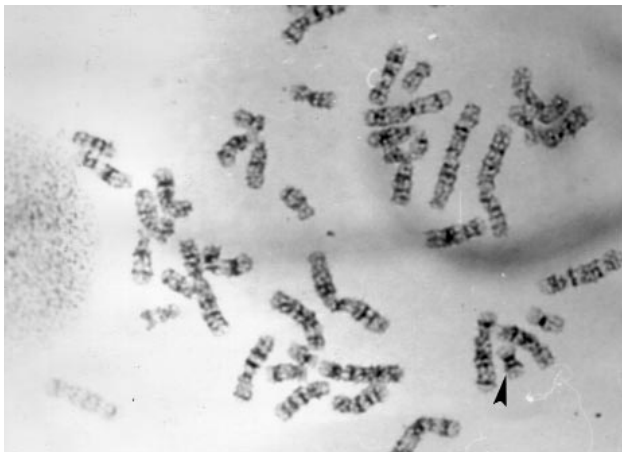

Figure 1. Metaphase plaque (GT-banding). The 21q;21q translocation is shown with an arrow.

the mother's and the father's chromosomal structures obtained from peripheral blood lymphocytes were found to be normal, we performed amiocentesis to eliminate gonadal mosaicism. In genetic counseling, the posibility of an elevated recurrence risk due to gonadal mosaicism in one of the parents should be considered (4). If one spouse was a carrier of 21q:21q translocation, this family would certainly have a baby with Down syndrome. On the other hand, nearly all 21q:21q translocations and isochromosomes (more than 95%) occur de novo and the larges class of de novo chromosomal rearrangements in Down syndrome is 21q;21q translocation (5). Furthermore, a Robertsonian translocation between two 21st chromosomes can not be distinguished from an isochromosome composed of genetically identical arms by cytogenetic analyses (6). Molecular techniques are necessary for differentiation between Robertsonian translocations and isochromosomes. To distinguish between Robertsonian 21q;21q translocation and isochromsome 21q, Restriction fragment length polymorphisms (RELPs) spanning the length of chromosome 21 are lost frequently used for distinguishing between Robertsonian translocations and isochrome 21q.

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