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Case Report

Uniparental disomy resulting from heterozygous Robertsonian translocation (13q14q) in both parents

Mir Davood Omrani, Soraya Saleh Gargari***

Abstract

Uniparental disomy (UPD) is a situation in which both members of a chromosome pair are inherited from one parent. This study has been conducted on a family with a five year-old healthy girl and a mentally retarded boy. The parents were first cousins and they both had Robertsonian translocation between their long arm of chromosome 13 and 14 [45, XY t (13q14q)]. Their affected son had a similar karyotype. Their daughter's karyotype revealed the presence of a homozygous Robertsonian 13/14 translocation 44, XX t (13q14), t(13q14q). According to the clinical findings it is possible to conclude that the affected boy suffers from UPD.

KEY WORDS: Robertsonian translocation, uniparental disomy, chromosome 14.

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In 1916, for the first time an American insect cytogeneticist, W.R.B. Robertson, stated that the translocations of chromosomes are the results of the fusions of two acrocentrics chromosomes. Therefore, in his honor this type of translocation was named Robertsonian (Rob) [1]. The frequency of this type of translocation in the general population in new borns is about 1 in 1000 [2]. The presence of this type of translocation in the parents could lead to the birth of children with uniparental disomy (UPD). UPD is an abnormal situation in which both members of a chromosome pair are inherited from one parent and the other parent's chromosome for that pair is missing [3]. UPD usually arises from the failure of the two members of a chromosome pair that are not able to divide properly into two daughter cells during the meiosis in the parent's germline (nondisjunction). Since the majority of the nondisjunction occurs in the maternal meiosis I,[4,5] it is more likely for a trisomy to consist of two maternal chromosomes and one paternal chromosome. The first report of UPD in humans was found in a child who had cystic fibrosis (CF) due to the inheritance of two identical copies of chromosome 7 from his mother and no contribution from his father's chromosome [5].

Maternal UPD 14 has been reported in association with mosaicism, Robertsonian translocations and isochromosomes [5,6,7]. Individuals with maternal disomy 14 have short stature, hypotonia, hyperextensible joints, scoliosis, minor facial dysmorphic features, mild developmental delay and precocious puberty [8]. Individuals with paternal disomy 14 have a more severe phenotype than those with maternal disomy 14; Which include mental retardation, skeletal abnormalities (that result in short-limb

*Associate Professor, Department of Genetics, Uremia University of Medical Sciences, Uremia, Iran.
**Assisstant Professor, Department of Obstetrics and Gynecology, Uremia University of Medical Sciences, Uremia, Iran.
Correspondence to: Dr Mir Davood Omrani, Associate Professor, Department of Genetics, Uremia University of Medical Sciences, Uremia, Iran. e-mail: davood_omrani@umsu.ac.ir

dwarfism with narrow thorax), it also includes decreased survival rates due to the respiratory difficulties, dysmorphic facies, and scoliosis [8]. The patients with paternal disomy 14 have been diagnosed following the identification of Robertsonian translocations or isochromosomes which involve chromosome 14.

The occurrence of this translocation in both parents is highly unlikely and we have only one report of this case by Martinez-Castro and his collogues in 1984 [9].

In this study, we present a family with translocation in both parents and their child.

Case report

The probands are a phenotypically normal couple who were seen because of their mentally retarded son. They have two children: a five year old healthy daughter with no clinical features and a mentally retarded son. The parents were first cousins (F = 1/16). In their medical record, it was noticed that they had a baby girl who died when she was six month-old. Major complaints of the baby were umbilical cord infection, pulmonary infection, pericarditis, thorax infection, persistent vomiting and developmental delay. They brought in their 9 year-old mentally retarded son for a genetic evaluation secondary to the developmental delay. He was born after an uncomplicated pregnancy with normal growth parameters. Except for hypotonia, his parents did not report any problem at the time of the delivery. By the age of 3, concerns about his motor and speech delays led to formal developmental testing which indicated mild global developmental delay. The possibility of UPD (14) was raised based on the triad of developmental delay, macrocephaly, and joint laxity which are the characteristics of this syndrome. According to the protocol of the ethical review board of the Uremia university, informed consent was obtained from his parents. All the boy's family members have been karyotyped using GTG banding protocol on peripheral blood lymphocytes. Using GTG banded chromosome typing, it was noticed that both parents had Robertsonian translocation between long arm of chromosome 13 and 14 (figure1). Their affected son had also translocation between chromosome 13 and 14 [45, XY t(13q14q)]. The healthy girl's karyotype revealed the presence of a homozygous Robertsonian 13/14 translocation and her karyotype was 44, XX t(13q14), t(13q14q) (figure2).

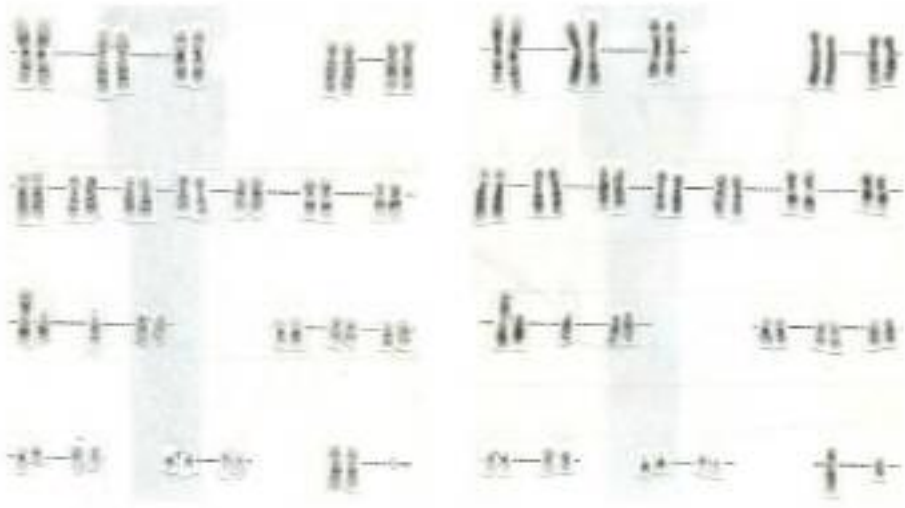

Figure 1. Chromosomal findings of the screened patients using GTG banded chromosome typing methods. As it is obvious from the picture in both parents (father right and mother left), Robertsonian translocation between chromosome 13 and 14 (Rob13q14q) was present.

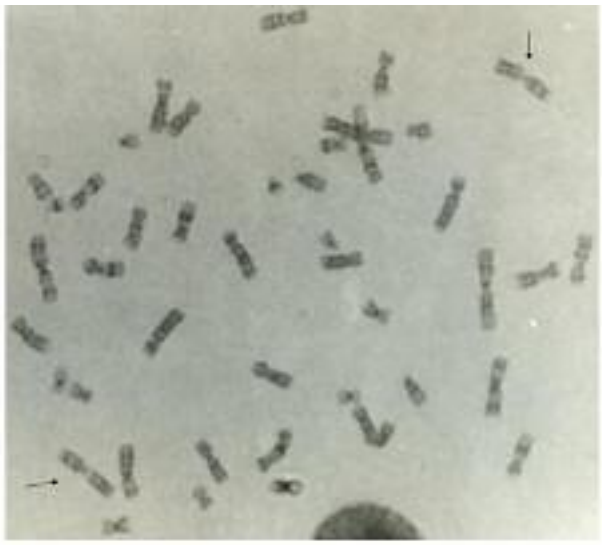

Figure 2. GTG banded chromosome typing in the daughter of the family showed that both translocations were inherited from her parents 44, XX t(13q14q) t(13q14q). Arrows show both affected chromosomes.

Discussion

The segregation of a Robertsonian (13p14p) or (13q14q) translocation in families with a single heterozygous carrier has been previously reported [10,11]. Martinez-Castro et al has reported a family with five affected children. In that family, both parents were heterozygous carriers like our case and they had five children with heterozygous and homozygous Robertsonian translocation (13q14q) [9]. According to their report, all children were healthy and even their marriage resulted in healthy but carrier offsprings [9]. Simoni et al [12] reported a family in which both parents, also cousins, were heterozygous carriers of the same reciprocal translocation (2;7). However, only the heterozygous carrier was found in their offspring. We have found no previous report of a family in which the presence of the same translocation in both parents had resulted in homozygous and heterozygous children. In the family under the study, their son's phenotype with mental retardation and growth delay is possibly due to the UPD. Individuals with paternal disomy 14 have a more severe phenotype than those with maternal disomy 14 which includes mental retardation, skeletal abnormalities (that results in short-limb dwarfism with narrow thorax), decreased survival rates due to respiratory difficulties, dysmorphic facies, and scoliosis. The boy's clinical feature is in accordance with the paternal disomy 14 symptoms. However, in order to clarify the results, it is necessary to carry out further experiments with FISH probes or molecular markers. The healthy girl's karyotype is 44, XX t(13q14q), (13q14q) which means she is homozygous for rob translocation.

A few cases of homozygous Robertsonian translocations 13q14q have been reported both prenatally and postnatally and it appears that it does not affect the phenotype (balanced). In our case, there is obviously an increased risk for trisomy 13, and possibly for spontaneous abortions. Otherwise, this girl is expected to have the possibilities of giving birth to normal babies. It is not possible to reach a definite conclusion by studying the medical history of the deceased child. However, it is possible that she was suffering from the UPD phenomenon which is a especial paternal disomy. By studying their family history analysis, it is possible to arrive at this conclusion that the mentioned phenomenon can not be just a chance occurrence and it could be due to the consanguinity of the parents since they are first cousins.

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