

Case Report: Potential Speciation in Humans Involving Robertsonian Translocations.

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Abstract

Approximately one person in 1,000 is a Robertsonian translocation carrier. This type of translocation most likely arises during egg (or more rarely sperm) formation. Most Robertsonian translocation carriers are healthy and have a normal lifespan, but do have an increased risk of pregnancy loss and children with trisomies. We have found a Robertsonian translocation family, one of them who came from a consanguineous marriage has the previously undescribed balanced human karyotype 44,XY,der(14;15)(q10;q10), der(14;15)(q10;q10). Many such rearrangements in natural populations of different species are known. It is well-known that the fitness of rob translocation carries is reduced, but rob translocation can provide material for evolution.

Keywords. Chromosome, Robertsonian translocation homozygosity, evolution

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Introduction

The frequency of Robertsonian translocation in newborn babies is approximately one in 1,000. Robertsonian translocation is an unusual type of chromosome rearrangement caused by two particular chromosomes joining together. In humans, it occurs in the five acrocentric chromosomes, 13, 14, 15, 21, and 22. During a Robertsonian translocation, the participating chromosomes break at their centromeres and the long arms fuse to form a single chromosome with a single centromere. The short arms also join to form a reciprocal product, which, in the acrocentric chromosomes, typically contains nonessential genes and repetitive sequences such as nucleolar organizing regions, and is usually lost within a few cell divisions.

Since Robertsonian translocation carriers have a balanced chromosomal complement, they are healthy and have a normal lifespan, and may be unaware of their unusual chromosome rearrangement. A Robertsonian translocation can be transmitted for many generations without detection. Robertsonian translocation carriers produce six kinds of gamete. One sixth of the gametes are normal, and lead to offspring with normal chromosomes. One sixth of the gametes contain the Robertsonian translocation, which is passed

to the offspring. The remaining 4 types of gametes lead to offspring with monosomy or trisomy. Because of this, Robertsonian translocation carriers do have an increased risk of pregnancy loss. While a few babies with trisomy 13 or 21 will survive, those with trisomy 14, 15, or 22 usually miscarry in the first twelve weeks.

Case report

This case report was occasioned by the ascertainment of a 25-year-old Chinese man (IV-1) married to a non-consanguineous woman with normal chromosomes (IV-2). This couple had had a son who died at age 6 months, was buried without an autopsy, but had had a chromosome study because of cerebral palsy. The karyotyping analysis of IV-1 is Authenticated by the Chinese Academic Committee of the state key laboratory of medical genetics with the previously undescribed balanced human karyotype 44,XY,der(14;15)(q10;q10),der(14;15)(q10;q10).

The parents of the proband are phenotypically normal first cousins, each a carrier of the same Robertsonian translocation (□-1, □-2). Their parents, a mutual uncle, and both grandparents are deceased, thus it is not possible to determine whether I-1 or I-2 was the carrier of the translocation.

The respective probabilities of □-1 and □-2 to produce as follow (Fig. 3).

- Normal gametes is 1/6
- Balanced translocation gametes: 1/6
- Unbalanced gametes is 4/6; and their probability of producing
- A normal karyotyping child is 1/36
- A child with a balanced Rob chromosome is 6/36
- A child with a disomy Rob chromosome is also 1/36
- A genetically unbalanced zygote is 28/36, will increase pregnancy loss in early stage

Figure. 1. Pedigree of the family transmitting Robertsonian translocation chromosome $t(14; 15)(q10;q10)$. Open hexagon designates a presumed carrier of $t(14; 15)(q10;q10)$. Filled hexagon designates a known carrier of $t(14; 15)(q10;q10)$. The proband, IV-1 (arrow), has disomy $t(14; 15)(q10;q10)$. The proband's wife, IV-2, has a normal karyotype. Their deceased son, V-1, was a carrier with karyotype $45,XY,der(14;15)(q10;q10)$.

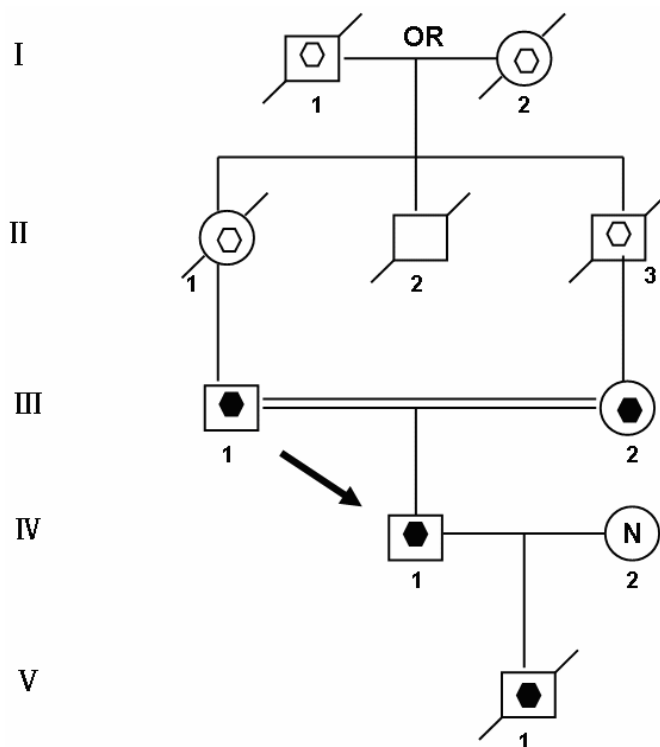


Fig. 1.

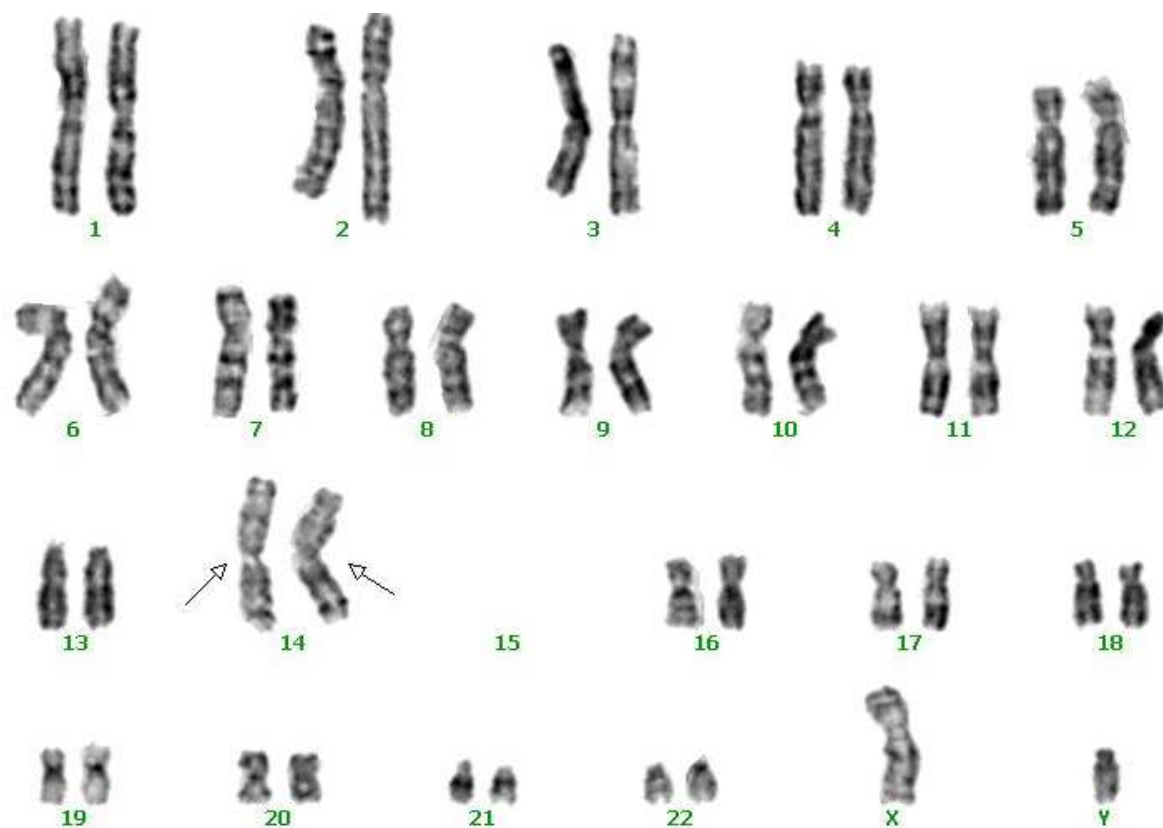


Figure 2. Karyotype of the proband of the study, $44,XY,der(14;15)(q10;q10),der(14;15)(q10;q10)$, having disomy for the Robertsonian translocation chromosome (arrows).

Sperm						
Ovum						

: 14th chromosome : 15th chromosome : Derivative chromosome (14q15q)

Figure 3. Possible chromosomal complements of the offspring of two individuals having karyotype 45,XN,der(14;15)(q10;q10)

Discussion

It is well-known that the fitness of rob translocation carries is reduced[2]; in some rob translocations the risk of unbalanced offspring may exceed 20%. The homozygous state of such a rearrangement presumably leads to infertility[3]. The concept of human aneuploidy syndromes as failed “attempts” at speciation was discussed by Neri and Opitz[4] in the context of trisomy “21”.

Rob translocation carries are phenotypically normal since they involve loss only of short arm material. Many such rearrangements in natural populations of different species are known, most famously in the house mouse, *Mus poschiavinus* (the “tobacco mouse”) being considered a distinct species [5], the genus *Muntiacus*, the cotton rats (*Sigmodon*) of North America [6], and even rams with the Massey rob fusion [7]. What is clear from these and many other studies over the last 70-80 years is that rob rearrangements can increase polymorphisms in a species, provide material for natural selection and even lead to speciation [8-10]. John [11] has made the point that the types of chromosome

rearrangements that occur as polymorphisms or as fixed permanent heterozygotes invariably involve meta- or submetacentric chromosomes. Those that distinguish species and serve to isolate these species involve telocentric or acrocentric chromosomes, which are self-sterilizing.

Robertsonian rearrangements are common chromosomal changes that can lead to rapid and efficient reproductive isolation between karyotypically similar populations, especially when many rob metacentric chromosomes display monobrachial homologies [12]. In the case of the *Muntjac*, little or no measurable genetic or morphological differences have been found [13]. Homozygosity for Robertsonian translocations in man has been described before. A fetus with two t(14;21) chromosomes was found by Dallapiccola et al. [14]. The related parents were heterozygous for the same translocation. Martinez et al. [15] described three adult sibs homozygous for t(13;14). Their parents were first-cousins and both were heterozygous carriers. Rajangam et al. [16] found a unique DS karyotype 45, XY, der(14;21)pat, der(14;21)mat, +21mat. Whereas translocation heterozygosity is associated with meiotic disturbances that cause infertility and subfecundity,

translocation homozygosity should not have any effect on meiosis—at least in theory[15].

The propositus (IV-1) is healthy and has a balanced chromosomal complement. Assessment of a semen sample from the propositus (IV-1) showed normal sperm number and morphology. We were not able to analyse a sperm karyotype, but given his karyotype of 44,XY,der(14;15)(q10;q10),der(14;15)(q10;q10), we assume his sperm karyotype to be consistently 22,X and 22,Y. Since the propositus is phenotypically normal with normal fertility, we consider his chromosomal rearrangement to be a balanced polymorphism [11]. The aberration can provide material for evolution.

The establishment of a new human subspecies with a diploid complement of 44 chromosomes could occur if a small population with the karyotype of the propositus underwent long-term reproductive isolation.

Conclusion

Although a Robertsonian translocation carrier has a full genetic complement, their fitness is reduced due to high probability of genetically imbalanced gametes. However, this type of translocation can provide material for human evolution. Long term isolation of a group of individuals who are homozygous for a particular Robertsonian translocation chromosome could theoretically lead to the establishment of a new human subspecies having a full genetic complement in 44 chromosomes.

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