brief report

Genetic counseling in adult carriers of a balanced chromosomal rearrangement ascertained in childhood: Experiences from a nationwide reexamination of translocation carriers

Iben Bache, MD[1], Karen Brondum-Nielsen, MD, DMSci[2], and Niels Tommerup, MD, DMSci[1]

Purpose: Prenatal diagnosis is offered to carriers of a balanced chromosomal rearrangement because it may predispose to offspring with an unbalanced karyotype. Therefore, carriers examined prenatally or in childhood should be informed before they reach reproductive age. We aimed to determine how many of the adult carriers ascertained in childhood currently know about their carrier status. **Methods:** We used data obtained by a questionnaire study reexamining carriers of a balanced reciprocal translocation. When a carrier was older than 18 years of age and had been examined in childhood, relatives were asked whether she/he knew of the translocation. **Results:** Among the 113 parents we interviewed, 10 carriers (9%) in 8 families had not been informed. In one of the eight families, an offspring with an unbalanced translocation was born 23 years after the father had been examined in childhood. **Conclusion:** Because of our findings, the practice of genetic counseling in Denmark has been changed: When a carrier of a balanced chromosomal rearrangement who was examined prenatally or in childhood turns 18 years of age, the parents will receive a letter reminding the family about the reproductive risk. ***Genet Med* 2007:9(3):185–187.**

Key Words: *balanced chromosomal rearrangements, genetic counseling, carrier testing, prenatal, childhood*

Balanced chromosomal rearrangements are one of the most frequent genetic abnormalities in humans: an estimated 0.52% of the population carries a balanced translocation or inversion.[1] These carriers can be ascertained before reproductive age in three situations: (1) children born after a prenatal chromosome examination, (2) children examined because of an abnormal phenotype, and (3) children with a normal phenotype examined because of a familial chromosomal rearrangement. Carrier testing of children in the third group was performed in many countries from the 1960s to 1990s but is no longer recommended.[2] Children in the first two groups are still tested.

Because balanced chromosomal rearrangements may predispose to an unbalanced karyotype leading to spontaneous abortions or seriously ill children, prenatal diagnosis is offered to carriers. However, when carriers have been prenatally or postnatally examined years before they reach reproductive age, their knowledge about their carrier status will often depend on whether the parents have informed them. We aimed to approximate how many adult carriers ascertained in childhood knew of their carrier status. We used data obtained by a questionnaire study of carriers of a balanced reciprocal translocation.

MATERIALS AND METHODS

As part of a separate study, we surveyed all postnatally examined Danish carriers of a constitutional balanced reciprocal translocation and sent questionnaires to those older than 18 years of age, living in Denmark, and previously informed of the chromosomal rearrangement.[3] The study was approved by the scientific ethical committee, and informed written consent was obtained from all respondents. When the carrier had been examined in childhood (before 18 years of age), we asked the relatives participating in the questionnaire study whether the carrier knew of her/his carrier state. These relatives, preferably the parents, were interviewed by telephone.

RESULTS

In total, 294 carriers were younger than 18 years of age when the chromosome examination had been performed. Among these, we excluded carriers with serious, early-onset disease ($n = 103$); who were dead ($n = 15$); who emigrated ($n = 7$); and who were still younger than 18 years of age ($n = 22$). Among the remaining 147

From the [1]Wilhelm Johannsen Centre for Functional Genome Research, Department of Cellular and Molecular Medicine, University of Copenhagen, Denmark; [2]Kennedy Institute-National Eye Clinic, Glostrup, Denmark.

Iben Bache, MD, Wilhelm Johannsen Centre for Functional Genome Research, Department of Cellular and Molecular Medicine, Panum Institute, University of Copenhagen, Blegdamsvej 3, 2200 Copenhagen N, Denmark. E-mail: iben@imbg.ku.dk

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Table 1
Characteristics of the 10 carriers who were not informed about their carrier status

Family	Ascertainment	Age when karyotyped (years)	Age when informed	No. of offspring before information	Cytogenetic examination of offspring
1	Newborn screening[4]	0	21	0	
1	Relative with balanced translocation	11	26	1	Not performed
1	Relative with balanced translocation	15	30	0	
2	Newborn screening[4]	0	34	0	
3	Newborn screening[4]	0	20	0	
4	Abnormal phenotype	0	27	1	Not performed
5	Relative with balanced translocation	7	30	2	Not performed
6	Relative with fragile X	10	32	0	
7	Relative with balanced translocation	0	26	0	
8	Relative with unbalanced translocation	6	29	1	Result: unbalanced translocation

carriers, 34 had no relatives included in the questionnaire whom we could interview. Thus, we were able to interview relatives of 113 carriers who had been examined in childhood. They had been karyotyped from 1967 to 1998 (median year 1980), and the number of years after the chromosome examination ranged from 5 to 36 with an average of 23.1 years.

Ten carriers (9%) in eight families did not know about their carrier state (see Table 1 for their ascertainment[4]). These carriers had been examined from 1970 to 1989 (median year 1980), and we interviewed their relatives 15 to 34 years (mean 22.6 years) after the chromosome examination. In four families, the parents had forgotten that their offspring had been examined, whereas in four families the parents had not understood the importance of telling their offspring. In total, five offspring (in four families) were born before the carriers were informed; one had an unbalanced translocation.

DISCUSSION

We contacted relatives of carriers of a balanced reciprocal translocation by questionnaire and telephone interview and found that 9% of the adult carriers examined postnatally in childhood did not know about their carrier status. Thus, despite an early chromosome examination having been performed in the families, there is, nevertheless, still a risk that a carrier will have a child with an unbalanced reciprocal translocation, as happened in one of the Danish families.

Genetic counseling of couples in whom one is a carrier of a balanced reciprocal translocation will include considerations about the risk of an unbalanced offspring. This risk depends on the mode of ascertainment, with approximately 19% when the proband is unbalanced and approximately 3% when the proband is balanced,[5] the chromosomes involved, and the localization of the breakpoints.[6] However, regardless of the estimated theoretic risk, the standard practice is to offer prenatal diagnosis to carriers of a balanced reciprocal translocation.

The original counseling strategies of the families varied because the nationwide cohort comprised carriers examined during a 30-year period and in six different laboratories. Unfortunately, we do not know how many of the eight families were counseled by a clinical geneticist. Our study included only postnatally examined carriers, but we received sporadic reports about lack of knowledge of their chromosome abnormality among prenatally examined carriers too. We did not include families with a balanced inversion, insertion, or Robertsonian translocation in this study, but it is likely that, here too, the information given to the offspring when they reach reproductive age may be inadequate.

One specific consequence of this survey is that we informed the parents in the eight families (with 10 non-informed carriers) of the necessity of telling the young generation about their carrier state, and the families were invited to further genetic counseling. A more general consequence is that we changed the practice in Denmark after discussion among the directors of the cytogenetic laboratories: when a carrier of a balanced reciprocal translocation, inversion, insertion, and Robertsonian translocation found prenatally or postnatally turns 18 years of age, the parents will receive a reminder letter. In this letter, the importance of informing the carrier of the potential reproductive risks involved is described and she/he is invited to genetic counseling. Postnatal carrier testing of children with a normal phenotype is no longer performed,[2] resulting in families with offspring who have not been examined but who have a high risk of being carriers. It is also important to remind these families that their children have a high risk of being carriers and therefore have a potential reproductive risk.

Reminding parents about their offspring's carrier status many years after the chromosome examination can most easily be performed systematically in countries that have a centralized ability to track the population. However, in most countries, there are clinical genetic services responsible for all individuals in a specified geographic area. If all carriers of a chromosomal rearrangement were reported to these services,

they would be able to remind the families when the offspring reach the appropriate age.

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