DOWN SYNDROME ASSOCIATED WITH A FAMILIAL 14/21 TRANSLOCATION

by

EJ HANNA, WP JOHNSTON, NC NEVIN

Department of Medical Genetics, The Queen's University of Belfast and Royal Victoria Hospital

Down syndrome (mongolism) is one of the commonest chromosomal abnormalities in man with an incidence of between 1 and 2 per 1000 live births. In Northern Ireland the incidence is 1 in 630\(^1\). About 95 per cent have 47 instead of 46 chromosomes with an extra chromosome 21 (Trisomy 21). A small proportion, between 2 and 5 per cent are due to an unbalanced chromosomal translocation, usually involving the D(13-15) group chromosomes, particularly chromosomes 14 and 21. About half of the cases of translocation Down syndrome are inherited and thus, other family relatives may carry the chromosomal translocation and have a high risk of having affected children. The purpose of this paper is to describe our recent experience with a family which illustrates the importance of cytogenetic examination in all Down syndrome infants, of family follow-up when an unbalanced translocation is discovered, and of providing genetic counselling for those relatives who are carriers.

PATIENTS

CASE 1. The propositus (Fig. 1. IV.1), a female, born 11 April 1980, was the
first born of a 27 year-old mother and a 28 year-old father. Birthweight was 3203 gms. at 38 weeks gestation. Clinical examination revealed the typical facial appearance of Down syndrome. Cytogenetic studies showed an unbalanced translocation, 46,XX,-14,t(14:21) (Fig 2). Blood from the parents revealed that the mother was a balanced translocation (45,XX,t(14:21) (Fig. 3).

**FIG. 2.** Karyotype of the unbalanced translocation. Arrow indicates the translocation (t(14q21q)).

**FIG. 3** Karyotype of the balanced translocation. Arrow indicates the translocation (t(14q21q)).
CASE 2. A female (Fig. 1. IV.19), born 7 July 1980, was the first born of a 24 year-old mother and a 28 year-old father. Birthweight was 3175 gms. at 40 weeks gestation. The baby had the typical facial appearance of Down syndrome. Cytogenetic studies showed an unbalanced translocation (46,XX-14t(14:21). Blood from the parents demonstrated that the mother had a balanced translocation (45,XX,t(14:21). The mothers of Case 1 and Case 2 were paternal first cousins.

Relatives of the families were visited and blood samples obtained for cytogenetic examination in a total of 21 other relatives. Apart from the above two Down syndrome infants (Case 1 and Case 2) no other relative was affected.

RESULTS

There was no difficulty in persuading the relatives to provide a blood sample for chromosome analysis once the situation had been carefully explained. Of the 21 relatives examined, 8 (7 males and 1 female) were discovered to have a balanced 14/21 translocation. Of the 10 balanced translocation carriers in the family, 7 had children. Three female balanced translocation parents produced a total of 6 children; 2 normal infants, 2 with balanced translocations, and 2 with Down syndrome. The four male balanced carrier parents produced a total of 15 children; 9 normal infants, 5 with balanced translocations, and one unknown (died in infancy).

DISCUSSION

The incidence of Down syndrome is between 1 and 2 per 1000 live births. Over 95 per cent of cases are caused by non-disjunction, the remainder resulting from translocation. Down syndrome due to translocation can only be distinguished from that due to Trisomy 21 by cytogenetic examination. Our family illustrates the importance of cytogenetic examination in all Down syndrome newborn and of follow-up of the relatives when an unbalanced translocation is found. Among cases of unbalanced translocation Down syndrome about half are inherited. When inherited, the risk of maternal carriers of a 14/21 translocation producing an infant with Down syndrome is approximately 10 per cent and about 2-3 per cent when the father is the carrier. Similar risks are involved when the translocation involves chromosomes 21 and 22. However, if either parent has a balanced 21/21 translocation all pregnancies will be abnormal since the only alternatives are the unbalanced translocation Down syndrome and the lethal monosomy 21. Our family also emphasises that the risk of Down syndrome offspring is greater when the mother carries the translocation. Both Down syndrome infants had been born to females with balanced 14/21 translocations. The four males with balanced 14/21 translocations had a total of 15 children, of whom 9 had normal chromosome constitutions, 5 had balanced 14/21 translocations, and one was unknown (died in infancy). When individuals in this family had been identified as having balanced translocations, they were advised of the risk of having an infant with the Down syndrome and of the availability of prenatal diagnosis by cytogenetic examination of cultured amniotic fluid cells in any future pregnancy.
SUMMARY

The finding of an unbalanced translocation t(14q21q) in two Down syndrome infants, born within three months of each other to mothers who were paternal first cousins, led to a clinical and cytogenetic investigation of the families. Chromosome examination in 25 individuals revealed 10 balanced translocation carriers, 3 females and 7 males. Both Down syndrome babies had been born to balanced female carriers. The study emphasises the importance of chromosome examination in all Down syndrome infants, and in relatives when an unbalanced chromosome constitution is discovered.

REFERENCES

1. Nevin NC. Aetiology of genetic disease. In Turnbull AC, Woodford FP, eds. Prevention of handicap through antenatal care. Amsterdam: Elsevier Excerpta Medica, 1976: 3-12.

2. Yunis JJ. Classical chromosome disorders In: New Chromosomal Syndromes. London: Academic Press, 1977.

3. Hamerton JL. Human cytogenetics. In: Clinical Cytogenetics, vol. 2. London: Academic Press, 1971.