Maternal transmission of translocation 2;21 associated with Down's syndrome

Saroj V Kotwaliwale, Vidya V Dicholkar, N D Motashaw

Abstract

An unusual 2;21 translocation associated with Down's syndrome is reported. The proband was a 3 year old boy, clinically diagnosed as having Down's syndrome and with a family history of Down's syndrome. Maternal age at the time of study was 28 years. Out of the four sibs with Down's syndrome three had died. Two pregnancies ended in first trimester miscarriage. The proband was found to have trisomy 21 associated with a 2;21 translocation inherited from his mother.

Down's syndrome was first described by Langdon Down in 1886¹ and was subsequently confirmed to be associated with an extra chromosome 21 by Lejeune *et al*² in 1959. The syndrome can be diagnosed at birth or shortly thereafter by the typical clinical features. The chromosome complement can be either frank trisomy 21, mosaicism, or trisomy owing to a D;G (13-15;21) or G;G (21;21) translocation. In addition, other translocations can be present. A case with an apparent translocation 21;1 associated with Down's syndrome was described by Kontras *et al*³ in 1966. We report a case of 2;21 translocation associated with Down's syndrome.

Case report

The proband, a 3 year old boy, was referred to the laboratory for cytogenetic analysis along with his parents. He was born at 8½ months' gestation by normal vaginal delivery. Maternal age at the time of his birth was 25 years. The child had delayed developmental milestones and had frequent respiratory problems. Clinical features included a flat occiput, epicanthic folds, depressed nasal bridge, and a protruding tongue. The hands were short and broad

with a simian crease. No cardiac anomaly was present. He was the fourth child of the family (fig 1). The first child was female and died at 1 year of age. The second and third were twin females. All of them had clinical features of Down's syndrome. However, cytogenetic analysis was not performed on them. These births were followed by two first trimester miscarriages in the mother. The father of the proband was an only child. The mother was the third in her sibship. No other family members had an abnormal child. It was not possible to question the relatives since they were out station patients.

CHROMOSOME STUDIES

Whole blood from the patient and his mother and father was cultured for 72 hours. Chromosomes were

Figure 1 Pedigree of a child with Down's syndrome whose mother is a 2;21 translocation carrier.

Figure 2 Chromosomes 2 and 21 in the mother and the proband. The abnormal chromosome is on the left.

Genetic Diagnostic Centre, 203 Bombay Air Conditioned Market, Tardeo Road, Bombay 400 034, India.

S V Kotwaliwale, V V Dicholkar, N D Motashaw

Correspondence to Dr Kotwaliwale.

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G banded using the method described by Rooney and Czepulkowski.⁴ A total of 50 metaphases out of 500 metaphases obtained were studied in each case. Chromosomal analysis of the child indicated trisomy 21 associated with a 2;21 translocation (47,XY,+21,t(2;21)(q21;q22.3)mat) (fig 2). Chromosome analysis of the mother indicated a 46,XX chromosome complement with a balanced translocation between chromosomes 2 and 21 (46,XX,t(2;21)(q21;q22.3)) present in all metaphases (fig 2). The father had a normal 46,XY karyotype.

Discussion

The clinical features and cytogenetic analysis of the proband clearly indicated that the child had Down's syndrome. The chromosome 21 together with translocation chromosome 2 at first appeared to be a large acrocentric chromosome. However, the banding

pattern clearly indicated a 2;21 translocation. The mother of the proband also had this translocation and 3:1 segregation gave rise to the proband. Chromosomal analysis of the dead sibs was not performed and, although all of them were abnormal, it cannot be said with certainty that these children had Down's syndrome. This was the only family, out of 105 cases of Down's syndrome studied in this laboratory during the last two years, in which Down's syndrome resulting from a 2;21 translocation was found.

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- 3 Kontras SB, Carrier GJ, Cooper RF, Ambuel JP. Maternal translocation of 21/1 translocation associated with Down's syndrome. *J Pediatr* 1966;69:635-9.
- 4 Rooney DE, Czepulkowski BH. *Human cytogenetics*. Oxford: IRL Press, 1986.