48,XY,21+,mar+mat: A Case of Trisomy 21 Associated with an Inherited Small Marker Chromosome*

GERALD J. BARGMAN, RICHARD L. NEU, HAROLD O. POWERS,† and
LYTT I. GARDNER

*From the Genetic and Endocrine Unit, Department of Pediatrics, State University of New York,
Upstate Medical Center, Syracuse, New York, U.S.A.*

A patient with Down's syndrome whose karyotype included a t(GqGq) translocation chromosome and a fragment has been reported by Penrose, Ellis, and Delhanty (1960). Subsequently, den Dulk *et al.* (1966) reviewed six patients with chromosome fragments associated with clinical abnormalities. None of these latter cases, however, had clinical pictures compatible with any of the established trisomies, such as those reported by Vislie *et al.* (1962), Frøland, Holst, and Terslev (1963), and Dekaban and Zelson (1968), as well as others. This communication describes a case of trisomy 21 associated with an inherited marker chromosome.

Case Report

The proband was a Caucasian infant, the product of a first pregnancy for a 21-year-old mother and a 24-year-old father. The mother's pregnancy was unremarkable until the end of her seventh month when her membranes ruptured spontaneously. This was associated with a brief episode of abdominal 'cramps' and minimal vaginal bleeding. She was treated with bed-rest and intermittent progesterone as well as tetracycline therapy for one month when delivery finally occurred. There was no known exposure to radiation. The infant was born after an estimated 34 weeks of gestation via low forceps vaginal delivery with a vertex presentation. Active labour was only four hours' duration and uneventful. Saddle anaesthesia was administered to the mother shortly before delivery. The infant's Apgar score was 8 at one minute. His birthweight was 2 kg.

The maternal grandmother has a history of 'hypothyroidism' and diabetes mellitus, otherwise the family's medical history is unremarkable.

Shortly after birth the infant was noted to have facial features and other physical findings consistent with

Down's syndrome. He had no difficulties until feeding was attempted at 12 hours of age. At that time the infant began to have frequent episodes of spitting up after feeding, and progressive abdominal distension. No meconium was passed. Duodenal atresia was shown by barium swallow x-ray examinations. At 6 days of age an operation was performed for correction of the duodenal atresia.

Cytogenetic Studies

Micromethod leucocyte cultures were made from the proband, mother, and father. Thirty metaphases were examined from each culture. The karyotype of the infant was 48,XX,21+,mar+. The father's karyotype was normal; that of the mother was 47,XX,mar+. The marker chromosome was observed in all well-spread metaphases from both mother and infant (Fig.), and was not constant in size. Subsequently, the chromosome complements of the maternal grandparents were examined and found to be normal.

Discussion

The marker found in this family could have been derived from any of the chromosomes in the complement. Satellites were not observed on any of the markers, as one might expect to find if they originated from acrocentric chromosomes. Since the marker appeared to have formed a ring in at least two of the metaphases examined, it seems probable that it resulted from breakage on both sides of the centromere. The marker is probably centric because it is present in every cell; the acentric material was lost in division shortly after the breakage occurred. The marker most likely arose from non-disjunction during a meiotic division in one of the maternal grandparents, or in the first mitotic division of the zygote which resulted in the mother. In the latter case, the cell missing the chromosome from which the marker originated would not be viable. The marker creates a trisomic state for the genetic material in the immediate vicinity of the

Received 7 November 1969.

* This study was aided by grants AM-02504, T1-AM-5277, and 5-TO-2-CH-1081 from the National Institutes of Health, U.S. Public Health Service.

† H.O.P. was a postdoctoral trainee of the National Institute of Arthritis and Metabolic Diseases.

FIG. A composite of G group and marker chromosomes taken from metaphases of the propositus (above) and his mother (below).

centromere, but does not seem to result in obvious clinical aberrations.

Summary

A premature infant with typical clinical features of Down's syndrome was found to have a 48,XY, 21+,mar+mat karyotype. The marker chromosome was found in all suitable metaphases from both infant and mother. It is suggested that the marker chromosome is centric in origin, resulting from breakage on both sides of the centromere.

REFERENCES

- Dekaban, A. S., and Zelson, J. (1968). Retardation in a child with an extra submetacentric chromosome fragment and partial mongolism. *Journal of Mental Deficiency Research*, 12, 216-225.
- den Dulk, G. M., Turner, B., Lee, C. and Quoye, J. (1966). Chromosomal abnormality: cases with additional chromosome fragments. *Medical Journal of Australia*, 2, 695.
- Frøland, A., Holst, G., and Terslev, E. (1963). Multiple anomalies associated with an extra small autosome. *Cytogenetics*, 2, 99-106.
- Penrose, L. S., Ellis, J. R., and Delhanty, J. D. A. (1960). Chromosomal translocations in mongolism and in normal relatives. *Lancet*, 2, 409-410.
- Vislie, H., Wehn, M., Brøgger, A., and Mohr, J. (1962). Chromosome abnormalities in a mother and two mentally retarded children. *ibid.*, 2, 76-78.