

Short communications

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Trisomy 21 mosaicism in a woman with two children with trisomy 21 Down's syndrome*

Summary. Trisomy 21 mosaicism was identified by fluorescent quinacrine banding in a phenotypically normal mother, who gave birth to two children with trisomy 21 Down's syndrome.

Trisomy 21 Down's syndrome associated with maternal mosaicism was first described by Smith *et al* in 1962. Since then there have been at least eight more reported cases of trisomy 21 Down's syndrome associated with maternal trisomy 21 mosaicism (reviewed by Aarskog, 1969). Similarly, paternal mosaicism has resulted in children with Down's syndrome (Hsu *et al*, 1971; Mehes, 1973).

We have recently detected another phenotypically normal mother with mosaicism through her two children who had trisomy 21 Down's syndrome.

Case reports

The mother, 39 years old in 1973, was the youngest in her sibship. Her mother was estimated to be more than 37 years old when she was born. She had slanted eyes, but otherwise no clinical features suggestive for Down's syndrome. Dermatoglyphics were normal. At age 25 she gave birth to a daughter (MV 140659) with typical clinical features of Down's syndrome. She then had three normal children from the same marriage. By a second marriage she had one healthy son and two first trimester spontaneous abortions, while the third marriage produced a son (SS 170573) with Down's syndrome. At that time she was 39 years old. The affected daughter and son had epicanthal folds, mongoloid slant of palpebral fissures, flat occiput, hypotonia, and typical dermatoglyphics.

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Cytogenetics

Chromosome analysis from peripheral leucocyte cultures of both affected children showed trisomy 21 in all 20 cells analyzed. Mosaicism of 46,XX/47,XX+G was found in the peripheral leucocyte culture of the mother. The trisomic karyotype was found in 10 of 45 cells examined. The extra G chromosome in the trisomic cells was identified as a No. 21 by quinacrine banding (Fig. 1).

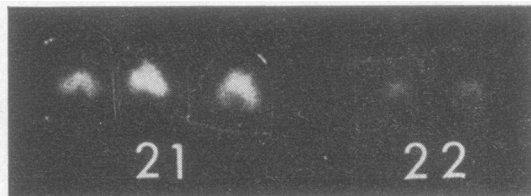


FIG. 1.

Discussion

It has been postulated that mosaic trisomy can arise by one of two mechanisms. The first is mitotic non-disjunction after the first cleavage division of an originally normal zygote, forming three types of cells having chromosome constitution of 45,-21;46 (normal) and 47,+21. The cell line with 45 chromosomes would not be viable because of the monosomy, thus resulting in 46/47,+21 mosaicism. The other possibility is meiotic non-disjunction during parental gametogenesis, forming a trisomic zygote which would then lose one of the extra chromosomes after the first mitotic divisions. This possibility appears more attractive, since it is supported by the fact that the birth of trisomy 21 mosaic individuals is often associated with advanced maternal age (Penrose and Smith, 1966).

Recently, Priest, Verhulst, and Sizkin (1973) suggested that the contribution of maternal mosaicism for trisomy 21 Down's syndrome is about 11%. Thus, in addition to the unknown contribution from paternal mosaicism makes it essential to search for parental mosaicism, particularly in young

couples who have children with Down's syndrome, since their risk of recurrence is considerably greater than that of non-mosaic parent.

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REFERENCES

- Aarskog, D. (1969). Down's syndrome transmitted through maternal mosaicism. *Acta Paediatrica Scandinavica*, **58**, 609-614.
- Hsu, L. Y. F., Gertner, M., Leiter, E., and Hirschhorn, K. (1971). Paternal trisomy 21 mosaicism and Down's syndrome. *American Journal of Human Genetics*, **23**, 592-601.
- Méhes, K. (1973). Paternal trisomy 21 mosaicism and Down's anomaly. *Humangentik*, **17**, 297-300.
- Penrose, L. S. and Smith, G. F. (1966). *Down's Anomaly*, ch. 11. Little, Brown, Boston.
- Priest, J. H., Verhulst, C., and Sizkin, S. (1973). Parental dermatoglyphics in Down's syndrome. A ten year study. *Journal of Medical Genetics*, **10**, 328-332.
- Smith, D. W., Thermon, E. M., Patau, K. A., and Inhorer, S. L. (1962). Mosaicism in mother of two mongoloids. *American Journal of Diseases of Children*, **104**, 534.

Three generations and seven family members with a t(21q22q) chromosome

Nine patients who had both structural and numerical chromosomal aberrations were found among 275 patients with Down's syndrome. All the structural aberrations were reciprocal translocations. Six presented fresh mutations and three were familial mutations transmitted through several generations. There were five D/G translocations and four G/G translocations.

Before 1972, we did not use banding techniques or autoradiographic methods, so we could not precisely identify the chromosomes in each translocation. In the last two years using the modified band-

ing method of Sumner, Evans, and Buckland (1971) and Wang and Fedoroff (1972), we have been able more precisely to identify three cases of reciprocal translocation. All three belonged to the G/G type; two were 21/22, while one of them was 21/21. One reciprocal translocation 21/22 was familial and the other a fresh mutation.

Our proband (III.14) and his family represent a remarkably rare familial type of Robertsonian translocation (Hamerton, 1971; Chapman, Gardner, and Veale, 1973). III.14 is the second child of young healthy parents (a 26-year-old mother and a 32-year-old father). The mother (II.15) comes from a large family (Fig. 1). The pregnancy passed normally and delivery was spontaneous at full term. The proband weighed 3030 g and started to breathe and cry after resuscitation.

Psychomotor development of the proband was retarded from the very beginning. At 8 months he

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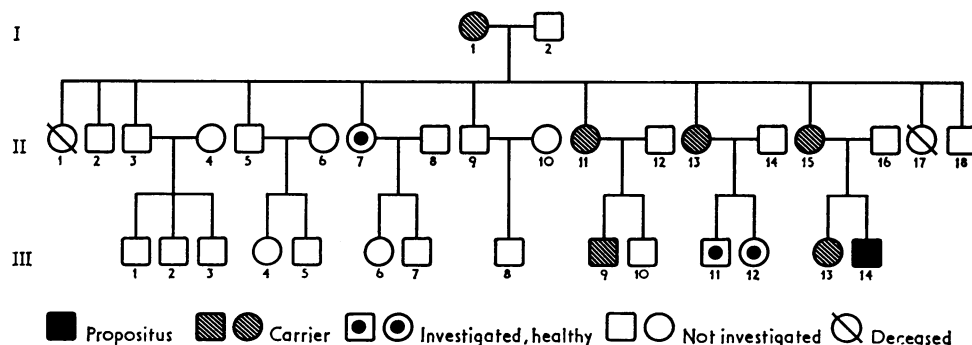


FIG. 1. Pedigree of the family.