Regular G21-trisomy in 3 sibs from mother with trisomy 21 mosaicism¹

SUMMARY This paper describes a family with 3 affected sibs with regular trisomy 21 Down syndrome. The condition seems to be transmitted from a phenotypically normal mother in whom G-trisomy mosaicism was identified. Giemsa banding depicted trisomy 21 mosaicism in cells from the mother. Chromosomes from the children showed a trisomy 21 in all the cells analysed.

In 1962, Smith et al. first described trisomy 21 Down syndrome associated with maternal mosaicism. Subsequently trisomy Down syndrome associated with maternal G-trisomy mosaicism has been reported in at least 12 instances. Aarskog in 1969 described a family with 2 affected sibs and made a review of cases published so far. In 1 of the families of this series the mother gave birth to 3 consecutive children with Down syndrome. Recently Kaffe et al. (1974) reported a case of trisomy 21 mosaicism in a woman with 2 children with trisomy 21 Down syndrome.

We would like to present a family in which 3 sibs show trisomy 21 Down syndrome. Chromosomes from the mother showed trisomy 21 mosaicism. Giemsa banding performed by the method of Seabright (1971), confirmed the presence of an extra G chromosome in the trisomic cells.

Case reports

The probands, 1 boy and 2 girls, were first seen at the genetics clinic at the ages of 13, 10, and 8, because of findings suggesting Down syndrome. They were the second, third, and fourth of 4 children (Fig. 1). The first one appeared as a normal 18-year-old youngster. Each affected child showed clinical features of Down syndrome such as brachycephaly, epicanthal folds, mongoloid slant of palpebral fissures, low-placed dysplastic ears, hypotonia, and typical dermatoglyphs.

The mother was 39 years old when she was seen for the first time in 1975. She was the eldest of a sibship of 6. Her mother was 26 years old and her father 23 years old when she was born. A paternal aunt gave birth to a child with clinical features of Down syndrome at the age of 41. She had 4 uneventful pregnancies, the first one at the age of 19 and the last one when she was 29 years old, and no abortions. Her first pregnancy ended with the birth of a normal boy. Five years later, at the age of 24 years, she gave birth to a boy with typical features of Down syndrome. She became pregnant again at the ages of 23 and 29 years and gave birth to 2 more children, both of them with clinical stigmata of Down syndrome. There was no history of drug ingestion, radiation exposure, or viral infection. Each child belongs to a different father. At the time of the interview in 1976 she was 39 years old. She displayed no stigmata of Down syndrome, and her intelligence was considered normal.

![Pedigree of the family.](image-url)

Fig. 1 Pedigree of the family.

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The second abnormal 45,-21, chromosome. Thus, chromosome constitution abnormal zygote from the mother with Giemsa banding. The 29% abnormal cases were 46,XX/47, XX+G karyotype (Smith et al., 1962) and in the women with Down syndrome. The XX+G karyotype is associated with advanced maternal age (Penrose and Smith, 1966). Therefore, an age-dependent factor may be involved in the formation, by primary non-disjunction, of a zygote with an extra chromosome.

According to Penrose (1963), Down syndrome may be classified in two groups, the maternal age-dependent group and the age-independent group. Most of the familial cases will be found in the age-independent group. Trisomy 21 Down syndrome associated with maternal trisomy mosaicism would be placed in the latter group. Thus, trisomy 21 mosaic mothers carry a considerably higher risk of having children with trisomy 21 Down syndrome. In addition to that, their risk of recurrence is greater than would be expected in non-mosaic women, as is suggested from the findings in the present family and those previously reported by Smith et al. (1962), Aarskog (1969), and by Kaffe et al. (1974).

It must be stressed that after the birth of a mongol child to a young couple, chromosome analysis should be carried out in both parents in order to rule out parental mosaicism.

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References

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