Turner/Down mosaicism

A case report

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Summary

A 45,X/47,XX, +21 mosaicism (80%:20%) in a young girl with clinical features of Down syndrome is reported. The proportion of 45,X:47,XX, +21 cells present in peripheral lymphocytes does not necessarily have a profound effect on the phenotype. A possible explanation for the occurrence of double aneuploidy is given.

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Double aneuploidy has been reported in several combinations, including Down/Klinefelter, Down/XXX[1] and Turner/Patau syndromes.[2] The Down/Klinefelter combination is the most frequent double aneuploidy recognised.[3]

Turner/Down mosaicism usually occurs as a phenotypical Down syndrome with cytogenetic mosaicism of different varieties.[4] The clinical features and cytogenetic findings in a patient with this condition are described in order to delineate this entity further, in particular with regard to morphological features in relation to cytogenetic findings.

Case report

An 8-year-old girl attending a school for the mentally handicapped, with clinical features of Down syndrome was referred for cytogenetic analysis to confirm the diagnosis.

The proband was the first child of unrelated parents and was born after an uneventful pregnancy. The mother was 24 years and the father 26 years of age at the time of her birth. Neither parent has any family history of Down or Turner syndromes.

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The mother later gave birth to a normal boy. This was followed by two miscarriages. At present the mother, aged 32 years, is 12½ weeks pregnant after *in vitro* fertilisation, infertility having become a problem.

Clinical examination revealed the child's height to be 109 cm, weight 18 kg and head circumference 48 cm. Craniofacial

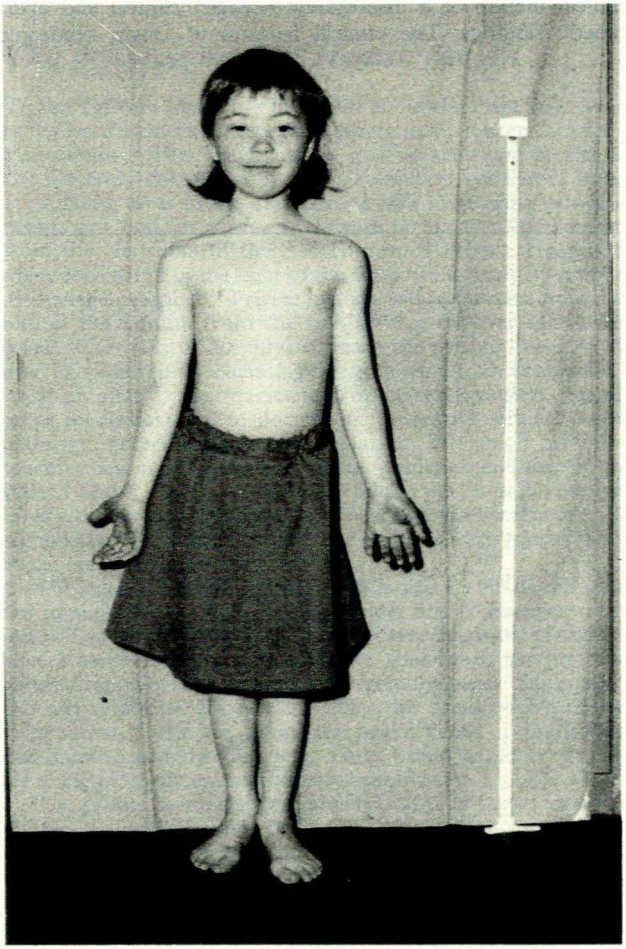

Fig. 1. The proband, aged 8 years.

features included brachycephaly, sparse hair with a low hairline and low-set ears. The face was round, with typical Down syndrome features — i.e. small, mongoloid palpebral fissures, Brushfield spots and flat nasal bridge. The mouth and teeth were normal. The thorax, cardiovascular system and external genitalia were normal. The upper limbs showed a simian palmar crease in the left hand, moderate brachydactylia and clinodactyly. The first two toes of the left foot were widely spaced. Moderate hallux valgus was present in the right foot (Fig. 1). Neurological examination revealed a patient with an affectionate nature and an IQ representative of Down syndrome.

Cytogenetic findings

Peripheral blood lymphocytes were obtained from the proband and her parents. Chromosome analyses were performed using trypsin-Giemsa banding. The analysis showed a normal karyotype in the parents. Initial chromosome analysis revealed a 45,X chromosome constitution in the proband (laboratory A). Because this was in disconcordance with the phenotype, the investigation was repeated (laboratory B). A total of 120 cells were examined, revealing a 45,X/47,XX, +21 mosaicism in the ratio 80%:20%. A buccal smear revealed a positive X-chromatin count, corresponding to the presence of an XX cell line in ectodermal tissue.

Discussion

Mosaicism should be considered whenever there is an atypical clinical picture or a discrepancy between clinical and cytogenetic findings. The clinical features of Down syndrome predominated in all 20 cases of Down/Turner mosaicism we could find reported, and in which the karyotype varied considerably.[3,4] Five of these cases showed the same chromosome constitution as our patient. The proportion of 45,X:47,XX, +21 does not necessarily have any bearing on the phenotype.[5]

A possible explanation for the occurrence of double aneuploidy in the same individual is as follows: prezygotic non-disjunction leads to a 47,XX zygote. Postzygotic anaphase lag of the X and 21 simultaneously results in a 45,X cell line.

Intrinsic factors causing a predisposition to abnormal chromosome segregation have been described. A gene for non-disjunction in humans has been suggested.[6] Regarding the latest pregnancy, we recommended mid-trimester amniocentesis on the grounds of a previous child with a chromosomal abnormality.

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