

Late replication studies and esterase D levels in a case of unbalanced X;autosome translocation, 46,X,t(X;13)(q27;q12)

The proband is a three year old Maori girl born to a 17 year old mother and a 20 year old father. Pregnancy was uneventful with forceps delivery at term. Birth weight was 3340 g. No external abnormality was observed other than one extra digit on each foot which was ligated before discharge. At the age of three years her height is 98.0 cm and weight 16 kg. She has been assessed as mildly mentally re-

tarded, functioning perceptually and cognitively at around the two year level. Her gross motor skills are significantly delayed (16 month level). She has poor equilibrium reactions in standing, runs clumsily, cannot jump, but manages steps. Expressive and receptive language is up to the 20 month level. Self care skills, emotional, and social behaviour are at the two year level. Hair and skull are normal. Her vision is good with a moderately high degree of astigmatism. She has a wide nasal bridge which is not inconsistent with her race. Her mouth, dentition, palate, and mucosa are normal. Her ears have attached lobes but are otherwise normal (fig 1a). The fingers are spindly with clinodactyly of the fifth finger (fig 1b). Her feet are normal with a minor degree of overlapping of the second and third toes. External genitalia, circulatory system, and chest x ray showed no abnormalities. Cytogenetic studies showed a complement of 46,X,der(X),t(X;13)(Xpter→Xq27::13q12→13qter) in all 200 cells analysed (fig 2a).

BrdU replication studies show the X portion of the der(X) to be late replicating in all cells. The 13q portion

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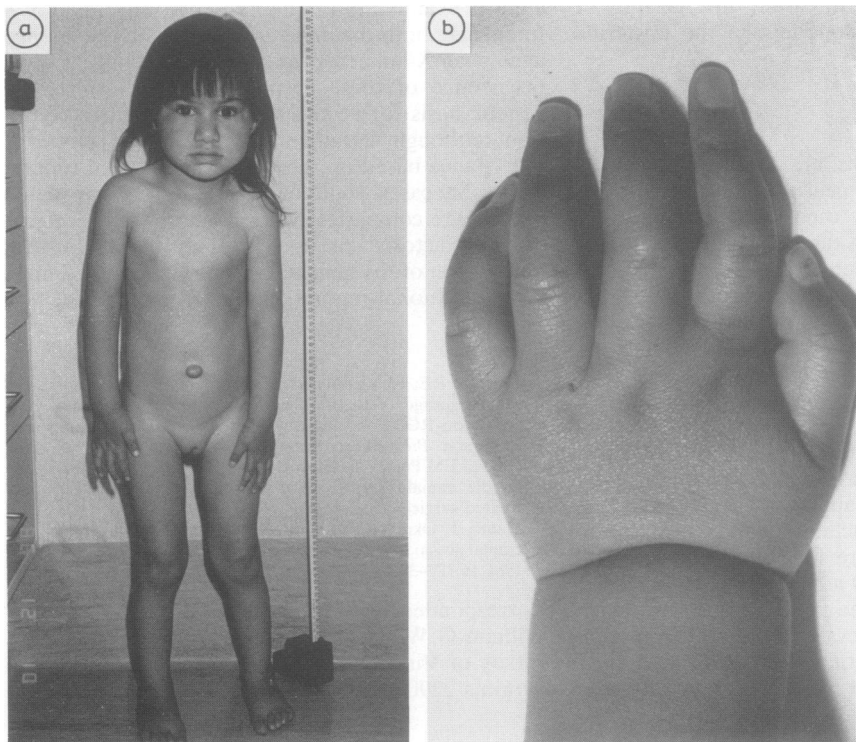


FIG 1 (a) Front view of index case. (b) Dorsal view of left hand of index case showing spindle shaped fingers and clinodactyly of the fifth finger.

the der(X) has a staining pattern comparable to the two normal chromosomes 13, with the exception of band 13q22 which is either faintly stained, as in a to e of fig 2b, or not visible at all. Parental chromosomes were normal. Electrophoresis of ESD showed the patient and her parents to be

type 1-1. Measurements of the level of red blood cell ESD in the patient showed an activity of 99.7 units compared to the maternal and paternal activities, which were 59.8 and 77.3 units respectively.

This case is another example of discontinuous spreading

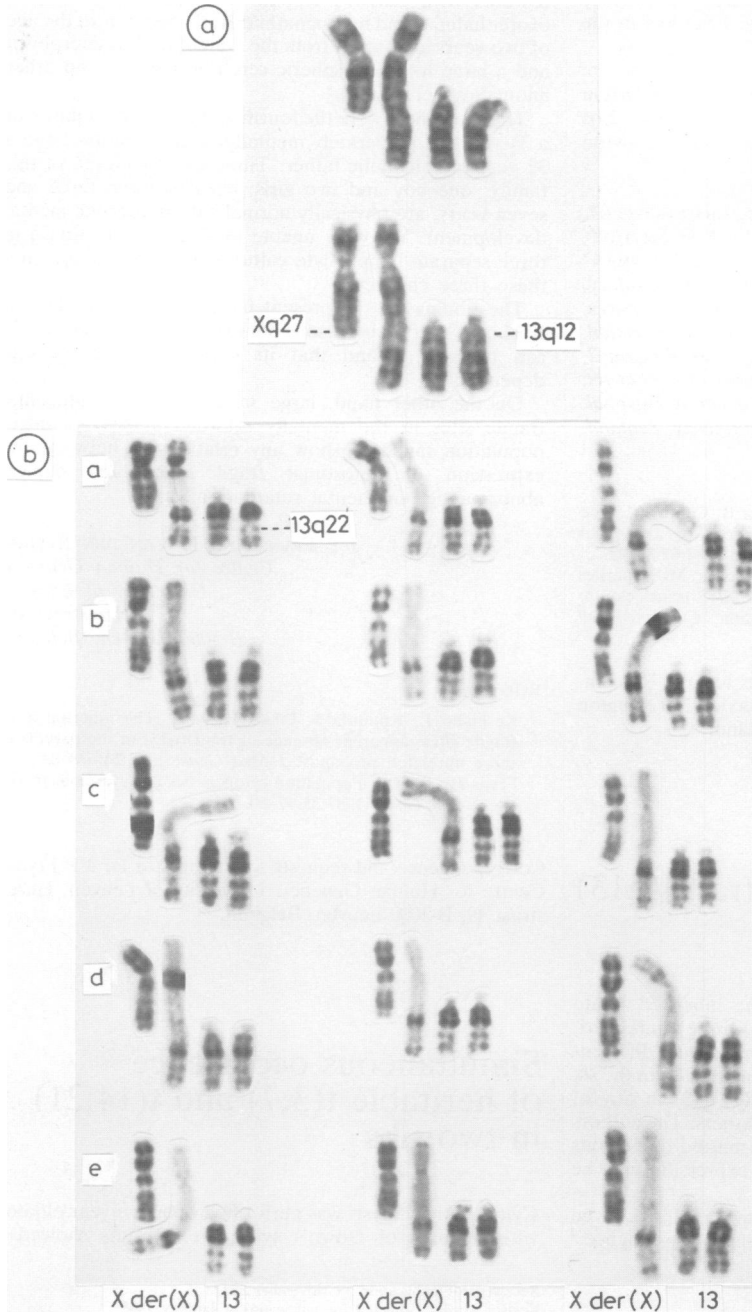


FIG 2 (a) GTG banded partial karyotypes from index case. Broken dotted lines indicate breakpoints. (b) Partial karyotypes from index case showing BrdU late replicating pattern in the X, der(X) and 13s. Note faint staining in a to e of band 13q22. In other metaphases band 13q22 is hardly visible.

of late replication. In the 13q portion of the der(X), band 13q22 shows faint staining, suggesting late replication and hence inactivation. The phenotype of our patient supports the replication pattern in that she has some but not all the features associated with trisomy 13q.¹

A 50% increase in her ESD activity, compared to that of the normal parents, confirms, as previously shown by Mohandas *et al.*,² non-inactivation of the ESD loci in the 13q portion of the der(X) chromosome.

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Is the expression of fra(2)(q13) age dependent?

In 1987 Keskiaho *et al.*¹ described the inherited folate sensitive fragile site fra(2)(q13) in three unrelated, mentally retarded children, two of them with different forms of epilepsy. Repeated chromosome studies in the six parents failed to detect the same fra(2)(q13) in any of them, except for one cell in one of the fathers. The authors concluded that fra(2)(q13) can be transmitted by persons not expressing it and that fra(2)(q13) expression may be age dependent.

In the fragile X screening programme of the Leuven Centre for Human Genetics we had a similar experience.²

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We detected a fra(2)(q13) in two dystrophic and profoundly retarded male sibs in 30% and 20% respectively of the cells in three different cultures. The boys were three months and 18 months old at the time of examination and presented with recurrent convulsions, failure to thrive, and similar dysmorphic craniofacial features with narrow, sloping forehead, long occiput, exophthalmia, and micrognathia. Both died before the age of two years and, apart from the craniofacial dysmorphism and a large interhemispheric cerebral hygroma, no other anomalies were found.

These brothers were the fourth and fifth born children of a 34 year old moderately mentally retarded mother and a 32 year old alcoholic father. Three other children of this family, one boy and two girls, aged between three and seven years, are physically normal with borderline mental development. We were unable to find the fra(2)(q13) in three separate lymphocyte cultures from the parents and these three children.

The findings in the present family confirm the data of Keskiaho *et al.*¹ that persons not expressing the fra(2)(q13) can transmit it and that its expression may be age dependent.

On the other hand, large scale studies of autosomal fragile sites in the mentally retarded versus a control population failed to show any relationship between the expression of autosomal fragile sites and clinical abnormalities or mental retardation.

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Simultaneous occurrence of heritable t(3;7) and t(14;21) in two sibs

Cytogenetic analysis was performed on a one year old boy with features of Down's syndrome. Results showed a

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