However, many of the features evocative of the trisomy 8 syndrome, such as the long face with everted lower lip, large dysplastic ears, and abnormalities of the skeletal system, are absent.

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‘Pure’ partial trisomy 2q in a male owing to malsegregation of a maternal translocation t(X;2)(p22·3;q32·1)

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SUMMARY This report describes a male infant with partial trisomy 2q: 46,Y,der(X),t(X;2)(p22·3;q32·1)mat. The phenotype was compatible with partial trisomy 2q syndrome. Replication studies showed a random X inactivation in the mother. Soluble isocitrate dehydrogenase (IDH-1) dosage was within the expected range for a trisomic patient and favours the assignment of this locus to the region 2q32→qter.

Fifteen cases of distal trisomy 2q have been described so far.¹ We report here a new case owing to malsegregation of a maternal translocation t(X;2)(p22·1;q32·1) in a male child. This case is

similar to that described by Turleau *et al*² in a female and, although the two families live in neighbouring villages, they are believed to have no common ancestor.

Case report

The proband was born in 1980 after a normal pregnancy. Birth weight was 2300 g, length 45 cm, and head circumference 30·5 cm. Apgar score was 1 at 1 minute and 8 at 5 minutes. Dysmorphic features were present and a very wide fontanelle, reaching the bridge of the nose, was noticed. Examination at the age of 17 months showed persistent growth retardation (weight 8400 g, –2 SD; length 73 cm, –2 SD) and microcephaly (head circumference 42 cm). The craniofacial features (fig 1) were typical of distal 2q trisomy syndrome,¹ especially the downward slanting palpebral fissures, hypertelorism, flat

FIG 1 The proband.

nasal bridge, short nose, and thin lips. Retraction of the upper right eyelid caused corneal ulceration which required plastic surgery resulting in a false appearance of ptosis.

There was micropenis and cryptorchidism. The upper limbs, especially the arms, were particularly short and the hands showed bilateral clinodactyly of the fifth finger and a unilateral single palmar crease. No visceral malformations were detected. There were no signs of ichthyosis. Psychomotor development was very delayed: the child could not sit and had no speech. His IQ was estimated to be about 50.

The proband has a normal brother (fig 2).

Another had died two days after birth of a complex cardiopathy but probably without associated dysmorphism. There were no other malformations among the members of the family. The mother has a normal phenotype and, though from a disadvantaged social background, her IQ seems to be within the normal range.

CYTOGENETIC STUDIES

The karyotype of the proband showed an Xp+. Examination of the mother's karyotype showed the presence of a balanced translocation: 46,X,t(X;2)(p22.3;q32.1) (fig 3). The proband was thus trisomic for the segment 2q32.1→qter. The maternal grandfather has a normal karyotype and the grandmother is dead. No other carriers were found among the subjects examined (fig 2).

X INACTIVATION STUDIES

The X inactivation patterns were studied in the mother on prometaphase chromosomes obtained after thymidine block and terminal BrdU incorporation.³ Among 31 lymphocytes analysed, the translocated X was early replicating in 16 cells and late replicating in 15 cells (fig 3). In the late replicating ones, a spreading of late replicating cells onto the translocated 2q segment was often observed. At the same time, X inactivation studies were repeated in the mother of the patient reported by Turleau *et al.*² The normal X was found again to be late replicating in all the 70 lymphocytes examined.

GENE DOSAGE STUDIES

Soluble isocitrate dehydrogenase (IDH-1) activity was assayed in the proband, his mother, and in the proband of Turleau *et al.*² It was compared with that of four other markers not assigned to chromosome 2. In the proband's red blood cells, the activity of IDH-1 was at a level of 183% compared to that in normal controls. It was normal in his mother. In the patient of Turleau *et al.*,² the activity level was 200%.

Discussion

The phenotype of our patient is compatible with the distal 2q trisomy syndrome which has now been clearly identified.¹ It must be pointed out that in our case the partial trisomy 2q is 'pure' because the breakpoint appears to be terminal on the X and furthermore the patient exhibited no features of distal nullisomy Xp (ichthyosis).

A comparison of the phenotype of the patient described by Turleau *et al.*,² a girl, with that of the present case should shed light on the consequences of X inactivation on the phenotypic expression of

FIG 2 Pedigree of the family.

FIG 3 Chromosomes 2 and X from the mother: $t(X;2)(p22-3;q32-1)$ (abnormal chromosomes on the right). (a) R bands. (b) Thymidine synchronisation and BrdU incorporation, acridine orange staining. Late replication of the normal X. (c) Same technique as (b), alternative pattern: late replication of Xp+. At the bottom, spreading of late replication onto the translocated 2q segment.

the autosomal trisomy. A reduction in the symptoms would be expected, owing to the spreading effect of X inactivation onto the translated 2q segment.⁴ In fact, it is difficult to appraise the consequences of this effect. The patient of Turleau *et al*² did not show milder symptomatology and the growth and mental retardation were rather more severe than in the present case.

Replication studies in the mother showed a random inactivation of the Xs. This is unusual in cases of balanced translocations but a survey of published reports shows that this situation is more often observed when the breakpoint in the X is located distally, as already indicated by Summit *et al*.⁵ Such random inactivation leads to a risk of functional autosomal monosomy by a spreading effect, as shown by the delay of replication of the autosomal segment in cells with a late replicating

translocated X. The dysmorphism and the mental retardation of the patient of Sands,⁶ for instance, are explained by this phenomenon, but this is not the case in the phenotypically normal mother of our patient.

Another interesting point is that the lymphocytes of the mother of the patient of Turleau *et al*,² carrying exactly the same translocation, showed constant inactivation of the normal X. This observation favours the hypothesis that the genic constitution of the subject can influence, to a certain extent, the 'choice' of which X becomes inactivated. Nevertheless, the recent data of Hellkuhl *et al*,⁷ showing variations of X inactivation patterns according to the nature of the tissues examined, call for caution in this respect.

The last point concerns the interpretation of the result of IDH-1 assays. The IDH-1 locus is defini-

tively assigned to the 2q32→qter region.⁸ The results of the assays in our proband and in the patient of Turleau *et al*² confirm this localisation. In the latter, no position effect, which would tend to give an activity level lower than expected for a trisomic subject, could be shown. This was also the case for esterase D in a patient of Mohandas *et al*,⁹ who was the carrier of a de novo unbalanced t(X;13)(q27;q12).

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Partial trisomy 12q24.31→qter

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SUMMARY Clinical details of a male child with the karyotype 46,XY,-4,+der(4),t(4;12)(p16;q24.31)mat are reported and compared with those of other known cases of partial trisomy of the distal region of 12q. This condition is apparently associated with mental and psychomotor retardation, widely spaced eyes, flat nasal bridge, low set ears, downturned mouth, micrognathia, loose skin at the nape, widely spaced nipples, simian creases, clinodactyly, abnormalities of the genitourinary system, alterations in the sacrococcygeal region, and deformities of the lower limbs. In the majority of the reported cases, the break-point was in the 12q24 region and resulted from adjacent 1 segregation of a maternal balanced translocation.

Case report

The proband was the second child of a 27 year old mother and a 45 year old father, both in good health and unrelated. The mother had no difficulty conceiving and had never miscarried. Pregnancy and delivery were uneventful at term and the birth weight was 1670 g.

At birth the infant was noted to have multiple congenital anomalies and was referred for clinical and cytogenetical evaluation. Clinical examination revealed dolichocephaly and peculiar facial features (fig 1), including prominent forehead, upward slanting palpebral fissures, convergent strabismus, hypertelorism, large and low set ears with poorly formed external lobules, high arched palate, wide mouth with downturned corners, beaked nose with a broad base, and micrognathia. No epicanthic folds were seen and the neck appeared long. Other abnormalities included a narrow chest with hypoplastic nipples, bilateral palmar simian creases, clinodactyly, large, proximally