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Inv dup (15) with mental retardation but few dysmorphic features

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SUMMARY We report a Scottish child with inv dup (15) and compare the clinical features with those of previously reported cases.

Since the first report by Parker and Alfi in 1972,¹ there have been 44 reports of patients with confirmed or suspected inv dup (15). The extra chromosomal material has been variously described, but in all cases there appears to be an additional G group sized chromosome in which both ends are derived from the short arm, centromere, and proximal long arm of chromosome 15. In most cases there are satellites at both ends of this extra chromosome.

We report the first patient from Scotland with similar cytogenetic findings.

Case report

The proband was referred for assessment of developmental delay. He was the third child of non-consanguineous Scottish parents. His father was 44 years old and his mother was 30 years old at the time of his birth. The pregnancy was uneventful

and spontaneous vertex delivery occurred at term. His birth weight was 3.43 kg.

All developmental milestones were delayed. He sat unsupported and crawled at the age of 10 months. He walked with support at 22 months. Speech development has also been delayed.

He underwent a right inguinal hernia repair at 12 months but otherwise has had good general health.

At 2.5 years of age examination revealed height, weight, and head circumference all on the 50th centile. His eyes had an antimongoloid slant and he tended to hold his head in dorsiflexion. Interpupillary distance was 4.8 cm (50th centile) and inner intercanthal distance was 2.6 cm (50th centile). Dermatoglyphs were abnormal with arches on five fingers. Apart from developmental delay, the remainder of his clinical examination was unremarkable.

CYTOGENETICS

Chromosome analysis of cultured lymphocytes by Giemsa banding, C banding, and DAPI/Distamycin A staining revealed a 47,XY chromosome constitution, with a small additional chromosome derived

FIGURE Karyotype of proband.

from the short arm, centromere, and proximal region of the long arm to q13 of two number 15 chromosomes. This chromosome was satellited at both ends and was present in all cells examined (figure).

The short arm and satellites at one end were clearly larger than those at the other, and both ends were observed to take part in satellite association. C banding confirmed that the chromosome was dicentric and suggested that the centromere with the smaller short arm and satellite was inactivated. DAPI/Distamycin A staining indicated that the chromosome included the centromere regions of two number 15 chromosomes.

Parental karyotypes were normal.

Discussion

Wisniewski *et al*² reviewed reports of inv dup (15) up to 1979. We identified 12 additional suspected cases reported before 1979 and a further six since that time.³⁻¹⁰ With the present report there are now 45 reported patients with confirmed or suspected inv dup (15).

In the more recent case reports, the use of anti-5-methylcytosine or DAPI/Distamycin A staining has

shown the additional chromosome to consist of a duplicated area of chromosome 15 which includes the short arm, centromeric heterochromatin, and proximal long arm. Thus, affected subjects are tetrasomic for loci in these regions of chromosome 15. The breakpoint on the long arm shows some variation but is often at q21→q23.

The clinical features of these patients are summarised in the table. Some phenotypic variation exists but, as in our case, most reports are of children with few or no dysmorphic features. Mental retardation is however universal. Although some children are only mildly retarded, most have been moderately to severely retarded. The degree of retardation has not correlated with the size of the additional chromosome. Abnormal tone, seizures, and behaviour disturbances are the other common features. The sex ratio is 1 male to 0.8 females. Both the birth history and birth weight are unremarkable. Major congenital malformations are notably absent in these patients.

Of these 45 patients, 29 had chromosomally normal parents. In six cases there was a familial translocation, in one family the mother was a

Case reports

TABLE Clinical features in 45 reported cases of inv dup (15).

	%
Mental retardation	98
Developmental delay	87
Abnormal tone	58
Seizures	53
Abnormal ears	51
Strabismus	49
Growth retardation	42
Behaviour disturbance	37
Abnormal dermatoglyphs	33
Antimongoloid slant	31
High arched palate	29
Abnormal speech	29
Epicanthus	20
Abnormal EEG	11
Facial asymmetry	7
Anteverted nares	5
Kyphoscoliosis	5

mosaic, and in the remainder parental karyotypes were not performed. In the non-inherited group, parental ages were stated in 20 families: for these the average maternal age at birth was 33.4 years and the average paternal age was 37.4 years. All of these de novo cases have been isolated events. The recurrence risk for parents with normal chromosomes thus appears to be low. To date there have been three reports of recurrence, two owing to parental translocation and one to maternal mosaicism. Those cases where a parental translocation was the cause had additional phenotypic features reflecting the partial trisomy or monosomy of the other chromosome involved in the translocation. In these situations amniocentesis is indicated for future pregnancies.^{2 8}

The origin of the extra chromosome in the non-inherited cases is unknown. Various theories have been postulated.¹¹ A study of the relative significance of birth order to maternal age and paternal age

might help to clarify the likely parental origin in view of the observed increase in mean parental ages.

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Interstitial deletion of the short arm of chromosome 4

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SUMMARY A 17 year old girl investigated for mental retardation and minor anomalies was found to have an interstitial deletion of 4p. Her clinical and cytogenetic findings are compared with previous reported case of interstitial 4p deletion and with terminal 4p— deletions (Wolf-Hirschhorn syndrome).

Before chromosome banding it was not possible to distinguish terminal and interstitial deletions and therefore few interstitial deletions have been reported. We describe a 17 year old girl with an interstitial deletion of segment p12p15 of chromosome 4. Francke *et al*¹ reported a similar patient with a deletion of segment 4p11p15. These patients show some similarity in clinical features suggesting that a recognisable phenotype may be associated with this deletion.

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