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Familial t(8;15)(p23·3;q22·3): report of two cases with dup(15)(q22·3→qter)

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SUMMARY Two affected first cousins with duplication of 15(q22·3→qter) are reported. This resulted from a familial t(8;15)(p23·3;q22·3) translocation. The findings in these patients are compared with each other and with six other published cases. Anthropometric and dermatoglyphic findings are summarised.

This report presents two patients with duplication 15(q22·3→qter). This occurred as the result of a familial reciprocal 8;15 translocation.

Case reports

CASE 1

This female proband weighed 3·73 kg (65th centile) at birth. The birth length was 50·3 cm (50th centile). The pregnancy, labour, and delivery were unremarkable. Microcephaly and a branchial cleft sinus were noted at birth. At eight months the OFC was 41 cm (−2 SD). Developmental delay was recognised at nine months. She sat at 10½ months. At one year her OFC was 43 cm (−2 SD). At 14 months her developmental age was seven to nine months. The branchial cleft sinus was excised at two years. At three and a half years she began to walk and to say words. Her developmental quotient was one year. At four years she had an eight word vocabulary and her OFC was 48 cm (−2 SD). Her OFC at 18 years was 51·5 cm (−1·8 SD).

She had a hypoplastic maxilla, hypotelorism, and narrow hands. At the age of 24 her height and

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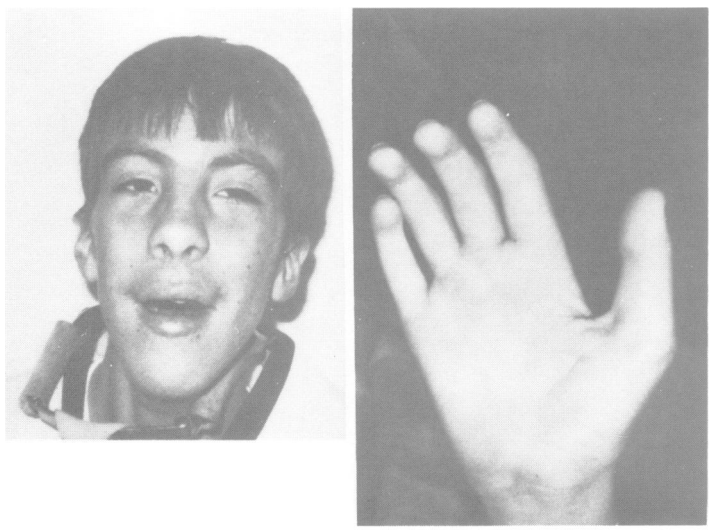

FIG 1 *Face and hand of case 2.*

weight were 173 cm (97th centile) and 47·3 kg (5th centile), respectively.

CASE 2

This male is the first cousin of the proband. The pregnancy, labour, and delivery were unremarkable. Birth weight was 3·41 kg (50th centile). The birth length was 53·3 cm (75th centile). He was noted at birth to have a long face with low set ears. He had a grade 2/6 systolic murmur, overlapping of the second and third fingers, and hyperextensibility. Dermatoglyphics were normal.

Cytogenetic studies were done elsewhere (before banding methods) and appeared to be normal.

At four months, he had hypotonia, downward slanting palpebral fissures, prominent epicanthal folds, bilateral preauricular sinuses, high arched palate, microcephaly, bilateral fifth toe deformity, VSD, and a hypoplastic facial structure.

The patient had surgical correction of his VSD. He also developed relatively severe asthma (numerous attacks and frequent admissions to hospital) and scoliosis.

Development was as follows: he sat at 12 months, spoke his first words at two years, and walked at three years. At the age of 11 the developmental quotient was three years.

At the age of 12 he was 147 cm tall (50th centile) and weighed 28·7 kg (5th centile). At 16 years his

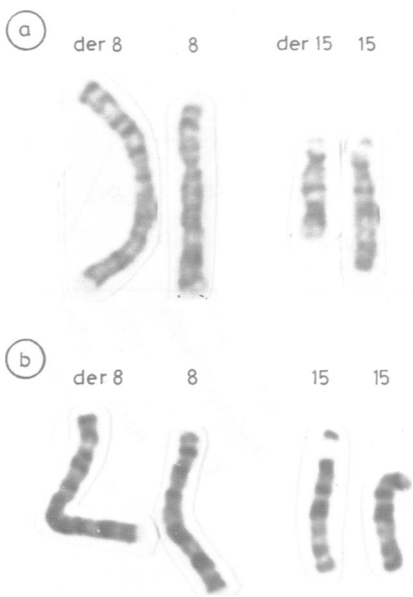

FIG 2 *Chromosome translocation from (a) balanced carrier and (b) unbalanced segregant.*

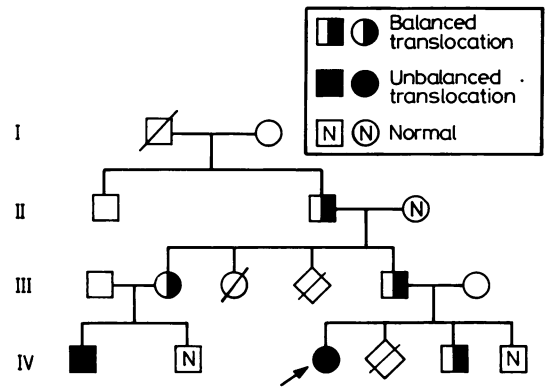

FIG 3 *Pedigree.*

TABLE *Clinical findings*

Clinical features	*Case 1*	*Case 2*	*Duplication 15q22→qter*[1–6]
Craniofacial			
Microcephaly	+	+	4/5*
Long narrow face	+	+	
Asymmetry of skull and face	−	−	4/4
Prominent forehead, occiput	−	−	4/4
Hypertelorism	−	−	
Downward slanting palpebral fissures	+	+	5/5
Synophrys	+	+	
Overfolding of superior helix	+	+	
Misshapen ears	+/−	+/−	4/4
Low set ears	−	+	3/3
Maxillary hypoplasia	+	+	
Micrognathia	+	+	3/4
Drooping lower jaw	+	+	
High arched palate	+	+	1/1
Prominent voluminous nose	−	−	4/4
Pronounced philtrum	+	+	2/2
Long upper lip	+	+	2/2
Broad neck	+	+	
Low anterior hairline	−	+	
Pectus excavatum	+	+	1/1
Scoliosis	+	+	1/1
Congenital heart disease	−	+	3/3
Extremities			
Abnormal fingers and toes	+	+	5/5
Broad thumbs	+	−	
Bilateral short distal phalanges of first finger	+	−	
Absent hypothenar eminence	+	−	
Narrow hands and feet	+	+	
Bilateral short second toes	+	−	
Bilateral tarsal deviation of big toe	+	−	
Bilateral camptodactyly of fifth toe	+	+	
Developmental delay	+	+	5/5
Dermatoglyphics			
Ridge dissociation	+	+	
Absent palmar *C* triradii			
Unilateral		+	
Bilateral	+		
Plantar hallucal fibular arch left foot	+	−	
Tented arch right foot	+	−	
Plantar zygodactyly with *b*, *c*, and *d* triradii absent on right foot	+	−	
c and *d* absent on left	+	−	
Two fingertip arches			
Left thumb	+	−	
Right index finger	+	−	
Total finger ridge counts	67	84	

*Number of patients with this feature present per number of patients with this feature mentioned.

OFC was 54 cm (−1·7 SD). At 18 years his height and weight were 158·8 cm (<3rd centile) and 34·1 kg (<<3rd centile), respectively.

His clinical features are shown in fig 1.

CYTOGENETIC STUDIES

Leucocytes were cultured in RPMI 1640 and harvested after the addition of colcemid and ethidium bromide for two hours. Cells were stained with GTG and analysed at an average band level of 525 bands.

The proband and her first cousin have the following cytogenetic findings: 46,XX,−8,+der(8),t(8;15)(p23·3;q22·3)pat and 46,XY,−8,+der(8),t(8;15)(p23·3;q22·3)mat. Cytogenetic studies of family members revealed a familial t(8;15)(p23·3;q22·3) translocation shown in fig 2. The grandfather, father, and brother of case 1 and the mother of case 2 are balanced translocation carriers. The sister of the carrier sibs (III.3) was born prematurely at seven months' gestation and died shortly after delivery (fig 3).

Discussion

The clinical features of two first cousins with duplication 15(q22·3→qter) are compared to other reported cases in the table. The features in common with the other reported cases include microcephaly, downward slanting palpebral fissures, synophrys, micrognathia, maxillary hypoplasia, drooping lower jaw, high arched palate, long upper lip, pectus excavatum, scoliosis, abnormalities of the hands and feet, and developmental delay. Findings that were not present in these cases but which have been consistently described in other cases include clinically obvious facial asymmetry (apparent by measurement in these cases), prominent occiput and forehead, and prominent, voluminous nose. One of the two cases has congenital heart disease, commonly described in this condition.

Dermatoglyphic findings are reported in the table. Since the findings differ considerably between the two cases, it appears that there may be no characteristic patterns in this condition. Both have

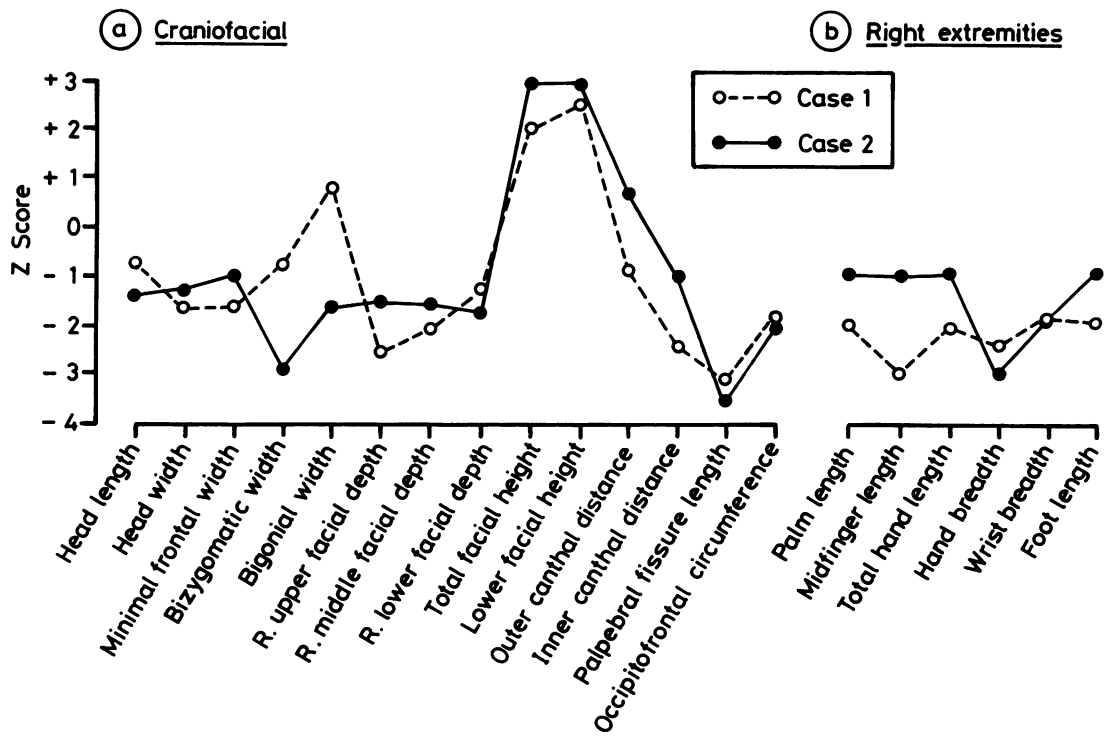

FIG 4 *Anthropometric pattern profiles. The Z score equals a standard deviation unit. The normal range is −2 to +2 with a mean of zero. The values are standardised for age and sex. (a) Face. (b) Right extremities.*

decreased ridge counts (−1·5 SD) and ridge dissociation (dotty appearance).

Anthropometric findings indicate that the two cases share similar facial pattern profiles (fig 4) which are significantly different when compared to normal controls. These differences include excessive facial height, shortened anterior-posterior facial dimensions, and short palpebral fissures. Both patients also have short and very narrow hands and narrow wrists.

These are the oldest reported cases of duplication 15(q22·3→qter). This may be due to the possibility that the duplication contains slightly less genetic material than the previously reported cases. These patients and those in published reports consistently show significant developmental delay, increased facial height, short, downward slanting palpebral fissures, microcephaly, pronounced philtrum and long upper lip, narrow hands, and abnormal fingers and toes. Longevity may be relatively normal in the absence of significant cardiac disease. The findings in these patients help to delineate the clinical features of duplication 15(q22·3→qter).

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