Case reports

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Simultaneous trisomy 9q3 and monosomy 5p in two children with der(5),t(5;9)(p15·1;q34·13): report of an extended family

D WELLESLEY*, I D YOUNG†, P COOKE‡, D F CALLEN§, AND A HOCKEY*

*Clinical Genetics Department, Irrabene and Princess Margaret Hospital, Perth, West Australia; †Department of Clinical Genetics, Leicester Royal Infirmary, Leicester; ‡Cytogenetics Unit, City Hospital, Nottingham; and §Cytogenetics Unit, Adelaide Children's Hospital, South Australia.

SUMMARY We present a family segregating for t(5;9)(p15·1;q34·13). Two cases with der(5),t(5;9), resulting in a partial duplication 9q34·13→qter and partial deletion of 5p15·12→pter, were ascertained. The phenotypes were consistent with features of both the cri du chat and trisomy 9q3 syndromes.

This case illustrates well the value of high resolution banding in the diagnosis of the severely handicapped child. Recurrent miscarriages, an alternative presentation for carrier families, are also a feature here. The authors would also like to stress the importance of the intercontinental collaboration to the diagnosis in this case.

Case reports

CASE 1

Case 1 was the first born child to unrelated Australian parents. The father was 24 years of age and the mother 25 years of age at delivery. There had been one previous early miscarriage. The proband was born at 37 weeks' gestation weighing 1·74 kg. The pregnancy was complicated by severe maternal anorexia and a total pregnancy weight gain of only 1·81 kg. Labour was rapid and the baby required oxygen at delivery.

She continued to have respiratory difficulties and so was referred to the neonatal unit at Princess Margaret Hospital, Perth, where she eventually required a tracheostomy for recurrent major apnoeic episodes and laryngeal hypoplasia. A large

part of her first two years was spent in hospital, with frequent chest infections and severe oesophageal reflux with vomiting after all meals.

From birth she was noted to be a very dysmorphic child with severe growth retardation, scaphocephaly with frontal bossing, and a marked occipital prominence. Her eyes have an antimongoloid slant and her mouth is small with a small philtrum and a high arched palate. She also has micrognathia and posteriorly rotated ears. She has arachnodactyly with syndactyly of the second and third toes bilaterally and bilateral single transverse palmar creases. There is very poor muscle development with hypotonia and virtually no subcutaneous tissue. She is profoundly mentally retarded (fig 1).

Now at three years of age she weighs 6·1 kg, is 76·5 cm long, and has a head circumference of 43 cm, all well below the 3rd centile. She sees and hears and responds well to her mother socially.

CASE 2

Case 2 was the product of the first pregnancy of healthy, unrelated English parents. Intrauterine growth retardation was noted during the third trimester and, after delivery at term, all growth parameters (weight 2·1 kg, length 46·5 cm, head circumference 31·5 cm) fell just below the 3rd centile.

The baby required extensive resuscitation after delivery and was in hospital for the first two weeks of life because of feeding problems.

During infancy she had frequent upper and lower respiratory tract infections in association with failure to thrive and marked developmental delay. She first smiled at three months but showed poor visual attention throughout life and was never able to sit independently. She died in her sleep at the age of 18 months shortly after undergoing surgery for correc-

FIG 1 Case 1 (a) at six months of age and (b, c) at three years of age.

tion of dislocated hips. Post mortem examination attributed death to asphyxia through aspiration.

Abnormalities noted at birth included a prominent forehead with deep set eyes, posteriorly rotated ears with preauricular tags, flexed wrists with long digits, bilaterally dislocated hips, and left talipes equinovarus. There was complete syndactyly bilaterally involving the second and third toes, and partial bilateral syndactyly between the third and fourth fingers. The baby's cry was described as high pitched and weak.

Additional findings at the age of one year, when all growth parameters were well below the 3rd centile (weight 5.3 kg, length 65 cm, head circumference 41 cm), were a high palate, irregular dental eruption, supraumbilical rectal divarication, hyperextensible fingers, and generalised hypotonia. No additional structural abnormalities were detected at necropsy.

CYTOGENETIC STUDIES

High resolution banding showed that a balanced translocation $t(5;9)(p15.1;q34.13)$ was segregating in this family (fig 2). The two affected subjects, III.2 and III.11, both had the karyotype $46,XX,der(5),t(5;9)(p15.1;q34.13)$ (fig 3). In III.2

FIG 2 Family pedigree.

FIG 3 Partial karyotype showing $t(5;9)(p15.1;q34.13)$. Idiogram of normal chromosomes 5 and 9 with breakpoints indicated by arrows. (a) Chromosome 5 and 9 from the father of case 1 showing balanced translocation $t(5;9)(p15.1;q34.13)$. Normal chromosome is on the left and translocated chromosome (with breakpoints indicated by arrows) on the right of each pair. (b) Chromosomes 5 and 9 from case 1 showing $der(5),t(5;9)(p15.1;q34.13)$. The derived chromosome 5 has the breakpoint indicated by an arrow.

TABLE Clinical features of our cases and other published cases.

	Case 1	Case 2	Trisomy 9q3*	Monosomy 5p*
Severe growth retardation	+	+	+	+
Severe mental retardation	+	+	+	+
Scaphocephaly	+	—	Dolichocephaly	Microcephaly
Hypotelorism	+	—	+	Hypertelorism
Deep set eyes	+	+	+	—
Anteverted nares	+	—	Beaked nose	—
High arched palate	+	+	+	—
Small philtrum	+	—	Normal philtrum	—
Small mouth	+	+	+	—
Microretrognathia	+	—	+	+
Posteriorly rotated ears	+	+	Large ears	Low set
Arachnodactyly	+	+	+	—
Syndactyly of toes 2 and 3	+	+	—	—
Amyotrophy	+	+	+	—
No contractures	+	+	Contractures	+
Microlarynx	+	Probable	—	+

*From de Grouchy and Turleau.⁴

the der(5) was inherited from the father and in III.11 from the mother.

Subject II.9 has mild to borderline mental retardation with hearing loss but no other dysmorphic features. He has a normal karyotype. All members of the West Australian branch of this family have now been tested. One normal female, II.10, had a normal karyotype; however all her other brothers have the balanced translocation, as do all their surviving offspring (fig 2).

The parents of case 2 have subsequently had a girl whose karyotype was recently tested and found to be normal.

Discussion

The absence of bands 5p14 and 5p15 have been implicated in the cri du chat syndrome¹⁻³ and the latter band is absent in our patient. Phenotypically our patients would not appear to be similar to the cri du chat syndrome,³ except for the laryngeal hypoplasia present in case 1. It was not known if she had the characteristic cat cry of this syndrome as she was always intubated before her tracheostomy.

The phenotype of these two cases shows remarkable similarity to published cases with trisomy 9q3⁴⁻⁷ (table). It would appear in both cases that the features are consistent with the simultaneous presence of both syndromes, the phenotype of trisomy 9q3 predominating.

It is of interest that in both cases initial banded karyotypes were normal, despite a high index of suspicion of a chromosomal abnormality. High resolution banding was necessary in both instances to discover the balanced and unbalanced translocations. Detection of the chromosome abnormality in this family has enabled them to consider further pregnancies knowing that accurate prenatal testing will now be available, either as chorion villus sampling or amniocentesis.

High resolution banding is not currently available

in Western Australia; prompted by the information from England regarding the karyotype of case 2, we were able to send the chromosomes of case 1 to Adelaide for high resolution banding and thus find for the family the cause of the patient's problems and the recurrent miscarriages in several members.

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Note added in proof

High resolution banding is now available in Western Australia for selected cases.

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Correspondence and requests for reprints to Dr D Wellesley, Clinical Genetics Department, Irrabene and Princess Margaret Hospital, 53 Ord Street, West Perth, Western Australia 6005.