Case reports

Journal of Medical Genetics 1988, **25**, 628–633

Deletion of a single chromosome band 4q26 in a malformed girl: exclusion of Rieger syndrome associated gene(s) from the 4q26 segment

T MOTEGI*, K NAKAMURA*, T TERAKAWA*, A OOHIRA†, K MINODA‡, K KISHI§, Y YANAGAWA*, AND H HAYAKAWA*

Departments of Pediatrics and Ophthalmology†, Tokyo University Hospital Branch; ‡Department of Ophthalmology, Teikyo University Ichihara Hospital; and §Department of Health Science, School of Health Sciences, Kyorin University, Japan.*

SUMMARY We report a malformed girl with a single chromosome band deletion of 4q26 in peripheral lymphocytes. This patient is the fourth case reported with an interstitial deletion involving 4q26 and has the smallest deletion of those reported. Deletion mapping indicates that psychomotor retardation, coloboma, prominent forehead, epicanthus, broad based nose, and broad, thin upper lip are associated with monosomy 4q26, and that gene(s) associated with Rieger syndrome can be excluded from the 4q26 segment.

To our knowledge there have been only three previously described cases of interstitial deletion 4q involving q26,^{1–3} although more than 20 cases of terminal deletion have been reported. We present here a malformed girl with a tiny interstitial deletion of 4q. The deletion involves only one band, 4q26, a very small part of chromosome 4.

Case report

The female proband (fig 1), the second of two sibs, was born in February 1985 to non-consanguineous parents; the mother was 32 and the father 39 years old. There was no family history of congenital malformations. The first and second pregnancies ended in miscarriage and stillbirth at 28 weeks' gestation, respectively. The older brother, born in 1980, was healthy. The pregnancy was uncompli-

FIG 1 Front view and profile of the proband at three months of age.

Received for publication 2 September 1987.
Accepted for publication 7 September 1987.

Case reports

629

cated and the birth at term was uneventful. Birth weight was 2360 g, length 48 cm, chest circumference 27 cm, and head circumference 32 cm.

Limb anomalies were noted at birth. They included cutaneous syndactyly of the third and fourth fingers on the left hand, absence of the second toe, and syndactyly of the third to fifth toes on the left foot. Ophthalmological examinations showed typical coloboma (coloboma iridis and coloboma choroideae) bilaterally and left microphthalmos. Facial profile included a prominent forehead, epicanthus, asymmetrical palpebral fissures (right > left), broad based nose, broad, thin upper lip, micrognathia, and incomplete development of the scaphoid fossa in the left auricle. The lower ribs on the left protruded and she had a cylindrical trunk and a narrow pelvis.

At one year five months she weighed 7.7 kg (−2 SD), height 74.5 cm (−1.5 SD), and head circumference 43 cm. DQ was 66 at 18 months. Dental development was normal at 22 months when 16 deciduous teeth were noted without any anomaly in shape or any caries. Mild malrotation of the left kidney was observed on IVP. Laboratory data including ESR, haematology, blood chemistry, serum immunoglobulin, brain CT, ABR, ECG, UCG, and urine analysis were all within normal limits. Plastic surgery on the malformed hand and foot was performed at one year five months and at two years three months.

Dermatoglyphic features included bilateral Sydney lines, fusion of the *b* and *c* triradii into a *bc*

triradius on the left hand, and axial triradii in the *r'* position. Total finger ridge count was 155.

CYTOGENETIC STUDIES

High resolution chromosome banding was performed on cultured peripheral lymphocytes with ethidium bromide pretreatment two hours before harvest, according to the method described by Ikeuchi.⁴ G and R bands were obtained using GAG and RBG banding, respectively. All cells examined, of which 18 G banded and 12 R banded were photographed and karyotyped, showed an interstitial deletion of the long arm of chromosome 4 with no evidence of translocation of the deleted segment to another chromosome. The karyotype was interpreted as 46,XX,del(4)(q26-00q27-00) (fig 2). The parents' chromosomes showed normal G banded karyotypes.

Discussion

The diagram in fig 3 shows the deleted segments in the four cases, including the present one, with interstitial deletion of 4q involving q26. The clinical features of these four cases are listed in the table. Somatic growth is normal in all but one. It is of interest to compare our patient's phenotype with the others, because our patient had a single band deletion of 4q26. Clinical findings observed in all of these cases include psychomotor retardation, coloboma, prominent forehead, epicanthus, broad based nose, and broad, thin upper lip. The cylindrical and narrow pelvis in the present case was also

FIG 2 Three pairs of chromosome 4 from the proband, (a) G banded, (b) R banded, and (c) high resolution G banded. The deleted chromosome is on the left in (a) and (b) and on the right in (c).

FIG 3 Deleted segments of cases with interstitial deletion of 4q involving q26.

TABLE 1 Clinical features of cases with 4q interstitial deletion involving q26.

	Serville and Broustet ¹	Mitchell et al ²	Ligutić et al ³	Present case
Deleted segment	4q24→q32	4q21.3→q26	4q23→q27	4q26
Sex	F	F	F	F
Birth weight (g)/gestational age (wk)	2800/41	3500/40	3400/40	2360/40
Psychomotor retardation	Severely retarded	DQ 75	IQ 80	DQ 66
Hypotonia	NS	+	+	—
Asymmetrical palpebral fissures	—	+	+	+
Coloboma	+	+	+	+
Microphthalmos	+	—	—	+(L)
Rieger syndrome	—	—	+	—
Prominent forehead	+	+	+	+
Epicanthus	+	+	+	+
Low set ears	+	—	+	+(L)
Broad based nose	+	+	+	+
Broad, thin upper lip	+	+	+	+
Micrognathia	—	+	+	+
Cardiac anomaly	—	A closing VSD	—	—
Limb anomaly	NS	Overlapping toes	Limited thumb abduction, planovalgus deformity	Syndactyly (L), oligodactyly (L)
Cylindrical trunk/narrow pelvis	+	NS	NS	+
Somatic growth	Failure to thrive	Normal	Normal	Normal
Parental karyotypes	Normal	Normal	Normal	Normal

NS, not stated; *apparent from photographs.

present in the case of Serville and Broustet.¹ The above findings may be attributed to the monosomy 4q26.

However, Rieger syndrome was observed in the case of Ligutić *et al*³ and gene(s) associated with this syndrome have been provisionally assigned to 4q23→q27.⁵ Both ophthalmological and dental examination ruled out Rieger syndrome in the present case. This suggests that gene(s) associated with Rieger syndrome can be excluded from the 4q26 segment.

Limb anomalies, such as cutaneous syndactyly and oligodactyly, were noted only in our patient and, therefore, the significance of the monosomy 4q26 in the limb anomalies in our case is unknown at present. Further reports of cases of 4q interstitial deletion are required to establish the clinical map of 4q.

References

- Serville F, Broustet A. Pericentric inversion and partial monosomy 4q associated with congenital anomalies. *Hum Genet* 1977;39:239–42.
- Mitchell JA, Packman S, Loughman WD, *et al*. Deletions of different segments of the long arm of chromosome 4. *Am J Med Genet* 1981;8:73–90.
- Ligutić I, Brečević L, Petković I, Kalogjera T, Rajić Z. Interstitial deletion 4q and Rieger syndrome. *Clin Genet* 1981;20:323–7.
- Ikeuchi T. Inhibitory effect of ethidium bromide on mitotic chromosome condensation and its application to high-resolution chromosome banding. *Cytogenet Cell Genet* 1984;38:56–61.
- McKusick VA. The human gene map 10 April 1986. *Clin Genet* 1986;29:545–88.

Correspondence and requests for reprints to Dr Tomiko Motegi, Department of Pediatrics, Tokyo University Hospital Branch, 3-28-6 Mejiro-dai, Bunkyo-ku, Tokyo, Japan 112.