Partial trisomy for 2q in a patient with dir dup(2)(q33.1q35)

D R Romain, N G Mackenzie, D Moss, L M Columbano-Green, R H Smythe, R G Parfitt, J W Dixon

Abstract

A 22 year old woman with partial trisomy for the long arm of chromosome 2 is described. The karyotype is 46,XX, dir dup(2)(q33.1q35) de novo confirmed by FISH using a chromosome 2 specific paint. Parental chromosome studies were normal. To our knowledge this is the first report of trisomy for this specific segment of 2q and only the sixth case of de novo direct duplication of 2q, one of which was mosaic. Clinical features include epicanthus, clinodactyly, scoliosis, broad, flat nasal bridge, thin upper lip, long philtrum, and short neck.

(J Med Genet 1994;31:652-653)

Case report

The proband is a female born at term by normal delivery on 15.6.70. Birth weight was 2600 g, head circumference 31 cm, and crown-heel length 47 cm (all less than the 10th centile).

Positional talipes was present at birth requiring bracing and splinting for approximately two years. There were no dysmorphic features noted at delivery. Antenatal history was uneventful. The mother's age was 40 years and the father's 41 years. Family history was unremarkable except for the mother's single miscarriage at 8 weeks' gestation, 15 years before the birth of the proband. All development was delayed. She sat unsupported at 9 months and first walked at 2 years. At 4 years her weight was 17 kg, height 103 cm, and head circumference 48.5 cm (50th centile). Hearing was assessed as normal but speech had not been attained. Gross motor development seemed to be somewhat more advanced than other areas. Physical examination showed hypertelorism and epicanthic folds but no other abnormalities were noted. Urinary amino acids were normal. Chest and skull x rays were normal. Chromosome studies were also reported as normal.

Speech was attained at 7 years of age. At 9 years following concern about her walking, skeletal x rays showed a long slow scoliosis with concavity to the left, which was thought to be secondary to the left leg being 4.6 cm longer than the right.

Currently at 22 years old, her weight is 85 kg (>90th centile) and height 160 cm (<25th centile). She has severe intellectual and physical impairment, with overall development between 3 and 5 years of age. Clinical features include epicanthus, clinodactyly of the fifth digit on the

Figure 1 Frontal and lateral facial appearance of proband.

Central Regional
Genetics Service,
Cytogenetics
Laboratory,
Wellington Hospital,
Private Bag 7902,
Wellington South, New
Zealand

D R Romain
L M Columbano-Green
R H Smythe
R G Parfitt
J W Dixon

Department of
Paediatrics, Wanganui
Hospital, Private Bag,
Wanganui, New
Zealand

N G Mackenzie
D Moss

Correspondence to
Dr Romain.

Received 28 January 1994
Revised version accepted for
publication 7 April 1994

left hand, broad feet, depressed nasal bridge, thin upper lip with cupid's bow, well developed, long philtrum, and short neck (fig 1).

Chromosome studies using high resolution G banding showed a 46,XX dir dup (2)(q33.1 q35) karyotype (fig 2). The chromosome 2 origin of the additional segment was confirmed by fluorescent in situ hybridisation (FISH) using a chromosome 2 specific paint. Parental karyotypes were normal.

Discussion

Direct intra-arm intrachromosomal duplications are very rare. Unequal interchange in meiosis between homologous chromosomes and unequal intrachange between chromatids of one

chromosome by an inversion or insertional translocation have been postulated as possible mechanisms of formation.

To our knowledge this is the first report of trisomy 2q for this specific segment and only the sixth de novo tandem duplication.¹⁻⁵ The majority of published cases have resulted from malsegregation of a translocation or insertion present in one of the parents. Hence the patients have duplication of 2q which may be accompanied by partial monosomy for other chromosomes.

The main clinical phenotype associated with trisomy 2q3 specifically has recently been reviewed.⁶⁻⁸ Our case shows many of these features (fig 1) namely, epicanthus, broad, flat, depressed nasal bridge, thin upper lip with cupid's bow, long philtrum with undefined pillars, short neck, clinodactyly and severe intellectual and physical impairment. She does not have pronounced frontal bossing or temporal depression, nor does she now show hypertelorism as noted at the age of 4 years. External genitalia is normal. Unfortunately a cell line is not available from this patient.

We thank H Lawton for typing this manuscript and the Audio-Visual Unit of Wellington Public Hospital for help with the illustrations.

Figure 2 High resolution G banded example of the dir dup (2q). The duplicated segment is indicated on the normal homologue between arrows.

1 Mu Y, Van Dyke DL, Weiss L, Olgac S. De novo direct tandem duplication of the proximal long arm of chromosome 2: 46,XX, dir dup(2)(q11.2q14.2). *J Med Genet* 1984;21:57-8.

2 Yu CW, Chen H. De novo inverted tandem duplication of the long arm of chromosome 2(q34→q37). *Birth Defects* 1982;38:311-20.

3 Schumacher RE, Rocchini AP, Wilson GN. Partial trisomy 2q. *Clin Genet* 1983;23:191-4.

4 Gardner RJM, Dockery HE, Fitzgerald PH, et al. Mosaicism with a normal cell line and an autosomal structural rearrangement. *J Med Genet* 1994;31:108-14.

5 Marchese S, Diggans G, Garver K, Stadler M. De novo 46,XX,dup(2)(q21→q31) ascertained by prenatal cytogenetic analysis. *Am J Hum Genet (Suppl)* 1984;36:1035.

6 Rivera AH, Cantu JM. Chromosome 2. Trisomy distal 2q. In: Buyse ML, ed. *Birth defects encyclopaedia*. Oxford: Blackwell Scientific Publications, 1990:331-2.

7 Ramer JC, Mowrey PN, Robins DB, Ligado S, Trowfighi J, Ladoa RL. Five children with del(2)(q31q33) and one individual with dup(2)(q31q33) from a single family: review of brain, cardiac and limb malformations. *Am J Med Genet* 1990;37:392-400.

8 Dahoun-Hadorn S, Bretton-Chappuis B. De novo inversion-duplication of 2q35-2qter without growth retardation. *Ann Genet (Paris)* 1992;35:55-7.