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

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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.

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 46.5 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
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)(q33.1q35) 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 intrachromatid interchange 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.3-5 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.

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