Partial trisomy 22 (q11.2-q13.1) as a result of duplication and pericentric inversion

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Abstract

A case of a 27 year old male with a duplication of part of the long arm of chromosome 22 (22q11.2-q13.1) together with a pericentric inversion of the same chromosome is reported. Particular phenotypic features of note include absence of speech, persistent self-injury, lack of daily living skills, colobomata, and very poor vision. Similarities between this case and other case reports of duplications of the long arm of chromosome 22 are discussed.

(J Med Genet 1995;32:306-308)

Complete trisomy 22 has very rarely been reported in live births,^{1,2} although it is a common finding in spontaneous abortions.^{3,4} The existence of such a chromosomal abnormality has, however, been questioned⁵ although there have been a number of recent reports of trisomy 22 confirmed by in situ hybridisation techniques.^{6,7} Partial trisomies for both the proximal and distal segments of the long arm of chromosome 22 have been described by a number of authors.⁸⁻¹⁰ We report a case of a duplication of part of the long arm of chromosome 22 (22q11.2-q13.1) together with a

pericentric inversion of the same chromosome.

Case report

The proband was a 27 year old male who had a moderate degree of learning disability and at the time of reporting was residing in a long stay unit for people with such impairment. Pregnancy and delivery had been normal, and although he was cared for at home for the first 11 years of his life, he spent subsequent years in long stay residential units. He had limited communication skills, poor mobility, and required help with all daily living skills. There was a longstanding history of persistent self-injury and hyperoral activity.

On physical examination he was less than 150 cm tall (<3rd centile) and weighed 70 kg (<50th centile). His head circumference was 52 cm, proportional for his height. He had a prominent forehead, low posterior hairline, prognathism of the lower jaw, tongue protrusion, and thick fleshy lips. In both eyes he had ectopic pupils with "pear shaped" colobomata with an abnormally pigmented retina and persistent pupillary membrane remnants. Vision was extremely poor in both eyes. His ears and nose appeared normal (figs 1 and 2).

He had bilateral single transverse palmar

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Received 18 July 1994
Revised version accepted for
publication 21 November
1994

Figure 1 AP view of craniofacial dysmorphism of proband.

Figure 2 Lateral view of craniofacial dysmorphism of proband.

Figure 3 Partial karyotype of proband illustrating normal (left) and abnormal (right) chromosomes 22: (A,B) G banding, (C) schematic idiogram.

creases with short hands and fingers; the distal phalanx of both thumbs was particularly short. He also had short feet and toes. There was a moderate thoracic kyphosis. The distribution of body hair was normal with a normal male pattern of pubic hair growth, although he had a small penis and testes.

He had three sibs, aged 32, 31, and 19 years, who were well. There was no family history of any mental or physical disorder. He was prescribed no medication and had no psychiatric disorder associated with his learning disability.

CYTOGENETICS

Cytogenetic preparations were obtained from phytohaemagglutinin stimulated lymphocytes from a peripheral blood sample. Cultures were set up and harvested by standard methods.

G banded analysis showed the presence of one normal chromosome 22 and a submetacentric chromosome of approximately the size of chromosome 16. C banding confirmed the presence of only a single centromere, while staining with silver nitrate¹¹ showed the presence of a nucleolus organiser region (NOR) in the middle of the long arm of the rearranged chromosome. Chromosome painting with a 14; 22 centromeric probe (D22Z3, Oncor) and with a chromosome 22 paint (Cambio) confirmed that all of the additional material was derived from chromosome 22.

The rearranged chromosome was interpreted as resulting from a duplication (probably an inverted duplication) of part of the long arm of chromosome 22 (from q11.2 to q13.1) followed by a pericentric inversion, although other interpretations are also possible. The karyotype of the proband is therefore 46,XY,dup(22)(q11.2→q13.1),inv(22)(p13q11.2) (figs 3 and 4). He is effectively trisomic for the region 22q11.2 to 22q13. Both parents have normal karyotypes.

A cell line has not been established from this patient.

Discussion

The majority of reported duplications of chromosome 22 involve the proximal segment of chromosome 22. Duplications of the distal

segment have been reported in only a few cases,^{5,8,12,13} but these cases have allowed the delineation of a distal 22q syndrome. Our patient appears to represent a duplication of 22q11.1 to q13, which has only been reported once previously to our knowledge.¹⁴

The phenotypic features of the present case have a number of similarities with the case of Taylor *et al*,¹⁴ notably absence of speech, persistent self-injury, lack of daily living skills, and very poor vision. The case of Taylor *et al*¹⁴ has some features not present in our case, which may be accounted for by (1) slight differences in the apparent breakpoints or (2) a larger duplication in the former.

However, the phenotypic features in our patient also overlap to some extent those reported in a case by Abeliovich *et al*⁸ and the duplication present in that case may also overlap the region duplicated in the present case. As in that case, our patient represents a "pure" duplication of 22q, in this case from q11.2 to q13.1, without involvement of any other chromosome segment. It is noteworthy that both our patient and that reported by Abeliovich *et al*⁸ have colobomata, which has been commonly reported in the "cat eye" syndrome (assigned to 22pter→q11).¹⁵

As suggested by Rivera,¹⁶ this case may represent a further case allowing the assignment of coloboma to the 22q11–12 interface. Other features in common with the case report by Abeliovich *et al*⁸ include prominent forehead and single transverse palmar crease. The case reported by Abeliovich *et al*⁸ also has a number of features in common with other reported cases of distal trisomy 22q (cleft lip and palate, micrognathia, etc) which was not observed in the present case and may therefore be accounted for by duplication of the region 22q13.1–qter.

The authors wish to thank Mary Strachan and Brian Byrne for technical assistance in this case.

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Figure 4 Partial karyotype of proband, illustrating normal (left) and abnormal (right) chromosome 22; (top) C banding, (bottom) NOR staining.

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