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

V P Prasher, E Roberts, A Norman, A C Butler, V H R Krishnan, D J McMullan

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.


Complete trisomy 22 has very rarely been reported in live births, although it is a common finding in spontaneous abortions. The existence of such a chromosomal abnormality has, however, been questioned although there have been a number of recent reports of trisomy 22 confirmed by in situ hybridisation techniques. Partial trisomies for both the proximal and distal segments of the long arm of chromosome 22 have been described by a number of authors. 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 hyperorality.

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...
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 sub-
metacentric chromosome of approximately the
size of chromosome 16. C banding confirmed
the presence of only a single centromere, while
staining with silver nitrate showed the pres-
ence 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) con-
formed 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) fol-
lowed 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 chro-
mosome 22 involve the proximal segment of
chromosome 22. Duplications of the distal
segment have been reported in only a few
cases, but these cases have allowed the
delineation of a distal 22q syndrome. Our
patient appears to represent a duplication of
22q11.1 to 13, which has only been reported
once previously to our knowledge.

The phenotypic features of the present case
have a number of similarities with the case
of Taylor et al, notably absence of speech,
persistent self-injury, lack of daily living skills,
and very poor vision. The case of Taylor et al 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 re-
ported in a case by Abeliovich et al and the
duplication present in that case may also over-
lap 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 Abeli-
ovich et al have colobomata, which has been
commonly reported in the "cat eye" syndrome
assigned to 22pter→q11.1.

As suggested by Rivera, this case may rep-
resent 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 include prominent forehead
and single transverse palmar crease. The case
reported by Abeliovich et al 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 ac-
counted for by duplication of the region
22q13.1–qter.

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