Partial trisomy 12q: report of a case and review

SUMMARY A malformed male infant with pure partial trisomy 12q (q24.1→qter), resulting from an unbalanced segregation of a paternal balanced translocation t(2;12)(q37;q24.1), is described. The cytogenetic and clinical abnormalities of the proband are compared with those of four previously reported cases of partial trisomy 12q, two of which also appear to have pure trisomy of segment 12q24.1→12qter.

There are, apparently, only four previously reported cases with any significant partial trisomy 12q,1-4 two of which appear to have no other chromosome imbalance.2-4 Here we describe the clinical and cytogenetic abnormalities in a new case of pure partial trisomy 12q, compare the findings with those in the four previous reports, and discuss the cause of the low incidence of this anomaly.

Case report

The proband was born after an uncomplicated pregnancy and delivery at 36 weeks' gestation. His parents, who already had a normal daughter, were unrelated and healthy. The mother was aged 22 years and the father 25 years. There was no family history of spontaneous abortions or stillbirths. At birth the proband weighed 2650 g and his Apgar score was 9. During the first week he received surgical correction of anal stenosis but otherwise his neonatal period was normal.

On presentation at the Clinica Pediatrica,
University of Catania at 5 weeks, his weight was 2850 g, length 46.5 cm, and head circumference 34.5 cm. He had an odd facies (fig 1, table), a short neck with redundant skin folds, clenched hands with overlapping fingers and clinodactyly of fingers 3 and 5, bilateral hammer toes, a sacral dimple, a small penis, and undescended testes. A cardiac systolic murmur was audible along the left sternal border and x-ray investigation revealed enlargement of the left third cardiac arch. Dermatoglyphic studies showed bilateral transverse single palmar creases and hypoplasia of the digital dermal ridges with a finger tip pattern of 5A, 4Lu, and 1W. Both eyes showed myopic refraction.

On re-examination at 4 months, the previously noted abnormalities were still evident and the child showed severe physical and psychomotor retardation.

**CYTOGENETIC STUDIES**

Chromosome preparations were obtained from peripheral blood using standard techniques and GTG banded with a method modified from that of Seabright. The karyotype of the father was shown to be 46,XY,t(2;12)(q37;q24·1) (sub-division of

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**TABLE**  Cytogenetic and clinical details in cases of partial trisomy 12q

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<tr>
<th></th>
<th>Hirschorn et al1</th>
<th>Prieur et al2</th>
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<td><strong>Cytogenetic findings</strong></td>
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<td>t(4;12)(q26;q12)</td>
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<td>Trisomy</td>
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<td>9p21→9pter</td>
<td>21p11→21pter</td>
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<td><strong>Clinical findings</strong></td>
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*Observed in photographs only.

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12q24 as in Sanchez et al5) and that of the proband
46,XY,der(2),t(2;12)(q37;q24·1)pat (fig 2). The
proband was thus trisomic for segment 12q24·1→
12qter with no detectable monosomy of 2q.

The karyotype of the mother was normal but the
family did not consent to cytogenetic investigation of
other relevant family members, who were, however,
phenotypically normal.

Discussion

Full trisomy 12 has not been reported in liveborn
subjects or in cytogenetic surveys of perinatal
mortalities9,10 and has only very occasionally been
detected in studies of spontaneous abortuses, in
embryos showing an early arrest of development.11,12
Similarly, trisomy 12 mosaicism has very rarely been
found.13

Cases with any significant trisomy of long arm
material of chromosome 12 are also extremely rare
with only four previous reports, all involving live-
born infants.1–4 In contrast, there have been many
liveborn cases with trisomy of short arm material of
chromosome 12, a few including the juxtacentromeric
region of 12q, for which a clinical syndrome has been
delineated.14 Conversely, in balanced translocations
of chromosome 12 there is far greater involvement
of the long arm than the short arm.15 This discrepancy
may be an indication of the lethality of additional
long arm material, which would account for the
almost complete non-viability of the full trisomic
condition. However, since the abnormalities in three
of the cases of partial trisomy 12q (present case2,3)
were compatible with an extended postnatal survival,
the relatively low frequency of partial trisomy 12q in
the liveborn population may be the result of factors
other than lethality, such as a high level of alternate
segregation with a low level of interstitial chiasmata.16

The case described here and the previous reports
of partial trisomy 12q are similar in resulting from
an alternate or adjacent 1 segregation (with and
without an uneven number of interstitial chiasmata
respectively6,9) of a parental balanced translocation
(table). The exchange point on chromosome 12 in
the cases described by Hobolth et al,2 Hemming and
Brown,4 and the present report appears to be at
q24·1, resulting in trisomy of an almost identical
segment of 12q. Furthermore, no monosomy of the
derived chromosome could be detected in the present
case and that of Hemming and Brown,4 because in
both instances either the parental translocation was
non-reciprocal or the exchange point was telomeric
in the recipient chromosome. In addition, the report
of Hobolth et al2 can also be considered to be a pure
trisomy of segment 12q24·1→12qter since the
absence of 21p, resulting from the reciprocity of the
parental translocation, is unlikely to have contributed
to the abnormal phenotype.17 However, in the cases
of Hirschhorn et al1 and Prieur et al9 the parental
translocations were both reciprocal and almost
symmetrical, resulting in trisomy of nearly the whole
of 12q with monosomy of the distal half of 4q, and
trisomy of segment 12q24·2→12qter with monosomy
of the distal half of 9p, respectively.

In the latter two cases it seems improbable that a
definite distinction can be made between the pheno-
typic expression of the partial monosomy and the
partial trisomy 12q. It is possible that in the case of
Hirschhorn et al,1 for which few clinical details are
available, both the partial monosomy 4q and the
partial trisomy 12q contributed to the abnormalities
reported. However, Prieur et al9 considered that the
clinical features in the case they described were, in
the main, consistent with the syndrome associated with
partial monosomy 9p.

It appears likely, therefore, that a phenotypic
comparison that only includes the cases with a pure
partial trisomy 12q (present case2,3) will be more
informative. The clinical features which appear to be
common to the present case and to either or both of
the other two are upward slanting palpebral fissures,2
poorly lobulated ears2,4 which are low set,2 flat nasal
bridge,4 long philtrum,2 micrognathia,2 short neck2
with redundant skin folds,2,4 simian creases,2,4
hammer toes,2 cryptorchidism,2 sacral dimple,4
hypotonia,4 cardiopathy,2 and psychomotor retardation2
(table).

Although there are as yet too few cases to delineate
a phenotype for partial trisomy 12q, it is probable
that the consistent features in the three cases with
pure trisomy of apparently the same segment
(q24·1→qter) of chromosome 12 will form the basis
of a clinical syndrome which will be defined further
with the accumulation of more data.

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References

1. Hirschhorn K, Lucas M, Wallace I. Precise identification
of various chromosomal abnormalities. Ann Hum Genet
Unilateral radial aplasia and trisomy 22 mosaicism

SUMMARY  A child with unilateral radial aplasia, asymmetry, other malformations, and severe physical and mental retardation is reported. In blood and bone marrow cultures a low mosaicism for trisomy 22 was found. In a few cells a chromosome 22 was missing. The importance of early cytogenetic analysis on large numbers of cells is emphasised, especially in cases of asymmetry where mosaicism is suspected.

Radial dysplasia is a relatively common limb malformation which has been associated with major anomalies in various systems, mostly genitourinary, skeletal, gastrointestinal, and cardiac. It may occur within a definite syndrome, for example, thrombocytopenia and absent radius (TAR), Holt-Oram syndrome, Fanconi’s anaemia, and VATERL association, and it has also been reported in chromosomal disorders like trisomy 13 and 18.1

We describe a child with total unilateral radial aplasia associated with a clustering of defects on the same side, in whom trisomy 22 mosaicism was demonstrated.

Case report

A 2900 g female child was born after a normal pregnancy and delivery to non-consanguineous parents of Arabic origin. The 25-year-old mother, the 36-year-old father, and the four other children were healthy. There was no history of any congenital anomaly in the family.

A clustering of malformations was evident on the left side including a small palpebral fissure with slight ptosis, hypotrophy of the cheek, a low set ear with abnormal configuration of the helix, and mild stenosis of the external auditory canal. Total left radial aplasia with absent thumb was present (fig 1). The left forearm, hand, and the four medial fingers were smaller than those on the right side and there was colateral clinodactyly of the little finger with only one transverse crease on the left.

Repeated blood counts, including platelet and

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Note added in proof

Since submission of this paper five cases of pure, or almost pure, partial trisomy of 12q24 have been reported.18–20 The many features common to these and to the three cases of pure partial trisomy described above support the suggestion in the concluding paragraph that pure trisomy of this region of chromosome 12 results in an identifiable clinical syndrome.

References


Case reports


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