‘Complete 5p’ trisomy: 1 case and 19 translocation carriers in 6 generations

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SUMMARY A description is given of a female infant with multiple malformations and mental retardation who died at 31 months. Cytogenetic studies indicate trisomy of the complete short arm of chromosome 5, resulting from the unbalanced segregation of a balanced translocation in the mother whose karyotype was interpreted as 46,XX,t(5;15)(p11;p12). The karyotype of the proband was designated 46,XX,der(5)t(5;15)(p11;p12)mat. Family studies indicate that the translocation had been present in the family for at least 6 generations.

Six cases of partial trisomy of presumptive 5p have been reported by Lejeune et al. (1964 and personal communication), Laurent and Robert (1966), de Capoa et al. (1967), and Noel et al. (1968).

We present a case which we believe to be the only recorded example of trisomy for the complete short arm of chromosome 5 (Brimblecombe and Lewis, 1966). The trisomic condition is the consequence of unbalanced segregation of a balanced translocation found in the mother and interpreted as 46,XX,t(5;15)(p11;p12).

Case history

The proband, Jennifer K, was born normally at term after an uneventful pregnancy, and weighed 2410 g. There was asymmetry of the face, with coloboma of the iris and microphthalmia affecting the left eye. The left ear was downwardly displaced and malformed, with a flattened helix (Fig. 1). Bilateral talipes equinovarus was present. At the age of 5 weeks a successful operation for pyloric stenosis was undertaken.

Her developmental progress was retarded so that by the age of 7 months her performance was that normally achieved by an infant of 2 months, and by the age of 30 months she had attained a developmental age of only 12 months. Her weight gain throughout was poor. She died suddenly at the age of 31 months, the cause of death being bronchopneumonia, which was confirmed at necropsy. The only additional abnormality found at this time was a small corpus callosum.

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Karyotypes from the proband were prepared from both peripheral blood and fibroblasts; karyotypes from the other members of the family were prepared from peripheral blood cultures only. In the proband each cell showed an unbalanced karyotype in which one D group chromosome was replaced by a sub-metacentric chromosome which was characterised by a conspicuous unstained segment in the short arm, proximal to the centromere. The abnormal chromosome was identified subsequently as one component of a balanced translocation carried not only by the

Fig. 1 Facies of proband, showing asymmetry, microphthalmia of left eye, and displaced and malformed left ear.
mother of the proband, but also by 16 other members
of the family; furthermore, it can be inferred from
the pedigree that another 2 members carried the
same balanced translocation abnormality (see
pedigree, Fig. 2). Autoradiographic studies indicated
that the translocation involved the short arms of
chromosome 5 and 15 (Fig. 3); more recent investiga-
tion using fluorescence and Giemsa banding
techniques have identified the breakpoints more
precisely as 5p11 and 15p12 (Fig. 4).

From these studies we conclude that the following
two karyotypes apply:

1. Karyotype of the proband:
   46,XX, der(5),t(5;15)(p11;p12)mat

2. Karyotype of the carriers:
   46,XX or XY, t(5;15)(p11;p12)

Investigation of blood groups and red cell enzymes
in the proband and 16 members of the family were
undertaken by Dr E. Robson. No correlation of any
significance was found.

A study of the dermatoglyphs of the proband was
made by the late Professor Penrose who reported
"On the finger-tips the pattern size was small, as is
commonly found in trisomies, but no other abnor-
malities were demonstrated."

Family studies (Fig. 2)

If we consider in Fig. 2, the relevant members of
generations IV to VI known to have normal pheno-
types (IV.1, 2, 4, 5, 6, 7, 8, 14, 15, 16; V.2, 3, 4, 8, 9,
10, 12, 13, 14, 15, 16; VI.1, 2, 3, 4, 5, 8, 10, 11, 12, 14,
15, 17, 18) are 34 and of these 34 individuals there are
5 females with a normal karyotype and 11 females
with the balanced translocation; of the male popu-
lation in this group, 12 have normal karyotypes and 6
did have balanced translocations. In the same 3 genera-
tions 13 individuals were stillborn or died in infancy
(IV.3, 9, 10, 11, 12, 13; V.1, 6, 7, 11; VI.6, 13, 16); of
these, 8 were male and 5 were female. We have been
unable to ascertain whether malformations were
present in 9 of these 13 individuals; of the remaining 4,
V.1 was stated by her mother to have been born with
abnormalities the details of which were neither known
to her nor recorded; VI.6 was a stillborn anence-
phalic; VI.13 had multiple skeletal abnormalities,
including scaphocephaly, bilateral talipes equinovarus,
and spina bifida occulta; and the fourth was the
proband whose malformations have already been
described.
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In all, 8 out of 10 female carriers (III.4, 6; IV.5, 8; V.8, 9, 10, 12) of the balanced translocation in generations III to V have had a total of 43 offspring; of these 13 are cytogenetically normal (9 male); 16 are translocation carriers (5 male); 12 were stillborn or died in infancy (8 male), and there were 2 miscarriages at approximately 20 weeks (sex unknown). There is only one male carrier of the balanced translocation who has had offspring; he has had 2 sons, 1 of whom is normal and 1 of whom is a carrier of the balanced translocation.

Discussion

Partial trisomy of presumptive 5p was first described in 2 sibs by Lejeune et al. (1964 and personal communication), 1 being a baby who died in infancy, and the other a girl who is still living but severely mentally retarded. Both these patients showed asymmetry of the jaw similar to that found in our proband. Laurent and Robert (1966 and personal communication) illustrated a third case with a similar asymmetry of the jaw. De Capoa et al. (1967) described a further 2 cases with minor clinical defects, and in their review underlined the non-specificity, wide range, and relative mildness (apart from mental retardation) of their abnormalities. Finally a sixth case has been described by Noel et al. (1968), with minor physical abnormalities but severe mental retardation.

These are all partial trisomies of presumptive 5p. Complete trisomy of the short arm of an unidentified B group chromosome has been described by Gustavson et al. (1954), the patient having severe multiple abnormalities and dying at the age of 3 months. Some of the patient's abnormalities were similar to those found in our proband, namely scaphocephaly, scoliosis, macroglossia, and malformations of ear and long fingers and toes. It is of interest that asymmetry of the jaw was not present in Gustavson's case.

On the other hand, some of these malformations, namely scaphocephaly, macroglossia, malformations...
of the ears, and narrow palpebral fissures were also found in 1 or more of 4 cases of 4p trisomy described by Schinzel and Schmid (1972), Owen et al. (1974), and Darmady and Seabright (1975).

Therefore, there, appears to be some overlap of the clinical findings in the trisomies of the short arm of the B group chromosomes so far reported, comparable with that found in the chromosomal abnormalities of other groups. It is probable that a distinct phenotype associated with trisomy of the complete short arm of chromosome 5 will only be distinguished from that of trisomy of the complete short arm of chromosome 4 as further cases are identified.

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References


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