Case reports

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Trisomy 5p: a second case occurring in a previously described kindred

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SUMMARY A second child with trisomy 5p has been born in the kindred reported by Brimblecombe *et al.*¹ The cytogenetic findings were similar to those of the index case except that the derivation was paternal instead of maternal. Improved banding techniques enabled more accurate designation of the breakpoints. The clinical and necropsy findings are described. Three non-specific phenotypic malformations and one brain abnormality, possibly specific, were common to both.

Case report

The proband (fig 1) was born by lower segment caesarian section for breech presentation and suspected large head to the second wife of a previously identified carrier of a balanced translocation.

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FIG 1 The proband.

She was first cousin to the child formerly described by Brimblecombe *et al.*¹ (fig 2). The pregnancy was uneventful and amniocentesis was not requested despite the fact that the father had received genetic counselling and had one phenotypically normal son with a similar balanced translocation by his first marriage. His second wife was not fully aware of the genetic implications of her husband's family history. At birth the proband weighed 2410 g, crown to rump length was 33 cm, crown to heel length was 50 cm, and head circumference was 36 cm. She was 6 days premature by dates and 35 days premature by Dubowitz scoring.² At transferral from a peripheral hospital she was found to be hypothermic (34.8°C) and to have the following phenotypic abnormalities: large head (circumference 36 cm), low set immature ears, micrognathia, macroglossia, mild bilateral microphthalmos, depressed nasal bridge, long fingers and toes, and widely spaced nipples. She was also snuffly and had a hoarse cry. After initial difficulty with feeding she was discharged at 7 days of age weighing 2370 g. She was re-admitted at 31 days for failure to thrive (weight 2530 g) and recurrent feeding problems thought to result from a poor nasal air entry. Head circumference was now 38 cm and sutures were

FIG 2 Cousin of the proband.¹

splayed and scalp veins prominent. She was treated conservatively. Six days later she was thought to have pneumonia and died at the age of 37 days.

Necropsy did not support the diagnosis of pneumonia. Death resulted from hypoxia caused both by pulmonary circulatory overload secondary to a large persistent ductus arteriosus and by a mechanical obstruction in the nasopharynx.

Additional malformations found were an extremely narrow nasopharyngeal space, slit-like in the AP dimension, and a septate uterus with duplex vagina. The fixed brain was abnormally heavy and large (631.5 g instead of about 400 g). The cerebellum was very small; it weighed 33 g and the brain stem 9.5 g. Fairly extensive microscopical examination was performed. No abnormalities were found in the large cerebral hemispheres, the dentate nuclei in the cerebellum were malformed, and there was a large cortical heterotopia in the left cerebellar hemisphere. A smaller cortical malformation was seen in the uvula. A very unusual feature was found in the sections of the basis pontis near the level of the emergence of the fifth nerve. Fibrillary astrocytic tissue had grown out of the sides of the pons into the adjacent leptomeninges.

Further data became available on the size of the head and the examination of the first child reported.¹ The head was large, with a circumference at 24 and 33 weeks of about 43 cm. The fixed brain at the age of 2½ years weighed 1319 g, of which the brain stem and cerebellum weighed 131 g. The left optic nerve was smaller than the right (the left eye was small).

Microscopical examination showed no developmental abnormalities in the cerebral hemispheres, brain stem, or cerebellum. In particular there was no evidence of any cerebellar cortical heterotopia.

DERMATOGLYPHS

The fingerprints of the proband were difficult to obtain on account of her age. Both thumbs, right forefinger, and possibly the left fourth finger had arches; the remaining fingers probably had ulnar loops. The pattern intensity was low and the total ridge count (if it were possible) would be low, in the order of 10 to 20. Palm and feet prints were unremarkable. These findings were the same as in her cousin.¹

CYTOGENETIC INVESTIGATIONS

The cytogenetic findings in the proband and the translocation carrier father were similar to those originally described in other members of this family, but improved banding techniques have enabled a more accurate determination of the breakpoints to be made. The karyotype descriptions, therefore, have been modified slightly from the original report. The karyotype of the father, known

previously to be a balanced translocation carrier, has been identified as: 46,XY,t(5;15)(p13;p13). The unbalanced karyotype of the proband, trisomic for the greater part of the short arm of chromosome 5, is described as 46,XX,der(15),t(5;15)(p13;p13)pat (fig 3). The conspicuous NOR band revealed by silver staining (fig 4) indicated quite clearly that the

FIG 3 (a) Partial karyotype of proband showing karyotype 46,XX,der(15),t(5;15)(p13;p13)pat. (b) Partial karyotype of father showing balanced translocation, karyotype 46,XY,t(5;15)(p13;p13).

FIG 4 Silver stained preparation showing NOR bands in proband: translocation chromosome arrowed.

FIG 5 Partial pedigree of family.

breakpoint in the short arm of chromosome 15 must be distal to the band p12 (thought originally to be the breakpoint) and is now, therefore, redesignated p13. The breakpoint in the short arm of chromosome 5 is more distal than originally thought and is located at p13.

Thus, the proband and presumably the case described previously are trisomic for the short arm chromosome segments p13→pter and not, as previously thought, for the complete short arm of the chromosome.

Family studies

The relevant section of the pedigree previously published¹ is shown in fig 5. The father V.13 of the proband VI.23 has the balanced translocation karyotype 46,XY,t(5;15)(p13;p13), as has his son VI.18 by his first marriage and his sister V.12, mother of the previously affected child VI.16.

Discussion

Despite the fact that this proband and the previously reported child¹ were first cousins and had apparently identical karyotypes, their abnormalities were similar in only four respects: macroglossia, malformed low set ears, long second to fifth fingers and toes, and large brains. Microphthalmos was unilateral and severe and associated with coloboma of the iris in the previous child and bilateral and mild in the proband. It is, however, impossible to compare adequately two infants when one survived for 31 months and the other for 37 days. We suggest that the facial appearance of the proband resembles cases of partial trisomy 5p previously described by Di Liberti *et al*³ more closely than does that of her cousin. Four of the six other malformations in the proband, micrognathia, low set malformed ears, flat nasal bridge, and long fingers and toes, have also been described not only in trisomy 4p but also in other chromosomal abnormalities. However 75% (sic) of 27 cases of trisomy 4p collected by Gonzalez *et al*⁴ had microcephaly, whereas four of 14 cases of

trisomy or partial trisomy 5p (PT5P) collected by Leschot and Lim⁵ had macrocephaly. Three occurred in one kindred described by Opitz and Patau⁶ where the proband had PT5P proven by her karyotype; two of her first degree relatives and three of her second degree relatives were presumed to have PT5P. The proband had macrocephaly and hydrocephalus resulting from the Dandy-Walker syndrome. Her sib had macrocephaly and a big brain without hydrocephalus and her mother's sister had macrocephaly and hydrocephalus, possibly resulting from an Arnold-Chiara malformation. The fourth was our previously described case,¹ and to these we can now add a fifth, our proband.

The large brain with PT5P seems to be unique, even though there are other instances of macrocephaly, and even though some are familial. This and the small cerebellum raises the possibility of a relation between a chromosomal abnormality and an alteration in growth of the nervous system. The malformations in the cerebellum in our proband were not specific. Lastly, there was the extensive astrogliosis in the leptomeninges on the sides of the pons. Small similar foci are said to be relatively common in malformed brains or in brains with cavitated lesions dating to the developmental period. According to Friede⁷ they are uncommon in otherwise normal brains. The appearances in our case are, to our knowledge, unique.

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