Case reports

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Partial trisomy 6q: case report with necropsy findings

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SUMMARY A male infant with partial trisomy 6q is described. This patient shares features with 12 previously reported cases including hypertelorism, cleft soft palate, bow shaped mouth, micrognathia, short, laterally webbed neck, clubbing of hands and feet, syndactyly, and growth retardation. In addition, visceral anomalies less frequently reported are described. These observations may extend the phenotypic characterisation of the trisomy 6q syndrome.

Trisomy for the distal part of the long arm of chromosome 6 was first reported by de Grouchy *et al*[1] in 1969. Since then, other cases of this unusual anomaly have been described. Only three case reports have included necropsy findings, since most children have survived infancy. The oldest patients were 16 and 23 years of age at the time of publication.[2] Our patient died shortly after birth.

Case report

The patient, the male child of a 27 year old mother and a 30 year old father, was born after 38 weeks' gestation by spontaneous vaginal delivery. Apgar scores were 0 at one and five minutes and 1 at 10 minutes. Physical examination of the infant at birth revealed a weight of 1095 g, length of 46·2 cm, and head circumference of 30 cm (all below the 10th centile for gestational age). Both the anterior and posterior fontanelles were widely open. The eyes were widely set. The neck was short with lateral webbing. Micrognathia, cleft soft palate, and glossoptosis (Pierre-Robin anomalad) were also present. The nasal bridge was flattened and the nose was short. The mouth was bow shaped. Both feet and the left hand were clubbed, with syndactyly of the second and third toes of the right foot. No other anomalies were noted (figs 1 and 2). Despite vigorous efforts at resuscitation the infant died without ever developing spontaneous heartbeat or respiration.

Parental history was significant in that they had been attempting pregnancy for five years with one spontaneous abortion (six years before the current pregnancy) at three months' gestation. A hysterosalpingogram and endometrial biopsy three years previously had shown polycystic ovaries.

The mother had received clomiphene (Clomid) eight months before this conception, which was achieved through husband-donor artificial insemina-

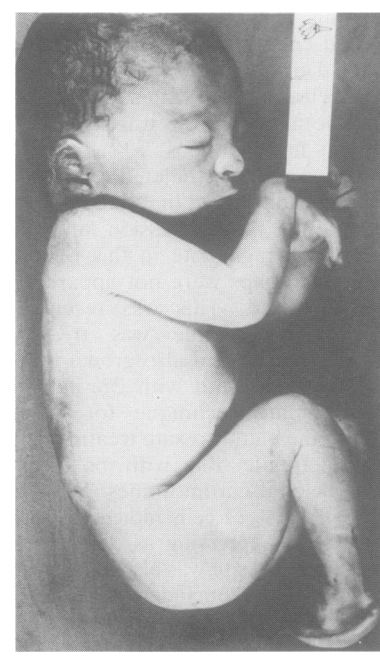

FIG 1 *Full body view of the infant showing clubbed feet, short neck, and micrognathia.*

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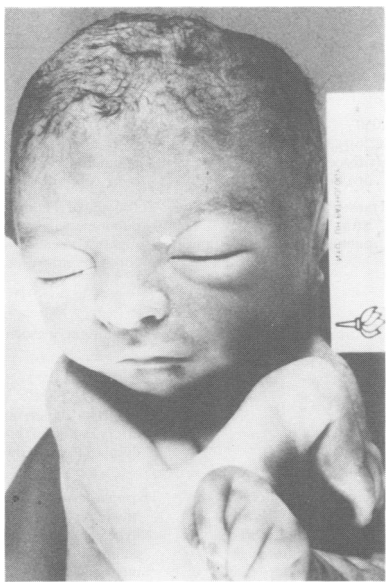

FIG 2 *The infant's face showing hypertelorism, broad nasal bridge, short nose, bow shaped mouth, micrognathia, and clubbed left hand.*

tion. The father had a history of oligospermia. Maternal history also included hypertension and pyelonephritis. No previous congenital abnormalities were noted in the family.

NECROSPY FINDINGS

Examination of the infant at necropsy revealed the external anomalies described above. Postmortem *x* ray examination showed bilateral cervical ribs, hypoplasia of the twelfth ribs, fusion of the third and fourth lumbar hemivertebrae, and mild brachycephaly. There was a 1·5×0·4 cm defect along the sagittal suture. Internal findings included tetralogy of Fallot with a unicuspid pulmonic valve, persistent left superior vena cava draining into the coronary sinus, and a displaced left coronary artery ostium (located superior to the sinus of Valsalva of the left anterior cusp of the aortic valve). Both kidneys were dysplastic with hypoplasia of the left renal vein and artery and the left ureter, and a right double ureter. The adrenal glands were grossly hypoplastic. The right mesocolon was absent. A small angiomatous malformation was noted in the right cerebral hemisphere. The brain was otherwise normal. Microscopical findings included amniotic fluid aspiration and pulmonary, renal, and subdural haemorrhage. The placenta was unremarkable.

CYTOGENETIC STUDIES

Material for chromosome analysis was obtained from samples of lung, kidney, and skeletal muscle. GTG banding showed that the short arms of one chromosome 3 were consistently longer than those of its homologue. In addition, there was a pericentric inversion of chromosome 9. The parents were then studied. The mother carried the inv(9); her karyotype was 46,XX,inv(9). However, the father's karyotype showed a balanced reciprocal translocation: 46,XY,t(3;6)(p26;q23). Thus, the child's karyotype was 46,XY,−3,+der(3),t(3;6)(p26;q23)pat, inv(9)mat (fig 3). He was effectively monosomic for the extremely small region 3p26→pter and trisomic for the region 6q23→qter.

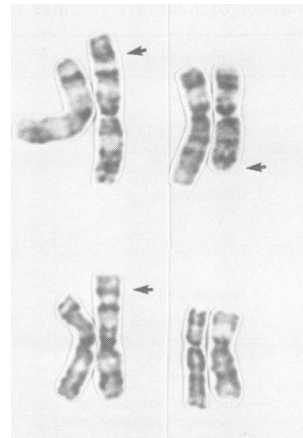

FIG 3 *Partial karyotypes showing chromosomes 3 and 6 from the father (upper row) and newborn infant (lower row). The derivative chromosomes (arrowed) are on the right in each pair.*

The paternal grandparents were not available for study. Two paternal uncles had normal karyotypes.

Discussion

Previous reports of trisomy of the distal part of the long arm of chromosome 6 have established it as a recognisable syndrome. The cases have in common mental retardation, microcephaly, hypertelorism, flat nasal bridge, micrognathia, short webbed neck, bow shaped mouth, joint contractures, camptodactyly, and low birth weight.[2–5] Many of these features are common to other chromosomal deletion and duplication syndromes. Only three previous case reports of partial trisomy 6 have included necropsy findings. Abnormalities seen in these earlier cases and in the current case are summarised in the table.

Of particular note is the similarity of the cardiac abnormalities in our case with that presented by Neu

TABLE *Comparison of necropsy findings of previously reported cases and present case.*

	Stamberg et al[3]	*Neu et al*[4]	*Duca et al*[5]	*Present case*
Sex	M	F	F	M
Birth weight (g)	1200	1280	2050	1095
Translocation	t(6;22)(q21;p13 or pter)mat	t(6;10)(q21;q26)mat	t(2;6)(q37;q25)mat	t(3;6)(p26;q23)pat
Central nervous system	Encephalocele	Absent olfactory tract and bulbs; hydrocephalus	Hydrocephalus; hypoplasia of corpus callosum	Angiomatous malformation, right cerebral hemisphere
Cardiovascular	Cardiomegaly	Persistent left superior vena cava; VSD; bicuspid stenotic aortic valve; preductal aortic coarctation	Transversely enlarged heart with VSD; enlarged pulmonary artery ostium	Tetralogy of Fallot, unicuspid pulmonic valve, persistent left superior vena cava, displaced coronary artery ostium
Respiratory	Non-lobated lungs	Non-lobated lungs	—	—
Gastrointestinal	Riedel's hepatic lobe; agenesis of gallbladder; omphalocele; imperforate anus	Malrotation of bowel	Gastric hypoplasia; hepatomegaly; megacolon	Absent right mesocolon
Genitourinary	Atresia of left ureteral orifice; hydronephrosis; ambiguous external genitalia	Hypoplasia of kidneys and ovaries	—	Hypoplasia of left ureter, renal artery, and vein; bilateral renal dysplasia; right double ureter
Other	Hypoplasia of adrenal glands; microcephaly; webbed neck; low set ears; hypertelorism; high arched palate; club feet	Accessory spleen; microcephaly; webbed neck; low set ears; microphthalmia; cleft lip and palate; bow shaped mouth; micrognathia; club foot; overriding toes	Microcephaly; short neck; hypoplasia of facial bones; hypertelorism; long philtrum; high arched palate; micrognathia; club foot	Hypoplasia of adrenal glands; brachycephaly; webbed neck; hypertelorism; cleft soft palate; bow shaped mouth; micrognathia; club feet and hand; rib and vertebral malformations

et al.[4] They reported persistent left superior vena cava, ventricular septal defect, bicuspid stenotic aortic valve, and preductal aortic coarctation. Cytogenetic analysis in the case of Neu *et al*[4] showed trisomy of 6q as a result of an unbalanced translocation between chromosomes 6 and 10. Our case involved trisomy of the same segment resulting from an unbalanced translocation of chromosomes 3 and 6. Translocations involved in other reported cases have involved chromosomes 2, 3, 11, 21, and 22. The consistency of phenotypic expression of trisomy 6q in the presence of such heterogeneity of translocation partners is convincing evidence that most of the malformations seen are not the result of any coincidental monosomy. Furthermore, the finding of cardiac anomalies in each of the cases necropsied suggests that they be included as a descriptive feature of trisomy 6q syndrome.

Chase *et al*[6] stated that the trisomy 6q syndrome is typified by chromosome breaks at 6q26. As other phenotypically similar trisomy 6q cases have been reported in which longer 6q fragments are triplicated,[7 8] it appears that the 6q terminus is crucial for the syndrome, and that additional genomic material from 6q does not consistently alter the phenotypic expression. The somewhat longer segment of 6q triplicated in our case may be relevant to decreased survival. It has been reported that the ratio of affected females to males is two to one[9]; our review of published reports shows that the sex ratio is approximately equal.

The subfertility of the translocation carrier in this case is of special note. Marmor *et al*[10] have reported azoospermia, oligospermia, and teratospermia in association with balanced autosomal translocations. Although translocations are said to be more prevalent among subfertile men than in the general population, sperm count was not significantly lower in translocation carriers than in the control subfertile men that they studied. Since the number of translocation carriers assessed for subfertility is as yet small, it is impossible to predict which translocations are most likely to interfere with fertility. The present case is unusual in that it is one of only two reported instances of paternally derived trisomy 6q.

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References

1 de Grouchy J, Emerit E, Aicardi J. Trisomie partielle pour le bras long d'un C(?6) par translocation t(Gp+;Cqs+). *Ann Genet (Paris)* 1969;**12**:133–7.

2 Clark C, Cowell H, Telfer M, Casey P. Trisomy 6q25→6qter in two sisters resulting from maternal 6;11 translocation. *Am J Med Genet* 1980;**5**:171–8.

3 Stamberg J, Shapiro J, Valle D, Kuhajda FP, Thomas G, Wissow L. Partial trisomy 6q due to balanced maternal translocation (6;22)(q21;p13) or (q21;pter). *Clin Genet* 1981;**19**: 122–5.

4 Neu RL, Gallien J, Steinberg-Warren N, Wynn RJ, Bannerman RM. An infant with trisomy 6q21→qter. *Ann Genet (Paris)* 1981;**24**:167–9.

[5] Duca D, Bene M, Ioan D, Maximilian C. Familial partial trisomy: 6q25→6qter. *J Genet Hum* 1980;**28**:31–7.
[6] Chase C, Jalal SM, Martsolf JT, Wasdahl WA. Duplication 6q24→6qter in an infant from a balanced paternal translocation. *Am J Med Genet* 1983;**14**:347–51.
[7] Fitch N. Partial trisomy 6. *Clin Genet* 1978;**14**:181–5.
[8] Tipton R, Berns J, Johnson W, Wilroy R, Summit R. Duplication 6q syndrome. *Am J Med Genet* 1979;**3**:325–30.
[9] Turleau C, de Grouchy J. Trisomy 6qter. *Clin Genet* 1981;**19**: 202–6.
[10] Marmor D, Taillemite JL, Van Den Akker J. *et al.* Semen analysis in subfertile balanced-translocation carriers. *Fertil Steril* 1980;**34**:496–502.

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Duplication 9p due to unequal sister chromatid exchange

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SUMMARY A case of trisomy 9p syndrome is reported. The karyotype showed a tandem duplication of the short arm and of the inverted heterochromatic block of chromosome 9. Unequal sister chromatid exchange seems to be the only possible cause of this finding.

Case report

The proband was referred for chromosome analysis when she was two years old because of multiple congenital malformations and psychomotor retardation. The parents were unrelated. The father was 37 and the mother 32 at the time of her birth. They had a normal 10 year old son. Two years before the birth of the proband a pregnancy ended in spontaneous abortion during the first trimester. The proband was born at 42 weeks' gestation by Caesarean section performed because of breech presentation.

Physical examination at two years showed an unusual facies with frontal bossing, deep set eyes, hypertelorism, bulbous nose, short philtrum, down turned mouth, large protruding ears, and short fifth fingers with clinodactyly. *X* ray examination showed delayed bone maturation and hypoplastic middle phalanges of the fifth fingers. Dermatoglyphic features included zygodactylous digital triradii *b* and *c*, bilateral simian creases, *t'* axial triradii on the left hand and *tt''* on the right hand. The patient was unable to walk, but could sit with support. Her mental development was subnormal. A clinical diagnosis of trisomy 9p syndrome was made.

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CYTOGENETIC STUDIES

Chromosome analysis performed on cultured peripheral lymphocytes showed 46 chromosomes with an aberrant chromosome 9 in all 102 divisions analysed. The rearranged chromosome showed a pericentric inversion of chromosome 9 of the common type (p11q13) and the presence of extra chromosomal material attached to the short arm. G banding, R banding, C banding, and the Goyanes technique,[1] a procedure for specific staining of chromosome 9 paracentromeric heterochromatin, showed that both the short arm and the inverted heterochromatic block were duplicated.

The position of the centromeres was shown by comparative analysis using both C banding and the Goyanes technique. The centromeres and the paracentromeric heterochromatin are both darkly stained using the first method, while with the second, only the paracentromeric heterochromatin of chromosome 9 is darkly stained, as the centromeres do not band.

The father and brother of the proband had normal chromosome complements, while the maternal karyotype was 46,XX,inv(9)(p11q13) (figure). Therefore, a tandem duplication of maternal origin was proposed, the karyotype being: 46,XX,dup inv(9)(p11q13)mat, (pter→p12::q13→p11::p24→p12::q13→p11::q21→qter) (figure).

Discussion

Trisomy 9p is responsible for a well known clinical syndrome that has been described in about 100 cases.[2] It may be a cause of familial mental retardation as in most cases it results from adjacent segregation of a parental translocation.[3]