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18q+, the progeny of a balanced translocation t(1;18)mat: case report with necropsy findings

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SUMMARY A female infant with additional genetic material on the long arm of chromosome 18 is described. Cytogenetic studies of the infant and her mother showed that the altered region resulted from an unbalanced translocation of part of the long arm of chromosome 1. This chromosomal abnormality has not been reported previously, according to a recent registry of abnormal chromosome patterns.¹ The patient had hydrops fetalis and multiple congenital abnormalities, involving the cardiovascular, respiratory, and skeletal systems, together with unusual facies. External features, radiological findings, and gross and microscopical examination at necropsy are presented and compared with previously reported cases of related but dissimilar chromosomal abnormalities.

Case report

The patient was a stillborn female infant born to a 29 year old white female (gravida 1) in the 34th week of

an uncomplicated pregnancy. The mother denied any history of fever, rupture of membranes, vaginal bleeding, hypertension, diabetes, smoking, or drug use. Her past medical history was unremarkable. During her pregnancy she took vitamins and iron. At the time of admission she had irregular uterine contractions. No fetal heart sounds were detected. Following rupture of the membranes, the amniotic fluid was seen to be tinged with blood. A few hours later she delivered a stillborn hydropic infant.

NECROPSY FINDINGS

Examination of the infant at necropsy revealed a hydropic female fetus of 34 weeks' gestation, weighing 2100 g (approximately 50th centile), and measuring 42 cm from crown to heel (approximately 10th to 25th centile). The head circumference was 30 cm (10th to 25th centile). External anomalies included low set ears, hypertelorism (fig 1), high arched palate, flexion of the second to fifth fingers of the right hand, and overlapping of the second over the first toe of the right foot. X-ray examination showed bony spicules in both proximal femora (fig 2) and cupping of the distal radius and ulna bilaterally (fig 3). Internal examination revealed approximately 150 cc of clear, serous fluid in the abdominal cavity and 10 cc of similar fluid in the

FIG 1 Facial appearance of patient showing hypertelorism and periorbital oedema.

FIG 2 X-ray of lower body of patient showing bony spicules in proximal femur bilaterally.

right pleural cavity. The organs were in normal positions. The organ weights were within the expected range for a 34 week gestation female fetus, except for the heart which weighed 18 g (normal 15.5), the liver 125 g (normal 98.1), and the thymus 1.5 g (normal 0.82). The heart showed hypertrophied right and left ventricles, dilated right and left atria, bicuspid aortic valve, mild stenosis of aortic and mitral valves, thickened pulmonary and mitral

FIG 3 X-ray of right arm of patient showing cupping of the distal radius and ulna.

valves, widened foramen ovale, and single (right) coronary ostium. The right lung showed only two main lobes with an accessory lobe attached to the upper lobe. There was only one umbilical artery. Haemorrhages were present in the viscera. The brain was markedly autolysed and therefore no sections were taken. Examination of the eyes showed persistence of the hyaloid system. The placenta weighed 680 g (normal 450 g) but did not appear hydropic microscopically. The umbilical cord contained one artery and one vein.

CYTOGENETIC STUDIES

Cytogenetic study was performed on successful cultures of fetal lung. GTG banding showed that one chromosome 18 had additional material on its long arm. The origin of that material could not be ascertained from study of the karyotype which was 46,XX,18q+.

Chromosomal studies of the mother showed there was an additional band at the q terminal region of chromosome 18 and a foreshortened terminal region on the q arm of chromosome 1. The karyotype was 46,XX,t(1;18)(q32;q22) (fig 4). The fetus had thus

FIG 4 Partial karyotypes of chromosome 1 and 18 pairs from (a) the mother and (b) the proband. The top row, despite overlaps on chromosomes 1b and 18a, is included because it is the best representation we have of the breakpoints at 1q32·1 and 18q22·2. The chromosome 1 pair of the proband is shown to illustrate, despite a considerable stretch artefactual disparity in length, that all bands are present in both chromosomes 1.

received the mother's normal chromosome 1 and the abnormal chromosome 18, resulting in an effective monosomy for the region 18q22→qter and trisomy of 1q32→qter.

A subsequent pregnancy, evaluated in the first trimester by chorionic villus sampling, has resulted in the birth of a phenotypically normal male infant. His karyotype shows the balanced translocation seen in the mother.

Discussion

The cytogenetic studies indicate that the extra material, consisting of 1q32→qter, replaced the 18q22→qter in the fetus. The phenotype of the fetus would, therefore, be expected to reflect features of trisomy 1q32→qter and of 18q- syndrome. The phenotypic manifestations reported for trisomy 1q32→qter and 18q- syndrome are summarised and compared with those of the present case in the table.

The most prominent features in the present case are the cardiovascular malformations. Deletion of the long arm of chromosome 18 has not been reported to cause cardiac abnormalities. On the other hand, partial trisomy of chromosome 1 is usually associated with cardiac abnormalities, most often a common truncus arteriosus and atrial septal defect.^{3 6 8} The present case shows less severe cardiovascular anomalies. In addition, the present case demonstrates a relatively mild degree of facial dysmorphism. Previously reported cases with 18q- syndrome or duplication of 1qter, although not showing consistent clinical appearances, have been more severely dysmorphic.²⁻¹³ Another observation of interest is the presence of the skeletal abnormalities seen in the postmortem x-ray films. These aberrations have not been reported either in trisomy 1q32→qter or in the 18q- syndrome. Bony spicules in the proximal femur are seen in Menkes' kinky hair syndrome and in I cell inclusion disease. Menkes' kinky hair syndrome is an X linked, single gene, recessive disorder in which copper absorption is impaired, resulting in abnormalities of hair, bone, and arteries, in conjunction with seizures and progressive cerebral deterioration.¹⁴ The same x-ray findings are seen in I cell inclusion disease, an

TABLE Comparison of features of trisomy 1q32→qter, 18q-, and the present case.

Phenotypic features	Trisomy 1q32→qter	18q- syndrome	Present case
Cardiovascular			
Common truncus arteriosus	+ ^{3 8}	—	—
Hypoplasia of mitral and tricuspid valves	+ ⁶	—	—
Atrial septal defect	+ ^{3 6 8}	—	—
Ventricular septal defect	+ ^{3 4 6 8}	—	—
Bicuspid aortic valve	—	—	+
Stenosis of aortic and/or mitral valves	+ ^{4 8}	—	+
Thickening of pulmonic and mitral valve cusps	—	—	+
Widened foramen ovale	—	—	+
Single (right) coronary ostium	—	—	+
Single umbilical artery	—	—	+
Respiratory			
Abnormal lobation of lung	+ ⁸	—	+
Skeletal			
Bony spicules of proximal femur	—	—	+
Cupping of distal ulna and radius	—	—	+
Craniofacial			
Hypertelorism	+ ^{2 3 5 7}	+ ^{10 11}	+
Low set ears	+ ^{2 4 5 7}	+ ¹¹	+
High arched or cleft palate	+ ^{2 5}	+ ^{10 11 13}	+
Others	+ ²⁻⁹	+ ¹⁰⁻¹²	—
Others			
Flexion of fingers	+ ^{5 8}	—	+
Long thin hands with tapered fingers	+ ^{3 4 7}	+ ^{12 13}	—
Widely spaced nipples	+ ^{4 9}	+ ^{12 13}	—
Genital abnormalities	+ ^{5 8}	+ ^{10 12 13}	—
Gastrointestinal abnormalities	+ ^{5 6 8}	—	—
Renal abnormalities	+ ^{3 8}	+ ¹⁰	—
Mental retardation	+ ²	+ ¹⁰⁻¹³	Not assessable
Thymic abnormality or absence	+ ^{3-5 8}	—	+

Note: numbers indicate reference.

inherited enzyme defect resulting in incomplete degradation of mucopolysaccharides.¹⁴ None of the other features of either disorder was present in the fetus. Cupping of the distal ulnae and radii is occasionally seen in a normally developing fetus, in addition to its association with copper deficiency.

The presence of hydrops in this fetus is of uncertain origin, but there is no evidence for an immunological basis. Its relation to the chromosomal abnormality is unclear. It is also difficult to explain the hydrops fetalis as a consequence of the relatively mild congenital heart disease.

The present case shows few features in common either with previously described cases of trisomy 1q32→qter or of 18q- syndrome. It represents a unique instance of a combination of cytogenetic findings with unexpected phenotypic features.

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