Partial monosomy 13q and partial trisomy 18p: case report with necropsy findings

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SUMMARY We describe a stillborn female infant with severe intrauterine growth retardation and multiple congenital anomalies. She was found to have a deletion of 13q22→qter and trisomy of 18p11-2→pter, resulting from a maternal balanced translocation.

Chromosome 13 has been studied extensively. Deletion and duplication syndromes involving numerous sites on 13q have been reported.¹⁻⁵ Aberrations of 18p are less common.^{6,7} Partial trisomy 18p and partial monosomy 13q in the same person have not been reported previously. The case described here had many of the clinical features found in monosomy 13q and a few that may be attributable to trisomy 18p.

Case report

The proband, a female, was stillborn at 36 weeks' gestation to a healthy 24 year old G2 mother and a 38 year old father. Both parents were phenotypically normal. The mother had had a previous first trimester spontaneous abortion. This pregnancy was remarkable for marked intrauterine growth retardation, first diagnosed by ultrasound at 27 weeks' gestation. At that time, fetal measurements were consistent with a gestational age of 20 weeks; follow-up ultrasound at 32 weeks showed a fetus of 22 weeks' size. Maternal serum viral titres were not evaluated, but there was no clinical evidence of infection. Fetal death was believed to have occurred on the day of delivery.

The baby weighed 709 g (below the 5th centile) and was noted to have multiple congenital anomalies (table, fig 1).

NECROPSY FINDINGS

A necropsy, including radiographical examination, was performed. X-rays (fig 2) showed many skeletal malformations, including handlebar clavicles,

abnormal shoulder articulations, hypoplastic thoracic cavities, hypoplasia of the distal phalanges and agenesis of the middle phalanges of both fifth fingers, bilateral syndactyly of the fourth and fifth metacarpals, hypoplasia and clefting of vertebrae C7 to T10, and abnormal rib articulations.

Internal findings were equally numerous. There was atresia of the duodenojejunal junction with dilatation of the duodenum and distal stomach and narrowing of the entire alimentary tract distal to the atretic point; agenesis of the right mesocolon and partial malrotation of the colon; failure of fusion of the ventral and dorsal buds of the pancreas; agenesis of the gallbladder and atresia of extrahepatic bile ducts with hepatic periportal fibrosis and cholestasis; tetralogy of Fallot with an atrial septal defect and persistent left superior vena cava which drained into the coronary sinus; and hypoplasia of the ductus arteriosus and of the lungs.

The kidneys were hypoplastic with a cortex of five to six glomeruli in thickness and no nephrogenic

FIG 1 The external appearance of the baby. Note scaphocephaly, protruding maxilla, microphthalmia, and hypertelorism.

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zone. A bicornuate uterus was present. The brain was normal but the spinal cord was hypoplastic. The following ophthalmological abnormalities were noted: in the left eye, malformation of the ciliary body, and in the right eye, persistent tunica vasculosa

TABLE Summary of clinical and necropsy findings.

Skeletal

Scaphocephaly
Protruding maxilla
'Handlebar' clavicles
Abnormal shoulder articulations
Hypoplasia, thoracic cavities
Digitalisation of thumbs
Clinodactyly, fifth fingers
Hypoplasia, distal phalanx, fifth fingers
Agenesis, middle phalanx, fifth digits
Club feet
Plantar flexure, left big toe
Overlapping flexed fingers, right hand
Syndactyly of fourth and fifth metacarpals
Hypoplasia and clefting of vertebrae C7 to T10
Dysplasia, endochondral bone formation, vertebrae, focal
Abnormal rib articulations
Dislocation, hips
Increased interspace between first and second toes and third and fourth toes, bilateral

Gastrointestinal

Atresia, duodenojejunal junction
Dilatation of duodenum and distal stomach
Narrowing of jejunum, ileum, colon, and anus
Malrotation of colon, partial
Agenesis, mesocolon, right
Hypoplasia, pancreas
Agenesis, gallbladder
Atresia, bile ducts, extrahepatic
Fibrosis, periportal, focal, liver
Haemosiderosis, liver, pancreas, kidneys

Cardiovascular

Tetralogy of Fallot
Ventricular septal defect, infracristal
Stenosis, pulmonic valve
Bicuspid pulmonic valve
Hypoplasia, pulmonary artery
Overriding aorta
Hypertrophy, right ventricle
Atrial septal defect, secundum type
Persistent left superior vena cava draining into coronary sinus
Hypoplasia, ductus arteriosus

Genitourinary tract

Hypoplasia, kidneys, bilateral
Bicornuate uterus

Central nervous system

Hypoplasia, spinal cord
Microphthalmia, bilateral
Persistent tunica vasculosa lentis
Dysplasia, retina, OD
Coloboma and reduplication, retinal pigment epithelium, OD
Malformation, ciliary body, OS

Others

Low set, malrotated ears
High palate
Hypoplasia, right nipple
Agenesis, left nipple
Imperforate ear canals
Simian crease, right hand
Hypertelorism
Hypoplasia, lungs

FIG 2 X-ray of the baby showing numerous skeletal malformations.

FIG 3 Partial karyotype of the infant and mother.

lentis, dysplasia of the retina, and coloboma and reduplication of the retinal pigmentary epithelium.

Examination of the placenta revealed a granulomatous villitis. No organisms were identifiable with special stains.

CYTOGENETIC STUDIES

Material for chromosomal analysis was obtained from fetal cardiac blood, skeletal muscle, and lung. GTG banding showed a deletion of 13q with the presumptive breakpoint at 13q22. The remainder of the karyotype was normal (fig 3).

The father had a normal 46,XY complement. The mother's karyotype showed a reciprocal translocation (13;18)(q22;p11-2) (fig 3). Thus, the infant's karyotype was: 46,XX,-13,der(13),t(13;18)(q22;p11-2)mat, and therefore she was monosomic for the region 13q22→qter and trisomic for the region 18p11-2→pter. Other relatives were not available for study. However, a partial family history was obtainable. The proband's maternal grandmother had had one early miscarriage and one normal daughter other than the proband's mother. This maternal aunt had two living, normal children. A third child had died at the age of 9 months with an 'eye tumour'.

The proband's mother has subsequently had another first trimester spontaneous abortion. No studies were performed on the conceptus.

Discussion

The combination of deletion of 13q22→qter and trisomy of 18p11-2→pter has not been previously reported. Deletion of the long arm of chromosome 13 contributes to a group of syndromes which have been well documented.¹⁻⁵ These may be categorised according to the location of the breakpoint. Perhaps the best known 13q- syndrome is that related to deletion of 13q14 and characterised by retinoblastoma.⁵ Patients with a more distal deletion, of the 13q3 segment, have also been described. These patients have a distinctive phenotype with many features common to our patient and others with deletion at 13q22,^{1,2} including intrauterine growth retardation, hypertelorism, eye anomalies (microphthalmia, colobomata, retinal dysplasia), protruding maxilla, short neck, skeletal malformations involving the ribs, spine, and pelvis, and malformations of the hands and feet.³⁻⁵ Hypoplasia or absence of the thumb with agenesis of the first metacarpal, which is a common feature of deletions occurring at 13q3,⁵ was not present in our case, although the thumbs and fingers were abnormal. Internal anomalies seen both in 13q3 deletion and in

our case include bicornuate uterus, congenital heart disease, hypoplasia of the kidneys, and aplasia of the gallbladder.

Hypoplasia of the pancreas as seen in this case has not previously been reported in association with 13q deletion. Two patients with trisomy 22 with absent pancreatic tail have been described.⁸ In another patient,⁹ absence of the pancreas was accompanied by intrauterine growth retardation, congenital heart disease, uterus didelphis, and aplasia of the gallbladder. Unfortunately, cytogenetic studies were not done.

Anal atresia is seen in 25% of cases of deletion 13q3.⁵ Our case had narrowing of the entire gastrointestinal tract distal to the duodenum, although this was probably secondary to the duodenojejunal atresia.

Paradoxically, many of these malformations have been also reported in association with duplication of all or part of chromosome 13. Common features include anomalies of the ribs and spine, microphthalmia, retinal dysplasia, cardiac malformations, intestinal malrotation, and bicornuate uterus.⁵

Trisomy of 18p has rarely been reported⁶ and generalisations about a specific phenotype cannot be made at this time. Abnormalities in common with our case include intrauterine growth retardation, hip abnormalities, club foot, high palate, and hypoplastic nipples. The first four of these features are seen in many other malformation syndromes, both chromosomal and otherwise; the last is occasionally encountered in trisomy 18⁵ and may constitute an aspect of the phenotypic expression of trisomy 18p11-2. It has been noted that clinical expression of trisomy 18 is not dependent on duplication of the short arm of 18,⁷ and the lack of overall resemblance of our case to patients with trisomy of all of chromosome 18 or of 18q confirms this. However, some of the features seen in this case have been reported in trisomy 18, namely, microphthalmia, congenital hip dislocation, cardiac malformations, biliary atresia, intestinal malrotation, bifid uterus, and atresia of the external auditory canal.⁵

The finding of granulomatous villitis is not explicable on the basis of clinical information. However, it has been suggested¹⁰ that non-specific inflammation of the placenta may be the result of maternal immunological factors when no evidence for uterine or systemic infection exists.

The majority of the malformations exhibited by our patient are specifically attributable to the loss of one third of 13q, rather than to the partial duplication of 18p, and it appears that the small amount of additional material contributed relatively little to this patient's phenotype.

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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