Partial duplication of 3q and distal deletion of 11q in a stillbirth with an omphalocele containing the liver, short limbs, and intrauterine growth retardation

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Abstract

We describe a female stillbirth with duplication of 3q21→qter and deletion of 11q23→qter resulting from an unbalanced segregation of a maternal t(3;11) reciprocal translocation. The proband had some of the clinical features consistent with those seen in patients with dup(3q) syndrome or distal del(11q) syndrome. Prenatal sonographic examination showed short limbs, intrauterine growth retardation, and an omphalocele containing the liver.

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Key words: omphalocele; dup(3q); del(11q).

Patients with dup(3q) syndrome usually have duplicated 3q segments within the region of 3q21→qter¹ and manifest mental and growth retardation, as well as multiple congenital anomalies, some of which overlap with Brachmann-de Lange syndrome,² for example, brachycephaly, synophrys, hirsutism, anteverted nares, downturned corners of the mouth, micrognathia, and high arched palate. The common congenital anomalies associated with 3q duplications are congenital heart defects (septal defects), renal malformations (polycystic kidneys or dysplasia), ocular malformations (strabismus, nystagmus, cataract, corneal opacities, colobomas of the iris, and anophthalmia), and limb anomalies (hypoplasia of the phalanges, camptodactyly, and clinodactyly).³ The duplications of 3q21→qter in most patients are the products of unbalanced segregations of balanced parental rearrangements involving other chromosomes and thus present with other chromosome aberrations.³ Only a few are de novo events with pure dup(3q).^{4,5} Despite the cytogenetic differences, the phenotypes are similar in cases with familial or de novo dup(3q).^{3,6} Recently, the critical region responsible for the typical dup(3q) phenotype has been localised to the interval 3q26.3-q27⁷ or 3q26.31-q27.3.⁸

Patients with del(11q) syndrome commonly have deletions of 11q23→qter and manifest developmental delay, psychomotor retardation, craniofacial dysmorphism (trigonocephaly, hypertelorism, a broad and flat nasal bridge, carp shaped mouth, high arched palate, micrognathia, and low set, malformed ears), congenital heart defects (ventricular septal de-

fects, truncus arteriosus, and aortic arch defects), renal anomalies (renal duplication and hydronephrosis), ocular malformations (ptosis, coloboma, strabismus, and telecanthus), limb anomalies (talipes equinovarus, clino- or camptodactyly, syndactyly, and palmar simian crease), and a short neck and widely spaced nipples.⁹ The distal 11q deletions in most patients have arisen de novo,⁹ but other cases of ring chromosome 11,¹⁰⁻¹² interstitial deletion of 11q23→q25,^{9,13} and unbalanced rearrangements^{9,14} involving chromosome 11 and other chromosomes also showed phenotypes typical of the distal deletion (11q) syndrome. The subband critical for the distal del(11q) syndrome is believed to be 11q24.1.^{9,13,15}

The combination of duplication of 3q21→qter and deletion of 11q23→qter has not previously been described. Here, we report a stillbirth with this chromosomal constitution and an omphalocele containing the liver.

Case report

The proband was stillborn at 35 weeks' gestation with a weight of 1568 g, and a length of 42 cm. She was the second child of a 24 year old woman and a 33 year old man. The parents are Chinese, non-consanguineous, and healthy. The mother had had one 3 year old healthy child and one miscarriage. She had a normal maternal serum α fetoprotein (AFP) level with multiples of the median of 0.91 and a normal maternal serum free β human chorionic gonadotrophin (β -hCG) level with multiples of the median of 0.58 at 15 weeks' gestation. Her pregnancy with this child was uneventful except that intrauterine growth retardation and short femoral length were noted during the third trimester. Prenatal sonography at 22 weeks' gestation showed a biparietal diameter of 5.6 cm (22 weeks), a femur length of 3.4 cm (20 weeks), and an abdominal circumference of 16.5 cm (21 weeks). At 33 weeks' gestation, the biparietal diameter was 8.2 cm (33 weeks), but the femur length of 4.9 cm (26 weeks) and the abdominal circumference of 23.6 cm (28 weeks) were significantly below the normal range. At 35 weeks' gestation, ultrasonography indicated intrauterine fetal death and a small omphalocele containing the liver.

Physical examination of this stillbirth indicated that her birth height and weight were below the 5th centile. She had a prominent,

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Figure 1 (Left) AP view and (right) lateral view of craniofacial dysmorphism in the proband.

keel shaped forehead (trigonocephaly), hypertelorism, anteverted nostrils, a long philtrum, a short broad nose with a wide, depressed nasal bridge, epicanthic folds, a carp shaped mouth with thin vermillion borders and down turned corners, and micrognathia (fig 1). Hypertrichosis of the cheeks and forehead extending to the temples and the back was evident. Malformed, low set ears (fig 1), short neck, and widely spaced nipples were present. Her limbs were short with cubitus vulgus and ulnar deviation, but there were no digital anomalies. Dermatoglyphics showed bilateral simian creases. A 3 × 4 cm omphalocele with an extracorporeal liver was present (fig 2).

Figure 2 Omphalocele with an extracorporeal liver.

Cytogenetic study was performed on Giemsa banded chromosomes from cultured chorionic villi cells and showed an abnormal chromosome 11 (fig 3). The proband's mother was found to have a reciprocal translocation between chromosomes 3 and 11, 46,XX,t(3;11)(q21;q23) (fig 4). Owing to an unbalanced segregation of this t(3;11), the proband had two normal chromosomes 3, one normal chromosome 11, and one derivative chromosome 11 resulting in duplication of chromosome 3q21→qter and deletion of chromosome 11q23→qter: 46,XX,der(11),t(3;11)(q21;q23)mat. The father had a 46,XY karyotype.

Discussion

Our patient had a dup(3q)/del(11q), which involved the critical regions of both dup(3q) and distal del(11q) syndromes, and thus manifested some of the characteristic features of dup(3q)/del(11q) such as hypertrichosis, trigonocephaly, hypertelorism, epicanthic folds, a carp shaped mouth, broad nasal bridge, micrognathia, anteverted nostrils, malformed, low set ears, widely spaced nipples, short neck, palmar simian creases, and talipes equinovarus. The short femoral length, intrauterine growth retardation, and omphalocele were obvious on ultrasonographic examinations. Prenatally, we did not detect any associated cardiac or renal malformations, although congenital heart defects are common in both dup(2q) and distal del(11q) syndromes. The life span of patients with a dup(3q) is variable and depends on the associated internal malformations.³ In the distal del(11q) syndrome, the majority of deaths in infancy are attributable to severe congenital heart defects, but in patients without cardiac disease or with successful treatment, the prognosis for survival is fair.⁹ The intrauterine fetal death in our case, however, suggests that the combination of these two syndromes is more detrimental.

The unusual feature in this case was the associated malformation of omphalocele with an extracorporeal liver. Chromosomal abnormalities have been reported in 10 to 40% of neonates with omphalocele, with a combined mean rate of 12%.¹⁶ Trisomy 18 and 13 are the most common chromosomal abnormalities but other aberrations such as trisomy 21, 45,X, triploidy, 47,XXY, 47,XXX, dup(1q), dup(3p), del(3p)/dup(3q), del(4p), del(4q), dup(4q), dup(5p), dup(6q), del(6q), del(7q), del(9p), inv(11), dup(15q), del(17p), dup(17q), and i(18q) have also been reported.¹⁶⁻²⁶ It is possible that the omphalocele and dup(3q)/del(11q) in our patient were purely coincidental. The relationship between omphalocele and both dup(3q) and distal del(11q) syndromes remains to be determined.

Several reports suggest that karyotypic abnormalities are more common in association with an omphalocele that contains only bowel compared with those that contain only liver.^{19 21 22 27 28} Moreover, the abnormal karyotypes in fetuses whose omphalocele contained only bowel were mostly full aneuploidies such as trisomy 18, 13, 21, 45,X, and 47,XXX

Figure 3 Partial karyotype of proband showing an abnormal chromosome 11.

Figure 4 Partial karyotype of the mother showing a reciprocal translocation involving one of the chromosomes 3 and 11 (arrows indicate the breakpoints).

except one case with a karyotype of 46,XY,-18,+i(18q).¹⁹ Getachew *et al*²⁸ described an omphalocele containing the liver in a fetus with an inversion of chromosome 11. Whether full or partial aneuploidies are associated with the difference in omphalocele content is unclear and will require additional cases and information to be elucidated.

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