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Short Communication

Prenatal diagnosis of de novo partial trisomy 18p and partial monosomy 18q recurrent in a family with fatal aortic coarctation

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ABSTRACT

Aortic coarctation is a life-threatening defect when it occurs with cardiorespiratory failure. Its genetic cause remains unknown. A woman was pregnant twice, both with male fetuses that had partial trisomy 18p, partial monosomy 18q, and aortic coarctation. The syndrome may relate to the aortic coarctation and pulmonary hypoplasia and is life-threatening. ArrayCGH analysis suggested a de novo 17.7 Mb deletion of chromosome 18q21.33→qter (58,413,193 bp to 76,116,029 bp) and a de novo 12.4 Mb duplication of chromosome 18pter→p11.21 (1543 bp to 12,438,430 bp) at the telomeric end of chromosome 18. To the best of our knowledge, the present chromosomal breakpoint with rearrangement has not been previously described. This chromosome aberration may be responsible for this syndrome.

1. Introduction

Aortic coarctation is aortic hypoplasia and is a life-threatening defect when it occurs with cardiorespiratory failure (Bronshtein and Zimmer, 1998). The coarctation of the aorta is a deformity of the aortic intima that often occurs on the aortic arch and descending thoracic aorta. The recurrence risk for sibs is approximately 1 in 200 for coarctation of the aorta (Boon and Roberts, 1976) and 5–8% for any form of congenital heart defect (Lynette, 2011). The heritability of aorta coarctation is estimated to be 58% (Boon and Roberts, 1976). There have been a few reports about chromosome abnormality (Turner syndrome and Noonan syndrome) that occurred with aortic coarctation (Chen et al., 2008; Vermeulen et al., 2005), but the genetic cause of aortic coarctation remains unknown.

This report describes a woman with inv (18), who had recurrent conceived fetuses with dup (18p)/del (18q) and aortic coarctation. We speculate that the abnormal fetal development that was observed was probably due to the presence of aberrant chromosomes and genes with copy number variation.

2. Methods

2.1. Clinical report

A 23-year-old, gravida 3, para 1, pregnant woman was referred to our Prenatal Diagnostic and Counseling Clinic at 38 weeks of pregnancy because of an abnormal fetal sonogram. A fetal heart Doppler ultrasound examination showed both aortic arch coarctation and left pulmonary hypoplasia (Fig. 1A). The diameter of the aortic arch was 2.5 mm, the ascending aortic diameter was 4.5 mm, and descending aortic diameter was 4.2 mm. The fetal heart was waxed and the cardiothoracic ratio was 49.3%. Sharp mitral regurgitation and gentle tricuspid regurgitation were observed. Moreover, left pulmonary hypoplasia was present. MRI also showed that the fetal heart was waxed, the volume of the lungs was minified, and pulmonary hypoplasia was present. Because of the birth defects, the infant was delivered vaginally at 38 + 5 weeks of gestation, weighed 2530 g (3209.5 ± 356.5) (Janssen et al., 2007), and length 52 cm (48.4 ± 2.0) with a head circumference of 35 cm (34.3 ± 1.7). Apgar scores were 9, 10 and 10 at the first, fifth and tenth minute, respectively. The fetal appearance was not obviously abnormal except for the ears being slightly low-set. Subsequently, the couple was happy and discharged with the live neonate. However, after 2 days, the baby died on the way to the hospital because of dyspneic respiration. The couple was not consanguineous and did not have congenital heart defects.

Two years prior to this, the woman had been pregnant and the fetus was delivered by cesarean section because of respiratory distress in the 39th week of pregnancy. The infant weighed 2400 g (3359.0 ± 390.4), and length 51 cm (49.4 ± 2.0) with a head circumference of 34 (34.8 ± 1.6). Apgar scores were 9, 10 and 10 at the first, fifth and tenth minute, respectively. The neonate had aortic coarctation that was detected by Doppler ultrasound examination, and his karyotype was 46, XY, der(18)(pter→q21.3::p11.2-pter). The neonate was born alive but died one day after birth because of pulmonary hypoplasia and fetal respiratory distress.

Abbreviations: FISH, Fluorescence in-situ hybridization; CGH, Comparative genomic hybridization; GTG, Giemsa trypsin Giemsa; FGR, fetal growth restriction.

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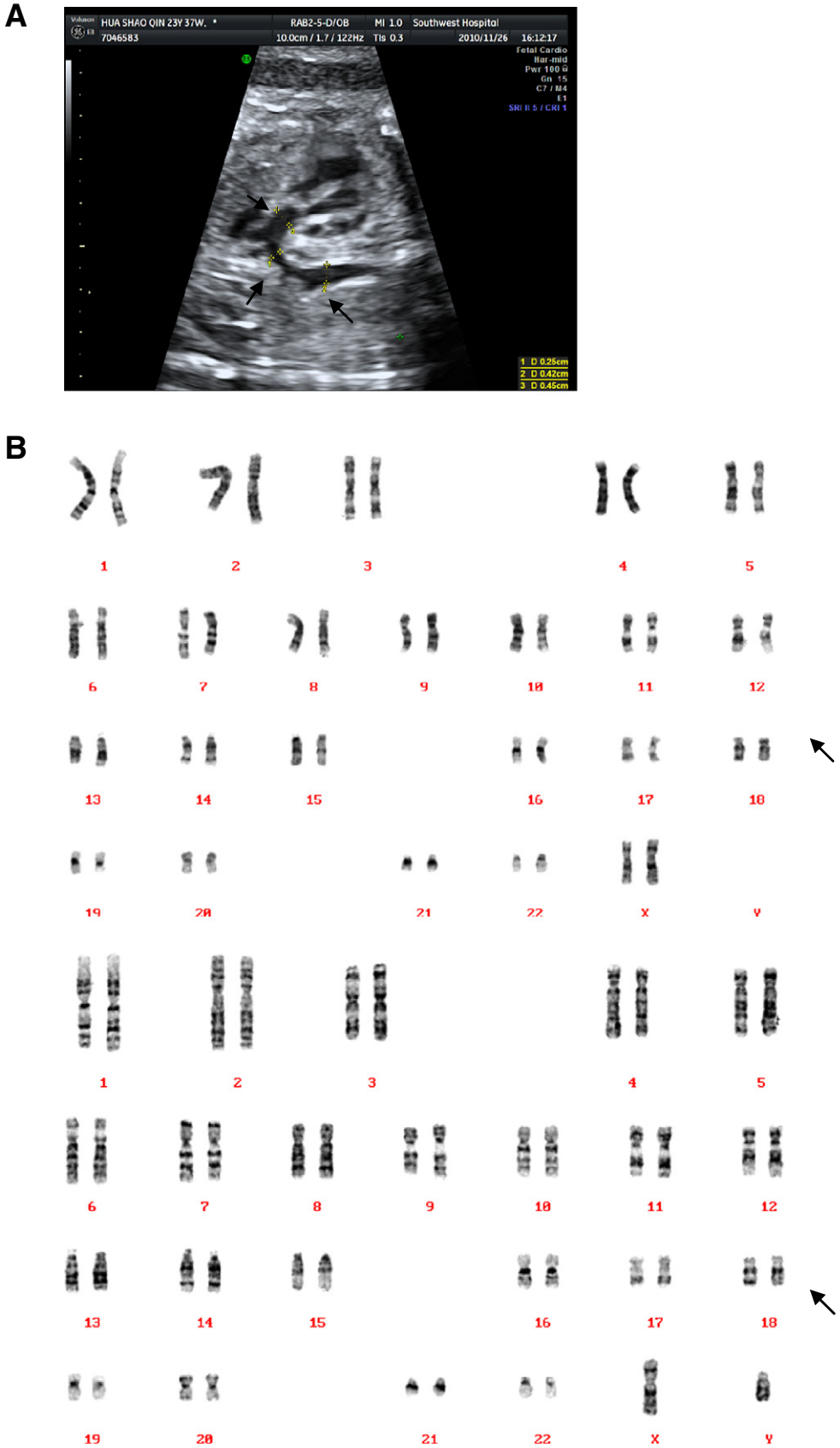

Fig. 1. (A) The abnormal echocardiography. The diameter of the aortic arch was 2.5 mm, the ascending aortic diameter was 4.5 mm and the descending aortic diameter was 4.2 mm. (B) Mother's chromosomes on above showing 46, XX, inv (18) (p11.2q21.3) and fetus' GTG banded chromosomes on below showing 46, XY, der (18) (pter→q21.3::p11.2-pter) (C) FISH analyses chromosomes using chromosome-specific probes for the 18p (red, KBI-30131) and 18q (green, KBI-30132). The red probe was shown on the 18qter and the green probe was shown on the 18pter in the mother's chromosome. In the fetal chromosome the red probe was shown on the 18pter and the telomere of 18qter. (D) CGH array shows a loss of 17.7 Mb at chromosome 18q21.33→qter and a gain of 12.4 Mb at chromosome 18pter→p11.21.