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Case Report

Prenatal diagnosis of 22q11.2 deletion syndrome associated with right aortic arch, left ductus arteriosus, cardiomegaly, and pericardial effusion

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ABSTRACT

Objective: To report prenatal diagnosis of 22q11.2 deletion syndrome with right aortic arch (RAA), left ductus arteriosus, cardiomegaly, and pericardial effusion in the fetus.
Case report: A 35-year-old woman, gravida 2, para 1, was referred to the hospital at 31 weeks of gestation because of abnormal ultrasound findings and whole-genome array comparative genomic hybridization report. G-banding chromosome analysis revealed a karyotype of 46,XX. Level II ultrasound at 22 weeks of gestation revealed RAA with the presence of the aortic arch on the right side of trachea at three vessels and trachea view, left ductus arteriosus, and mild right side pyelectasis. Cardiomegaly and pericardial effusion were also found 2 months later. Array comparative genomic hybridization detected a 2.743-Mb deletion at 22q11.2 region. Multiplex ligation-dependent amplification detected deletion in the DiGeorge syndrome critical region of chromosome 22 low copy number repeat 22-A–C. Metaphase fluorescence *in situ* hybridization on lymphocyte in cord blood confirmed deletion in 22q11.2 region.
Conclusion: Chromosome abnormalities have been found in patients with RAA. Prenatal diagnosis of RAA with or without intracardiac or extracardiac anomalies should include a diagnosis of 22q11.2 deletion syndrome.

Introduction

The common abnormalities found in patients with 22q11.2 deletion include congenital heart disease (74%) especially conotruncal malformations such as tetralogy of Fallot, interrupted aortic arch, ventricular septal defect and truncus arteriosus, palatal abnormalities (69%), characteristic facial features (48.7–100%), learning difficulties (70–90%), and immune deficiency (77%) [1–4]. About one-third of patients have urinary tract abnormalities including renal agenesis or multicystic dysplastic kidney (32%), hydronephrosis (16%), vesicoureteral reflux, or an irregular bladder (20%) [5,6].

Fetuses with 22q11.2 deletion have variable congenital anomalies. Here we present our experience of prenatal diagnosis of 22q11.2 microdeletion syndrome with right aortic arch (RAA), left ductus arteriosus, cardiomegaly, and pericardial effusion in the fetus.

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Case Report

A 35-year-old woman, gravida 2, para 1, was referred to the hospital at 31 weeks of gestation because of abnormal ultrasound findings and whole-genome array comparative genomic hybridization (aCGH) report. Her husband was aged 36 years. She and her husband were healthy and nonconsanguineous. There was no family history of congenital heart defect. She underwent amniocentesis at 18 weeks of gestation due to advanced maternal age. G-banding chromosome analysis revealed a karyotype of 46,XX. Level II ultrasound at 22 weeks of gestation revealed RAA with the presence of the aortic arch on the right side of the trachea at three vessels and trachea view, left ductus arteriosus, and mild right side pyelectasis (Figure 1). The aCGH was suggested for further study then, however, the patient declined. Follow-up ultrasound at 30 weeks of gestation showed no pyelectasis, but RAA with left ductus arteriosus, cardiomegaly, and pericardial effusion (Figure 2). Repeated amniocentesis was performed for aCGH and Multiplex ligation-dependent amplification (MLPA). aCGH showed a 2.743-Mb deletion at 22q11.2 region (Figure 3) including 42 Online Mendelian Inheritance in Man genes: *DGCR6*, *PRODH*, *DGCR2*, *DGCR14*, *TSSK2*, *GSC2*, *SLC25A1*, *CLTCL1*, *DVL1P1*, *HIRA*, *MRPL40*, *UFD1L*, *CDC45*, *CLDN5*, *SEPT5*, *GP1BB*, *TBX1*, *GNB1L*, *TXNRD2*, *COMT*, *ARVCF*, *MIR185*, *DGCR8*, *TRMT2A*, *RANBP1*, *ZDHHC8*, *RTN4R*, *DGCR6L*, *GGTLC3*, *RIMBP3*, *ZNF74*, *SCARF2*, *MED15*, *PI4KA*, *SERPIND1*, *SNAP29*, *CRKL*, *LZTR1*, *THAP7*, *P2RX6*, *SLC7A4*, and *BCRP2*. The MLPA detected a deletion in the DiGeorge syndrome critical region of chromosome 22 low copy number repeat (LCR) 22-A–C. The pregnancy was subsequently terminated. The fetus had facial dysmorphism of hypertelorism, prominent nasal root, broad nasal bridge, bulbous nasal tip, and short philtrum. Metaphase fluorescence *in situ* hybridization (FISH) was made by using Vysis LSI TUPLE 1 (HIRA) spectrum orange/LSI ARSA spectrum green probe set (Abbott Laboratories, Abbott Park, IL, USA) on lymphocyte in cord blood for confirmation. The result was 46,XX.ish del(22)(q11.2)(TUPLE 1-) (Figure 4).

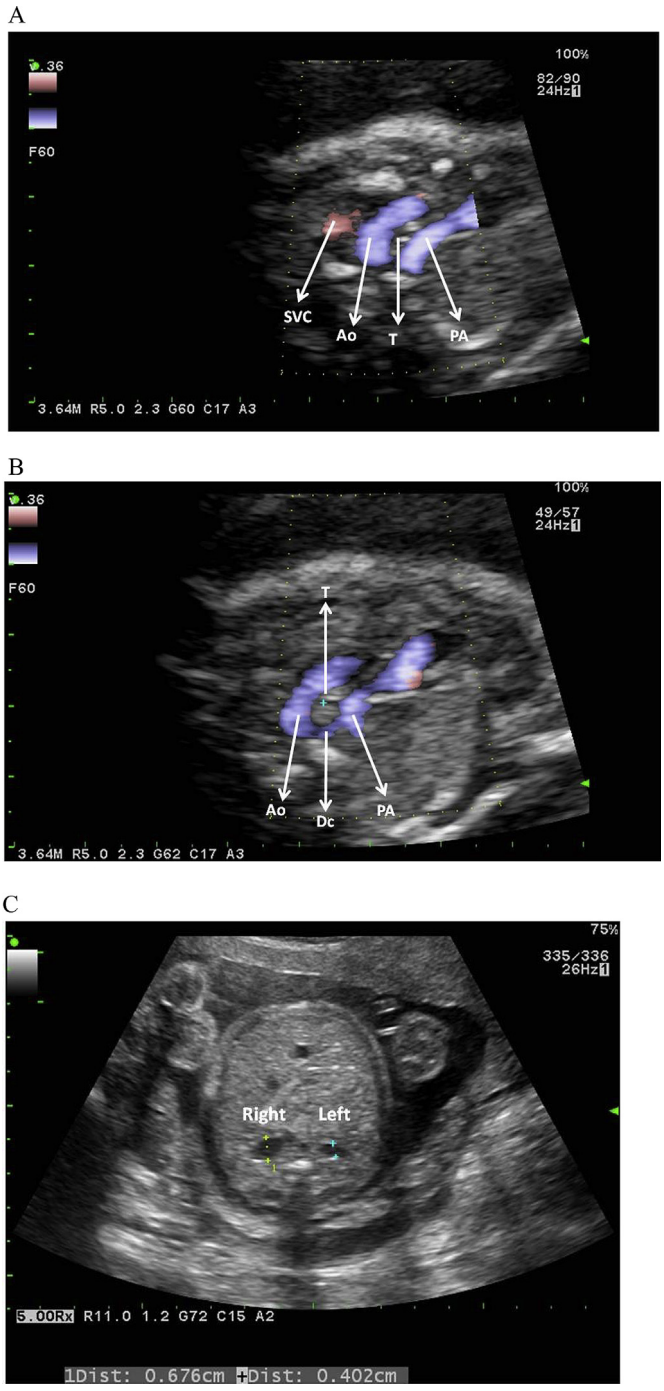

Figure 1. Level II ultrasound at 22 weeks of gestation shows (A) right aortic arch with aorta located at the right side of trachea, (B) left ductus arteriosus, and (C) mild right side pyelectasis. Ao = aorta; Dc = ductus arteriosus; PA = pulmonary artery; SVC = superior vena cava; T = trachea.

Discussion

The peculiar aspect of the present case is that the initial ultrasound findings showed RAA with left ductus arteriosus, and mild right pyelectasis without other significant intracardiac or extracardiac anomalies. Cardiomegaly and pericardial effusion were found 2 months later.

RAA in patients with 22q11.2 deletion syndrome is very rare. The overall incidence of RAA is 0.1–0.37% of all pregnancies [7,8]. In pregnant woman with risk factors of fetal congenital heart disease, 0.6% (98/16332) of patients were diagnosed with RAA, occupied 5.0% of all cardiac abnormalities [9,10]. However, probably because of the improving image of prenatal ultrasound, the number of RAA cases has increased gradually in recent years [10,11].The prevalence of isolated RAA in 22q11.2 deletion were reported to be about 9–12% in postnatal clinical patients [12,13]. The incidence of the prenatal diagnosed isolated RAA in 22q11.2 deletion syndrome is 3.8% (2 of 53 patients) [14].

Chromosome abnormalities has been found in 15.3–30% of the patients with RAA [10,15]. The reported chromosome abnormalities include 22q11.2 deletion, 47,XXY, trisomy 13, chromosome 13 deletion, 16p11.2 imbalance, 4p16.3 imbalance, and trisomy 21, with 22q11.2 deletion being the most common [10,16,17]. McElhinney et al [15] reported that 30% of the patients with RAA and normal intracardiac anatomy had 22q11.2 deletion. Miranda et al [10] reported different incidences of extracardiac and chromosome abnormalities between the patients with or without normal intracardiac anatomy. The incidence of extracardiac and chromosome abnormalities in patients with isolated RAA is relatively lower than patients with RAA and other structural congenital heart defect. In fetuses of RAA with normal intracardiac anatomy, the incidence of extracardiac anomalies and chromosome anomalies were only 11.1% (3 of 27 patients) and 3.7% (1 of 27 patients, with 3q29 duplication), respectively. The incidence of extracardiac anomalies and chromosome anomalies in patients of RAA with structural congenital heart defect were 39.4% and 19.7% respectively [10].

Here we present a rare case of prenatal diagnosed 22q11.2 deletion syndrome in a fetus with RAA, left ductus arteriosus, mild