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Prenatal Diagnosis of Crossed Pulmonary Arteries with a Postnatal Diagnosis of CHARGE syndrome

Riza Madazli[1], Funda Oztunc[2], Hakan Erenel[1], Didem Kaymak[1], Serpil Eraslan[3], and Hulya Kayserili[3]

[1]Istanbul University- Cerrahpasa Cerrahpasa Medical Faculty Department of Obstetrics and Gynecology Division of Perinatology
[2]Istanbul University-Cerrahpasa
[3]Koç University School of Medicine

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Abstract

Crossed pulmonary arteries (CPA) is a rare abnormality in which the ostium of the left pulmonary artery is located rightward and the ostium of the right pulmonary artery is leftward. CPA has been reported only once at prenatal period and has not been associated with CHARGE syndrome as yet. Prenatally left pulmonary artery was seen to pass beneath the ductus and directing towards the left side and pulmonary artery bifurcation could not be demonstrated at the same plane. Postnatal echocardiography reconfirmed the presence of CPA. Bilateral choanal atresia, genital hypoplasia, hearing loss with facial and external ear asymmetry and psychomotor retardation of the newborn led to clinical diagnosis of CHARGE syndrome and was confirmed by gene analysis.

Introduction

Crossed pulmonary arteries (CPA) is a rare congenital anomaly in which the ostium of the left pulmonary artery (LPA) originates from the right portion of the main pulmonary artery (MPA), while the ostium of the right pulmonary artery (RPA) originates from the left portion of the MPA (1). The LPA and RPA then crisscross one another along their courses to their corresponding lungs. CPA is often associated with other congenital heart defects, extracardiac abnormalities, chromosomal anomalies and genetic syndromes (2,3).

The CHARGE syndrome is a multiple congenital malformation syndrome occurring in 6–7 per 100,000 live births and presenting with a variable combination of ocular coloboma (C) congenital heart defects (H), choanal atresia (A), retardation of growth and development (R), genitourinary defects and/or hypogonadism (G), and ear anomalies with or without deafness (E) (4). We present a case of CPA diagnosed prenatally in which postnatal diagnosis of CHARGE syndrome was made by neonatal clinical findings along with a de novo heterozygous 71,5kb duplication in CHD7 gene, which is the first reported duplication case to the best of our knowledge.

Case report

A 30-year-old nullipara was referred due to suspicion of abnormality of the fetal heart at 22 weeks of gestation. The four-chamber view was normal. The RPA was seen to arise from the MPA in the right ventricular outflow tract view, where the LPA could not be demonstrated. On the three-vessel view of the heart, an aberrant vessel with an arterial Doppler flow pattern directed to the left side of the fetus was observed. Evaluation of the proximal part of this vessel revealed that it was LPA. LPA was observed to arise from the right and superior portion of the MPA and then curved to supply the left lung and the diagnosis of CPA

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was made (Figure 1a,b,c,d). There were no additional abnormalities. Karyotype, chromosomal microarray analysis and 22q11.2 deletion was normal. Pregnancy was followed-up and male neonate was delivered at 37 weeks of gestation with a birth weight of 2.420 kg. Physical examination of the newborn revealed bilateral choanal atresia, genital hypoplasia and undescended testes. Auditory brainstem response test of the newborn was normal. Postnatal cardiac echocardiography reconfirmed the diagnosis of CPA. Pulmonary artery bifurcation was not seen in the parasternal short-axis view and moving the probe up 1 or 2 intercostals in the high parasternal view and sweeping from superior to inferior showed the LPA ostium located in the right and above the RPA and running to the left side (Figure 2a,b). The newborn had an operation for bilateral choanal atresia at postnatal 5th day and discharged in healthy condition at postpartum 7th day and was followed-up by the genetic department due to multiple malformations. Neuromotor retardation was diagnosed in the infant at the age of 6 months. Audiometry test was repeated and showed a loss of 50 decibels and 30 decibels hearing loss in the left and right ear respectively. Due to the suspicion of CHARGE syndrome CHD7 gene analysis was performed. Multiplex ligation-dependent probe amplification (MLPA) revealed heterozygous duplication of exons 3 to 30 in CHD7 gene and the diagnosis of CHARGE syndrome was made at the age of 8 months. MLPA analysis was also performed to the parents revealing normal results demonstrating de novo mutation in the patient.

Discussion

CPA has been reported only once at the prenatal period and CPA has not been associated with CHARGE syndrome as yet (1). CPA may be due to embryonic pulmonary total counterclock wise rotation or faulty differential growth during the partitioning of the truncus arteriosus into the aorta and pulmonary trunk (2,5). CPA is often associated with cardiac abnormalities especially the conotruncal, aortic arch and septal defects and chromosomal anomalies including 22q11 deletions trisomy 18, partial monosomy Xq, and partial trisomy 1q (2,5,6). CPA is also reported to be associated with genetic syndromes such as Noonan, Costello, Frank Ter Haar, Holt–Oram and VACTERL syndromes (2,5). The first antenatal CPA case has been reported by Xiong et al. due to suspicious abnormal three-vessel and trachea view of the fetal heart when the ductus appeared extremely small (1). The authors stated that, the key to the prenatal diagnosis of this rare condition is to reveal the true relationship between the LPA and RPA. In the case reported herein, three vessel view of the fetal heart was abnormal with LPA passing beneath the ductus and directing towards the left side of the fetus and furthermore LPA and RPA bifurcation could not be demonstrated at the same fetal heart plane. We suggest that abnormal three vessel view and not being able to demonstrate the bifurcation of pulmonary arteries in the same plane are important clues for prenatal diagnosis of CPA.

CHARGE syndrome, is an autosomal-dominant malformation syndrome in which several organ systems are variably involved (4). Loss of function mutations in CHD7 gene cause CHARGE syndrome and heart defects occur in approximately 75% of patients with a pathogenic CHD7 mutation (7). The types of heart defects are variable, but atrioventricular septal defects and conotruncal defects are relatively overrepresented (8). Best to our knowledge, this is the first case of CHARGE syndrome accompanied with CPA. Recent literature has emphasized the poor accuracy of a prenatal diagnosis of CHARGE syndrome (7,9). We also could able to diagnose CHARGE syndrome postnatally after the identification of choanal atresia, genital hypoplasia, neuromotor retardation and hearing loss after delivery.

As a conclusion, abnormality in the three vessel view of the fetal heart is important for the prenatal diagnosis of CPA. Detection of crossed pulmonary arteries needs careful and detailed examination of the fetus to exclude fetal structural and chromosomal abnormalities and genetic syndromes including CHARGE syndrome.

References

1-Xiong Y, Gan HJ, Liu T et al. Prenatal diagnosis of crossed pulmonary arteries. Ultrasound Obstet Gynecol 2010;36:776-777.

2- Babaoglu K, Altun G, Binnetoglu K et al. Crossed pulmonary arteries: a report on 20 cases with an emphasis on the clinical features and the genetic and cardiac abnormalities. Pediatr Cardiol 2013;34:1785-1790.

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3- Cuturilo G, Drakulic D, Krstic A et al. The role of modern imaging techniques in the diagnosis of malposition of the branch pulmonary arteries and possible association with microdeletion 22q11. 2. Cardiol Young 2013;23:181-188.

4- Busa T, Legendre M, Bauge M et al. Prenatal findings in children with early postnatal diagnosis of CHARGE syndrome. Prenat Diagn. 2016;36:561-567.

5- Zhang J, Gao Y, Huang G et al. The Role of Echocardiography in Diagnosing Crossed Pulmonary Arteries. J Cardiol Diagn Res 2018; 1: 3-9.

6- Chaturvedi R, Mikailian H, Freedom RM. Crossed pulmonary arteries in tetralogy of Fallot. Cardiol Young 2005;15:537.

7- Legendre M, Abadie V, Attie-Bitach T, et al. Phenotype and genotype analysis of a French cohort of 119 patients with CHARGE syndrome. Am J Med Genet C Semin Med Genet. 2017;175:417-430.

8- Corsten-Janssen N, Scambler PJ. Clinical and molecular effects of CHD7 in the heart.Am J Med Genet C Semin Med Genet. 2017;175:487-495.

9- Millischer AE, Sonigo P, Attie T et al. Fetal MRI findings in a retrospective cohort of 26 cases of prenatally diagnosed CHARGE syndrome individuals. Prenat Diagn. 2019;39:781-791.

Figures to Legands

Figure 1a

Proximal part of the left pulmonary artery (open arrow) arises from the right portion of the main pulmonary artery and then curved to left side of the fetus.

Figure 1b

On the three vessel view of the heart, an aberrant vessel (distal part of left pulmonary artery) is directed to the left side of the fetus

Figure 1c

The right pulmonary artery originates from the left portion of the main pulmonary artery and then curved to right side of the fetus.

Figure 1d

Illustration of crossed pulmonary arteries

Ao, aorta; DA, ductus arteriosus; LPA, left pulmonary artery; MPA, main pulmonary artery; RPA, right pulmonary artery; VCS, vena cava superior.

Figure 2a

On the parasternal short axis view of the heart, left pulmonary artery arises from proximal part of main pulmonary artery (arrow) and it is directed to the left side of the newborn

Figure 2b

Left pulmonary artery arises from main pulmonary artery and it is directed to the left side of the newborn

RA, right atrium; LA, left atrium; Ao, aorta; LPA, left pulmonary artery; MPA, main pulmonary artery; RPA, right pulmonary artery

Figure 1a

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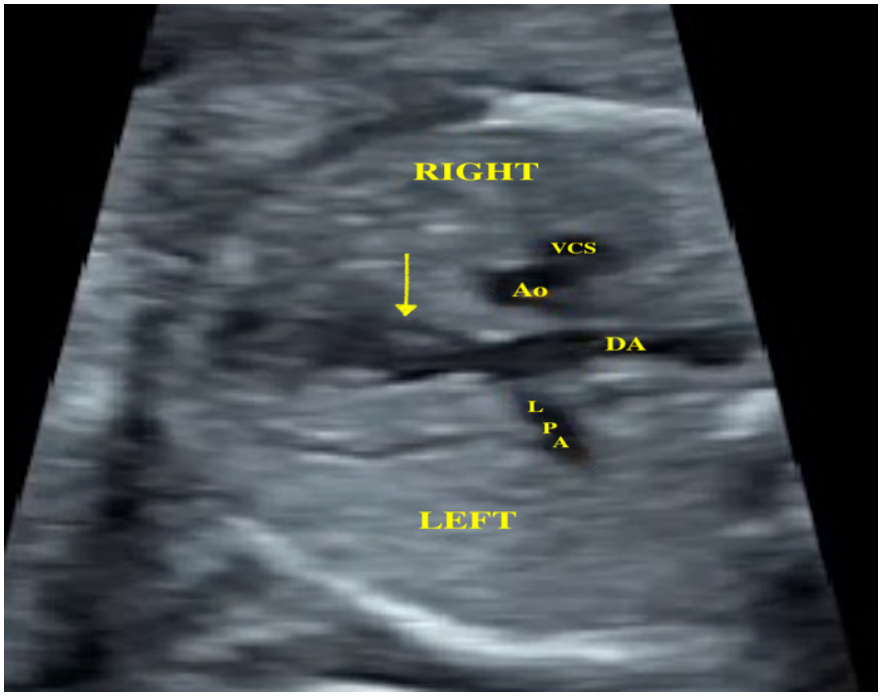


Figure 1b

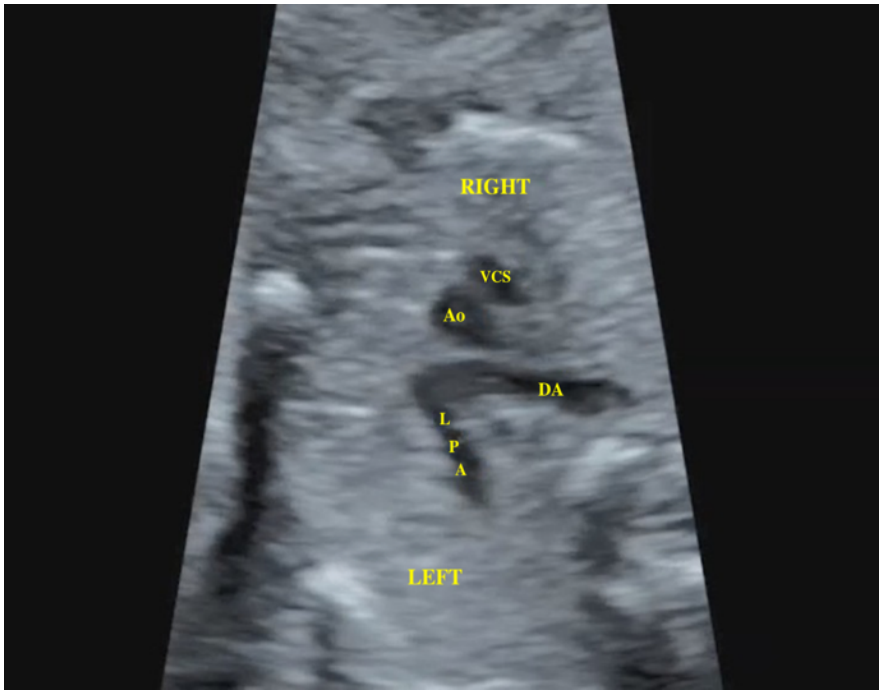


Figure 1c

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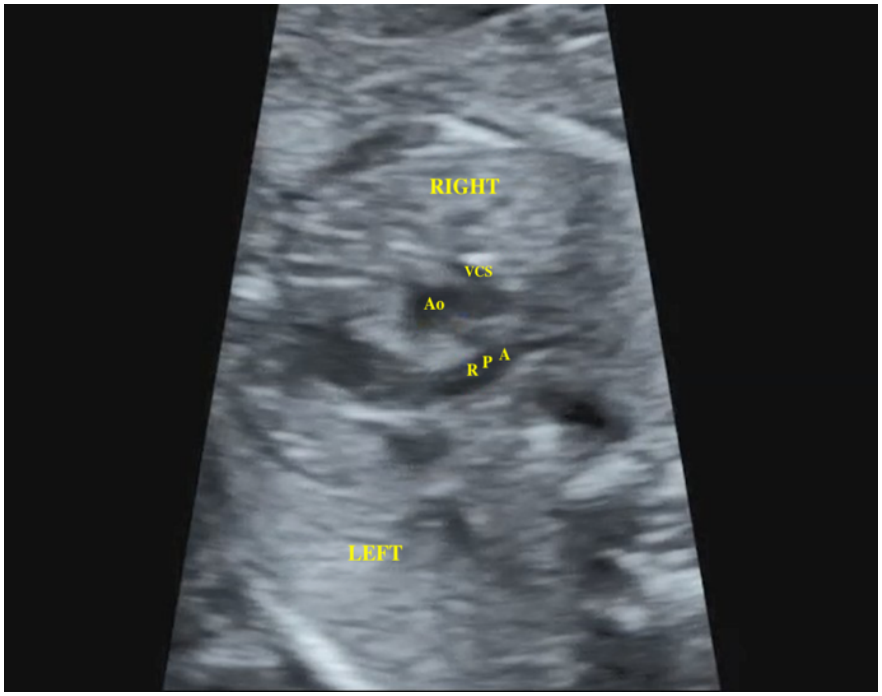


Figure 1d

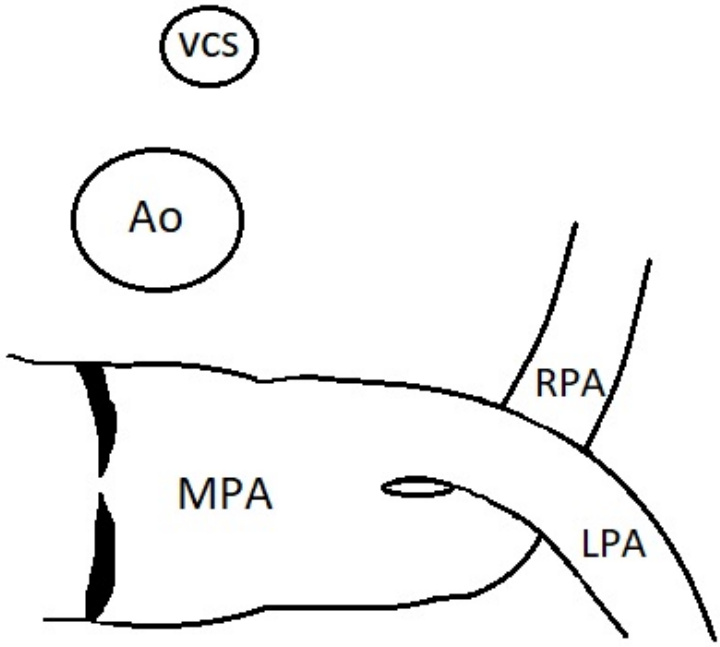


Figure 2a

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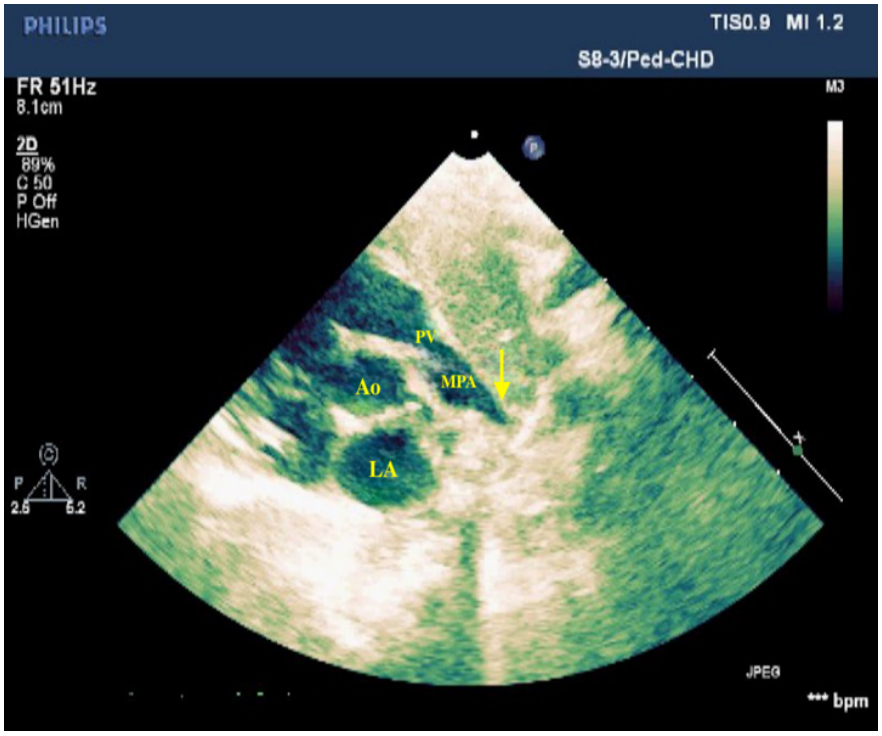


Figure 2b

