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REPORT

Prenatal diagnosis of tetralogy of Fallot with pulmonary atresia using: Fetal Intelligent Navigation Echocardiography (FINE)

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ABSTRACT

Tetralogy of Fallot with pulmonary atresia, a severe form of tetralogy of Fallot, is characterized by the absence of flow from the right ventricle to the pulmonary arteries. This cardiac abnormality is challenging and complex due to its many different anatomic variants. The main source of variability is the pulmonary artery anatomy, ranging from well-formed, confluent pulmonary artery branches to completely absent native pulmonary arteries replaced by major aorto-pulmonary collateral arteries (MAPCAs) that provide all of the pulmonary blood flow. Since the four-chamber view is usually normal on prenatal sonography, the diagnosis may be missed unless additional cardiac views are studied. Fetal Intelligent Navigation Echocardiography (FINE) is a novel method developed recently that allows automatic generation of nine standard fetal echocardiography views in normal hearts by applying "intelligent navigation" technology to spatiotemporal image correlation volume datasets. We report herein for the first time, two different cases of tetralogy of Fallot with pulmonary atresia having variable sources of pulmonary blood flow in which the prenatal diagnosis was made successfully using the FINE method. Virtual Intelligent Sonographer Assistance (VIS-Assistance®) and automatic labeling (both features of FINE) were very helpful in making such diagnosis.

Introduction

Tetralogy of Fallot is comprised of a subaortic ventricular sepal defect, overriding aorta, and infundibular pulmonary stenosis. A severe form of this congenital heart defect is tetralogy of Fallot with pulmonary atresia (TOF/PA), characterized by absence of flow from the right ventricle to the pulmonary arteries. This is one of the most challenging and complex cardiac defects due to its many different anatomic variants. The main source of variability is the anatomy of the pulmonary arteries. On prenatal ultrasound, the four-chamber view is usually normal and therefore, the diagnosis may be missed unless additional cardiac views are examined in detail. A novel method developed recently, known as Fetal Intelligent Navigation Echocardiography (FINE), allows automatic generation of nine standard fetal echocardiography views in normal hearts by applying "intelligent navigation" technology to spatiotemporal image correlation (STIC) volume datasets. We report herein for the first time, two cases of TOF/PA with variable pulmonary arterial anatomy in which the FINE method successfully demonstrated the features of this condition prenatally.

Case 1

A 31-year-old woman (G2, P0010) was referred to our research ultrasound unit at 30 weeks. Her past medical history was significant for childhood asthma and iron deficiency anemia. For both cases presented herein, the women were examined at Detroit Medical Center/Wayne State University, and the Perinatology Research Branch of NICHD, NIH, DHHS. They were enrolled in a research protocol approved by the Institutional Review Board of NICHD, NIH, and by the Human Investigation Committee of Wayne State University. Both women

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Supplemental data for this article can be accessed here.

provided written informed consent for the use of sonographic images for research purposes.

The patient had a body mass index (BMI) of 38.2, which is classified as severely obese [1]. Four-dimensional (4D) sonography with STIC was performed, in which multiple STIC volume datasets of the fetal heart containing gray-scale information were acquired from the apical four-chamber view by transverse sweeps through the fetal chest. The acquisition time was 12.5 seconds, while the acquisition angle was 35 degrees.

A single STIC volume dataset considered to be of highest quality was chosen for analysis by the FINE method [2]. Since its original invention [2], FINE has been integrated into a commercially available ultrasound platform (UGEO WS80A; Samsung Healthcare, Seoul, Korea) and is known as 5D Heart technology. Using the Anatomic Box® feature, seven anatomical structures of the fetal heart were marked on the screen, which generates an internal geometrical model of the heart [2]. The structures that were marked in sequential order are: (1) cross-section of the aorta at the level of the stomach; (2) cross-section of the aorta at the level of the four-chamber view; (3) crux; (4) right atrial wall; (5) pulmonary valve; (6) cross-section of the superior vena cava; and (7) transverse aortic arch. Once the marking process is completed, FINE allows automatic generation and display of nine standard fetal echocardiography views simultaneously in a single template: (1) four chamber; (2) five chamber; (3) left ventricular outflow tract; (4) short-axis view of great vessels/right ventricular outflow tract; (5) three-vessels and trachea (3VT); (6) abdomen/stomach; (7) ductal arch; (8) aortic arch; and (9) superior and inferior venae cavae [2]. Such cardiac views in this template are known as *diagnostic planes*. Yet, the FINE method also includes a tool known as *Virtual Intelligent Sonographer Assistance (VIS-Assistance®)*, which can be activated for each cardiac diagnostic plane [2–5]. VIS-Assistance® allows operator-independent sonographic navigation and exploration of surrounding structures in the diagnostic plane (i.e. "virtual" sonographer) in the form of a video clip, and therefore improves the quality of fetal cardiac examination. We have previously reported the value of VIS-Assistance® when congenital heart defects are present [2,6].

Automatic labeling of the nine echocardiography views (i.e. diagnostic planes), anatomical structures, left and right sides of the fetus, and cranial and caudal ends is an additional and optional feature of the FINE method [2,3]. Such labeling helps sonologists to recognize anatomical structures, especially when a cardiac defect is present.

Upon examination of the nine echocardiography views, we noted that five views were abnormal (Figure 1, Supplementary Movie 1). The 3VT view showed a severely hypoplastic pulmonary artery with dilated transverse aortic arch. The pulmonary valve appeared hyperechoic and closed throughout the cardiac cycle. As is typical, the four-chamber view appeared normal, and VIS-Assistance® demonstrated two pulmonary veins connecting normally to the left atrium. In the left ventricular outflow tract view, there was a subaortic ventricular septal defect (VSD) with overriding of the ventricular septum by the dilated aortic root. In addition, the aortic valve appeared thickened and dysplastic with "stiff" valvular excursion, suggesting aortic stenosis. The short-axis view of great vessels/right ventricular outflow tract showed pulmonary atresia with a severely hypoplastic pulmonary artery, as well as a tiny ductus arteriosus. In this view, the pulmonary valve tissue again appeared hyperechoic and closed throughout the cardiac cycle. The ductal arch demonstrated similar findings. In the aortic arch view, the aortic root was dilated and there was a prominent ascending aorta. It is noteworthy that automatic labeling of the cardiac anatomy was correct for all nine echocardiography views.

In contrast, real-time fetal echocardiography performed during the same visit was very difficult and suboptimal because of the maternal BMI, as well as prominent shadowing from the fetal upper extremities, ribs, and sternum over the chest. Moreover, aortic stenosis was not apparent during this examination. Yet, there was an opportune moment in which STIC volume datasets without shadowing artifacts could be successfully obtained within a short period of time.

The fetus was appropriately grown for gestational age, and the amniotic fluid volume was normal. The patient was offered noninvasive prenatal testing, as well as amniocentesis and fluorescent in situ hybridization (FISH) for 22q11.2 deletion syndrome, but she declined all testing. Serial ultrasound examinations for fetal growth were performed during the pregnancy and were within normal limits.

Delivery and postnatal course

At 38, 5/7 weeks, the patient underwent a spontaneous vaginal delivery and delivered a viable female neonate weighing 2930 grams. Apgar scores were 8 and 9 (at 1 and 5 minutes, respectively). Genetic testing for 22q11.2 deletion syndrome was negative. Postnatal transthoracic echocardiography on day one of life confirmed the diagnosis of TOF/PA with a large perimembranous VSD and overriding aorta (Supplementary Figure S2). The

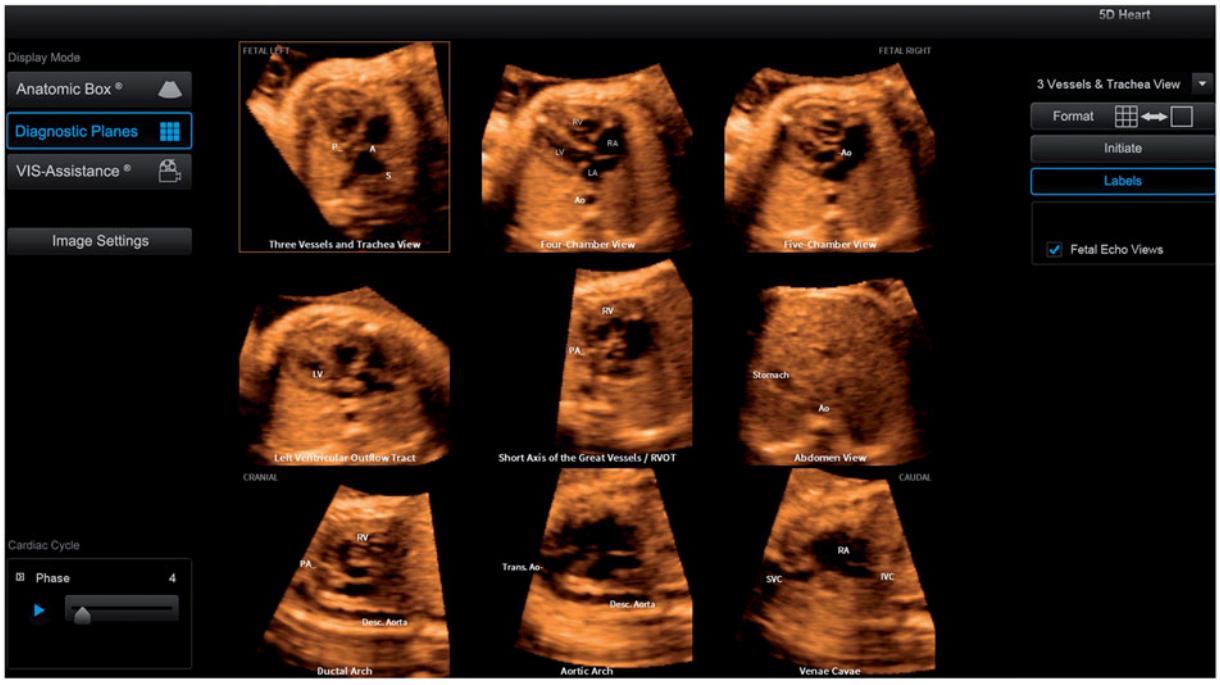

Figure 1. Application of the Fetal Intelligent Navigation Echocardiography (FINE) method to a spatiotemporal image correlation volume dataset of a fetus with tetralogy of Fallot and pulmonary atresia at 30 gestational weeks (Case 1) (also see Supplementary Movie 1). Diagnostic planes or Virtual Intelligent Sonographer Assistance (VIS-Assistance®) with automatic labeling are shown, in which five echocardiography views are abnormal. The three-vessels and trachea view shows a severely hypoplastic pulmonary artery with dilated transverse aortic arch. The pulmonary valve appears hyperechoic and closed throughout the cardiac cycle. The four-chamber view appears normal. VIS-Assistance® demonstrates two pulmonary veins connecting normally to the left atrium (not shown here). In the left ventricular outflow tract view, there is a subaortic ventricular septal defect with overriding of the ventricular septum by the dilated aortic root. In addition, the aortic valve appears thickened and dysplastic, suggesting aortic stenosis. The short-axis view of great vessels/right ventricular outflow tract view shows pulmonary atresia with a severely hypoplastic pulmonary artery, as well as a tiny ductus arteriosus. The pulmonary valve tissue again appears hyperechoic and closed throughout the cardiac cycle. The ductal arch view demonstrates similar findings. In the aortic arch view, the aortic root is dilated and there is a prominent ascending aorta. It is noteworthy that automatic labeling was correct for all nine echocardiography views. A: transverse aortic arch; Ao: aorta; Desc: descending; IVC: inferior vena cava; LA: left atrium; LV: left ventricle; P: pulmonary artery; PA: pulmonary artery; RA: right atrium; RV: right ventricle; RVOT: right ventricular outflow tract; S: superior vena cava; SVC: superior vena cava; Trans: transverse.

aortic valve leaflets appeared dysplastic, with narrowing seen in the supravalvar area. Spectral Doppler interrogation revealed a moderate degree of stenosis across the aortic valve and supravalvar region, with color Doppler aliasing seen from the turbulent flow across this area (Supplementary Figure S3, Supplementary Movie 2). In addition, echocardiography demonstrated the presence of multiple sources of blood supply to the lungs from the aorta, including what appeared to be a small patent ductus arteriosus (PDA) giving rise to severely hypoplastic native pulmonary arteries. The neonate was placed on continuous prostaglandin E1 infusion to maintain ductal patency.

Cardiac catheterization on day five of life confirmed the diagnosis and further delineated the distribution of pulmonary blood flow. Angiography demonstrated the presence of severely hypoplastic native confluent pulmonary arteries supplied by a small PDA (with preferential supply to the left lung) (Supplementary Figure S4). Additionally, there was a major aorto-pulmonary collateral artery (MAPCA) arising from an anomalous right subclavian artery to perfuse the right lung (not shown in Supplementary Figure S4). Despite the severe degree of pulmonary artery hypoplasia, initial attempts at surgical repair were undertaken by performing pulmonary arterial unifocalization and Blalock-Taussig shunt placement, along with relief of the supravalvar aortic stenosis. However, the neonate expired after a relatively short postoperative course due to persistent hypoxemia and hemodynamic compromise. An autopsy was not performed.

Case 2

A second patient was referred at 22 weeks to our unit in which the FINE method also successfully demonstrated the features of TOF/PA. For the gray-scale STIC volume, six echocardiography views were abnormal

(Supplementary Figure S5, Supplementary Movie 3). When the color Doppler STIC volume was analyzed by FINE [6], multiple echocardiography views demonstrated color flow in the aorta, but absent flow in the area of the main pulmonary artery, confirming the diagnosis of pulmonary atresia. Further details about Case 2, as well as the Discussion section can be found as Supplementary material: (1) FINE as a method to diagnose congenital heart disease; (2) variable anatomy of the pulmonary arterial circulation with TOF/PA; and (3) associated findings, prognosis, and outcome.

In conclusion, TOF/PA is a complex and heterogeneous cardiac defect with many anatomic variants, especially in the pulmonary arterial circulation. We report herein for the first time, two cases of TOF/PA with variable pulmonary arterial anatomy in which the FINE method successfully demonstrated the features of this cardiac abnormality in the prenatal period.

Disclosure statement

No potential conflict of interest was reported by the authors.

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