Atypical Circular Shunt and Diffuse Emphysema in a Fetus with Double-Outlet Right Ventricle and Absent Pulmonary Valve

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INTRODUCTION

Absent pulmonary valve syndrome (APVS) is a rare congenital cardiac anomaly commonly associated with pulmonary artery dilation, bronchial compression, and poor outcomes. Although overall operative mortality has improved, the management of APVS associated with airway compression remains challenging.[1] In this report we describe a fetus with a diagnosis of absent pulmonary valve with severe pulmonary regurgitation, double-outlet right ventricle with malposed great arteries, and patent ductus arteriosus (PDA), yielding a circular shunt with severe pulmonary and aortic dilation and tracheal and bronchial compression with diffuse obstructive emphysema.

CASE PRESENTATION

A 31-year-old G1P0 woman was referred to our institution for a second opinion at 32 and 1/7 weeks' gestation. She had a history of infertility, and the pregnancy was assisted by in vitro fertilization. She had been followed to date in her home state, where she had been offered no intervention because of the high likelihood of fetal or immediate postnatal demise. Karyotype performed at the home institution was 46,XY.

Severe cardiomegaly was noted, with a cardiothoracic circumference ratio of 0.70. Dextrocardia was present, with the cardiac apex pointing rightward (Figure 1A). There was no evidence of hydrops. There was atrial situs solitus with normal systemic and pulmonary venous return. The atria had a superior-inferior relationship, with the left atrium situated leftward and inferior and the right atrium situated rightward and superior. The atria were normally sized, with an aneurysmal atrial septum that bowed from the right atrium into the left atrium. A patent foramen ovale with right-to-left shunting was present.

The atrioventricular relationship was concordant without crisscross atrioventricular valves (the left atrium connected via the inferiorly positioned mitral valve to the left ventricle, and the right atrium connected via the superiorly positioned tricuspid valve to the right ventricle; Video 1). Trivial tricuspid regurgitation and trivial mitral regurgitation were noted.

The ventricles also had a superior-inferior relationship, with the left ventricle positioned inferior to a superior double-outlet right ventricle (Figure 1B). Both ventricles were severely dilated, hypertrophied, and trabeculated, with a non-compaction-like appearance and mildly depressed systolic function. A large subpulmonary ventricular septal defect (VSD) and multiple muscular VSDs were present.

Bilateral conus was present. The aorta arose from the right ventricle anteriorly and leftward of the main pulmonary artery (Video 2). The pulmonary valve was severely dysplastic or "absent," with severe pulmonary insufficiency (Figures 1A and 1C, Video 3). The pulmonary valve annulus measured within normal limits, with a Z score of -1.4.[2]

There was flow acceleration across the aortic valve with a peak velocity of 2.4 m/sec, although the valve morphology and annular dimension were normal (Z score = 1.5), suggesting that increased flow may be the etiology of the increased velocity. There was no significant aortic regurgitation.

The main pulmonary artery was severely dilated, with a Z score for gestational age of 5.0. The left pulmonary artery measured 16.3 mm (Z score = 20.8), and the right pulmonary artery measured 11.7 mm (Z score = 12.8). The aortic arch was left sided, with normal branching.

The ascending aorta and transverse arch were also severely dilated at 13.6 mm (Z score = 9.8) and 12.5 mm (Z score = 12.1), respectively. Retrograde flow from the distal aortic arch to the proximal left pulmonary artery through a short, very large ductus arteriosus that resembled a distal aortopulmonary window was observed (Figure 2, Video 4). The aortic isthmus, which was distal to the ductus arteriosus, and descending aorta measured only mildly dilated (Z score = 2.3 and 2.4, respectively).

Middle cerebral artery Doppler imaging showed flow reversal in diastole (Figure 3A). The umbilical artery and ductus venosus Doppler tracings had low end-diastolic velocities (Figures 3B and 3C). The umbilical vein tracing was normal (Figure 3D).

Fetal magnetic resonance imaging was performed at 32 and 1/7 weeks' gestation to assess lung volume. The proximal bronchi could not be visualized in the setting of severe pulmonary artery dilation; however, the distal bronchi were not dilated, as would be expected in the setting of proximal obstruction. The total lung volume was normal for gestational age at 82 mL. Follow-up fetal echocardiography performed at 35 and 3/7 weeks' gestation was similar to the first, with a main pulmonary artery Z score of 7.7 and an ascending aortic Z score of 16.7.

Analysis of flow patterns revealed a unique in utero circular shunt, likely explaining the severe aortic and ventricular dilation that was noted in conjunction with pulmonary artery dilation. Flow across the aortic valve coursed to the distal aortic arch; although some flow progressed to the head and neck vessels and to the descending aorta, a large volume of blood was directed across the ductus arteriosus into the left pulmonary artery. Much of the blood then coursed retrograde from the left pulmonary artery across the pulmonary valve in diastole into the right ventricle. This blood was then ejected into the
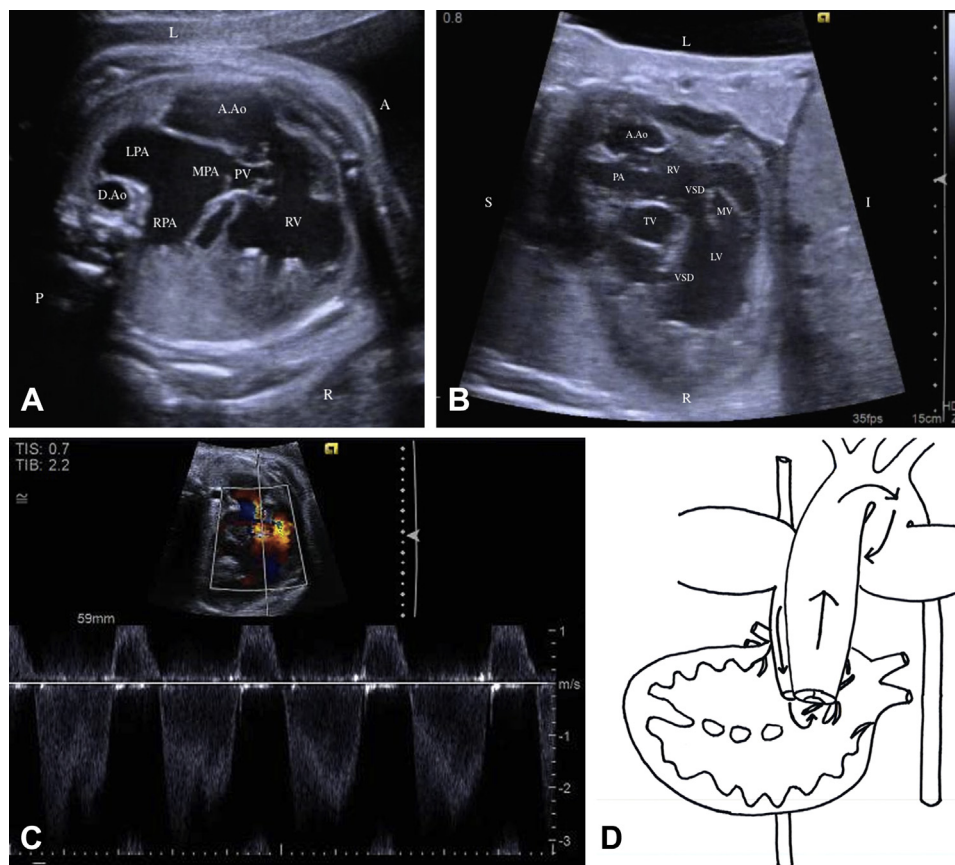
Figure 1 **(A)** Axial view. **(B)** Coronal view. **(C)** Pulsed-wave spectral Doppler tracing of the pulmonary valve. **(D)** Hand-drawn diagram with *arrows* representing the direction of blood flow in the circular shunt. *A*, Anterior; *A.Ao*, ascending aorta; *D.Ao*, descending aorta; *I*, inferior; *L*, left; *LPA*, left pulmonary artery; *LV*, left ventricle; *MPA*, main pulmonary artery; *MV*, mitral valve; *P*, posterior; *PA*, pulmonary artery; *R*, right; *RPA*, right pulmonary artery; *RV*, right ventricle; *S*, superior; *TV*, tricuspid valve; *VSD*, ventricular septal defect.

aorta, creating the circular shunt (Figure 1D). Accordingly, the isthmus and descending aorta distal to the ductal connection were only mildly dilated. Calculated output across the aortic valve was 1,100 mL/min (524 mL/min/kg on the basis of estimated fetal weight). Normal estimated aortic output at the gestational age of the fetus would be 179 mL/min/kg; thus, this output was about 2.9 times expected. Of note, the calculated prograde flow across the pulmonary valve was 1,500 mL/min (714 mL/min/kg), resulting in a severely increased combined cardiac output of 2,600 mL/min, or 1,238 mL/min/kg. We postulate that the increased flow across the pulmonary and aortic valves was due to the added volume from the pulmonary regurgitation (composed of retrograde pulmonary flow and retrograde flow from the ductus) plus expected outputs.

Given the severity of the fetus's congenital heart disease and secondary pulmonary disease, we counseled the family that we agreed with their home institution that the fetus would most likely die in utero or shortly after birth and recommended no intervention. The parents were devastated and requested that our team pursue anything possible for their only child, conceived after a history of prolonged infertility. We agreed to a stepwise care plan contingent upon the neonate's stability at each step, and with the stipulation that we would convert to comfort care at any step if we felt that support was futile.

The mother was induced at 38 weeks' gestation, with cardiology and neonatology present in the delivery room. The 3.2-kg infant was delivered via forceps-assisted vaginal delivery and emerged depressed, with Apgar scores of 1 and 3 at 1 and 5 min of life, respectively. The infant was intubated immediately upon delivery, and umbilical lines were placed. Initial arterial blood gas showed a severe respiratory acidosis with a pH of <6.8 and a pCO_2 of >100. Repeat arterial blood gas after placing the child in the prone position showed a pH of 6.92 and pCO_2 of 70, and oxygen saturations were in the 80s. The catheterization laboratory and operating room teams were placed on standby while the infant underwent computed tomographic angiography, which confirmed the intracardiac anatomy and showed severe narrowing of the distal trachea, carina, and proximal main stem bronchi in inspiration and complete occlusion of the distal trachea and main stem bronchi in expiration (Figure 4). There was severe bilateral air trapping, with left greater than right pulmonary interstitial emphysema.

The neonate was admitted to the pediatric cardiovascular intensive care unit to determine if either spontaneous or interventional closure of the ductus arteriosus would improve cardiovascular status. Over the next 36 hours, the PDA began to constrict. Despite improving cardiovascular status, the child struggled with oxygenation and ventilation despite neuromuscular blockade and prone positioning. On the second day of life, the patient developed a left-sided pneumothorax and underwent pigtail catheter placement. On the third day of life, after continued worsening ventilation and oxygenation and ongoing discussions with the parents about the futility of continued intervention, the family elected to withdraw care. The family declined autopsy.
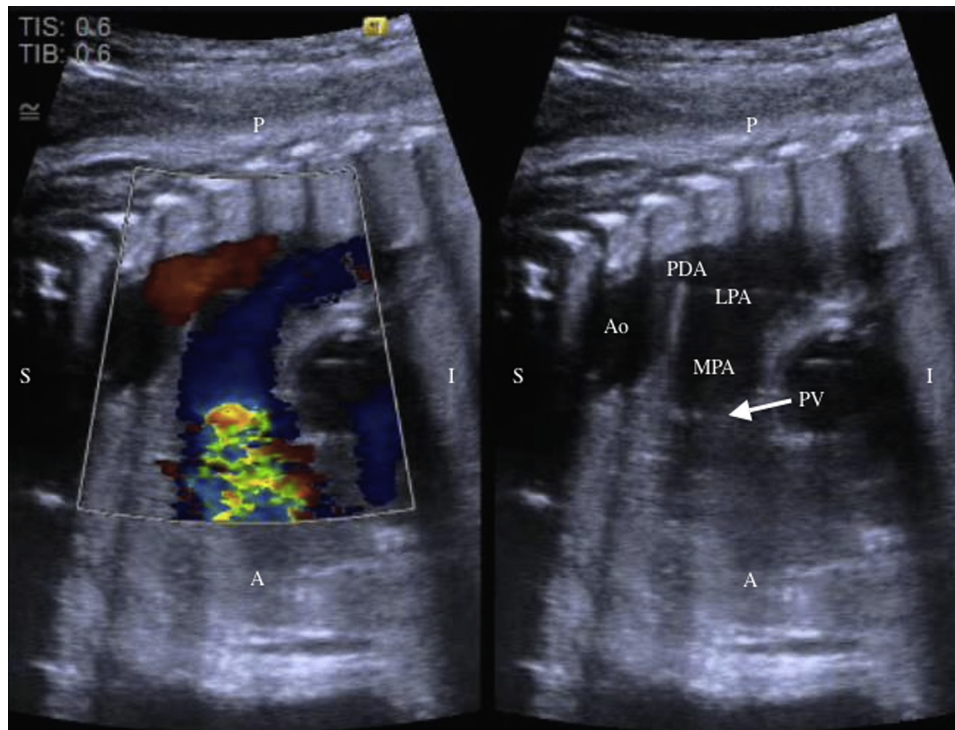
Figure 2 Color compare off-axis view in color Doppler and two-dimensional imaging. *A*, Anterior; *Ao*, aorta; *I*, inferior; *LPA*, left pulmonary artery; *MPA*, main pulmonary artery; *P*, posterior; *PDA*, patent ductus arteriosus; *PV*, pulmonary valve; *S*, superior.

DISCUSSION

In this case study, we describe a rare variation of APVS with superior-inferior ventricles with a double-outlet superior right ventricle with the aorta leftward and anterior to the pulmonary artery, multiple VSDs, and PDA. To our knowledge, this combination of lesions has not been previously described. This unique anatomy created circular shunt physiology, resulting in a significant volume load to the ventricles, ascending aorta and proximal arch, main pulmonary artery, and ductus arteriosus. Severe main and branch pulmonary artery dilation was seen, as is commonly described in APVS, but because of the unique circular shunt in this case, severe aortic and ventricular dilation was also present. A case series by Wertaschnigg *et al*[3] previously described a similar circular shunt in a patient with absent pulmonary valve and tricuspid atresia, VSD, and a PDA.

APVS is frequently accompanied by dilation of the main and branch pulmonary arteries, leading to tracheal and/or bronchial compression with varying degrees of respiratory distress.[4-6] Our patient had diffuse obstructive emphysema affecting all lobes with blebs, resulting in severe respiratory distress and pneumothorax after birth. Although the family had been counseled that a very poor outcome was anticipated, there was some hope that the cardiovascular status would improve with closure of the ductus arteriosus; however, the instability from a respiratory standpoint was, ultimately, the impetus for withdrawal of care. Although previous studies described some degree of respiratory distress secondary to lobar atelectasis, air trapping, and emphysema with APVS secondary to tracheobronchial compression, especially in those with tetralogy of Fallot with APVS, this is the first case to describe diffuse emphysema of all lung segments in a patient with APVS without tetralogy of Fallot. Recent studies have suggested that, contrary to prior reports, there is not a direct correlation between proximal branch pulmonary artery size and poor outcome or respiratory distress at birth.[7-9] It has been suggested that larger pulmonary valve annular dimension, by itself or relative to aortic valve annular dimension, may lead to worse outcomes.[7-9] In our patient, the pulmonary valve annular dimension was not large (Z score $= -1.4$) and small in proportion to the aortic valve. Given the lack of consistent evidence of cardiac predictors of the degree of lung involvement and respiratory distress, it has been speculated that underlying pulmonary parenchymal disease may play a role.[7] In a case series by Rabinovitch *et al*,[10] autopsy of three patients with APVS (two with tetralogy of Fallot and one with transposition of the great arteries) demonstrated abnormal pulmonary artery hilar branching, with compression of the intrapulmonary bronchi. All three neonates had respiratory difficulties from birth. Hilar branching appeared normal on our patient's computed tomographic angiogram. The patient's family refused autopsy, but this case highlights the need for future research in the area of lung disease with APVS.

The final question surrounding this case is an ethical dilemma: is it reasonable to offer a family hope in the form of a possible intervention when the predicted outcome is so poor? In this case, we initially, like the family's home institution, advised the family that the baby would most likely die in utero or shortly after birth and did not offer any intervention. When the family demonstrated that they were not ready to make this decision, we devised a stepwise plan for possible intervention if the neonate was stable enough to proceed. In a case such as this, with anatomy so unique that there is no standard of care in terms of management, and a prior case of AVPS with PDA having improving hemodynamic status with closure of the ductus arteriosus, we believed that honoring the family's wishes was reasonable until we felt that further intervention was futile. Chervenak and McCullough,[11] who write extensively on the topic of perinatal ethics,
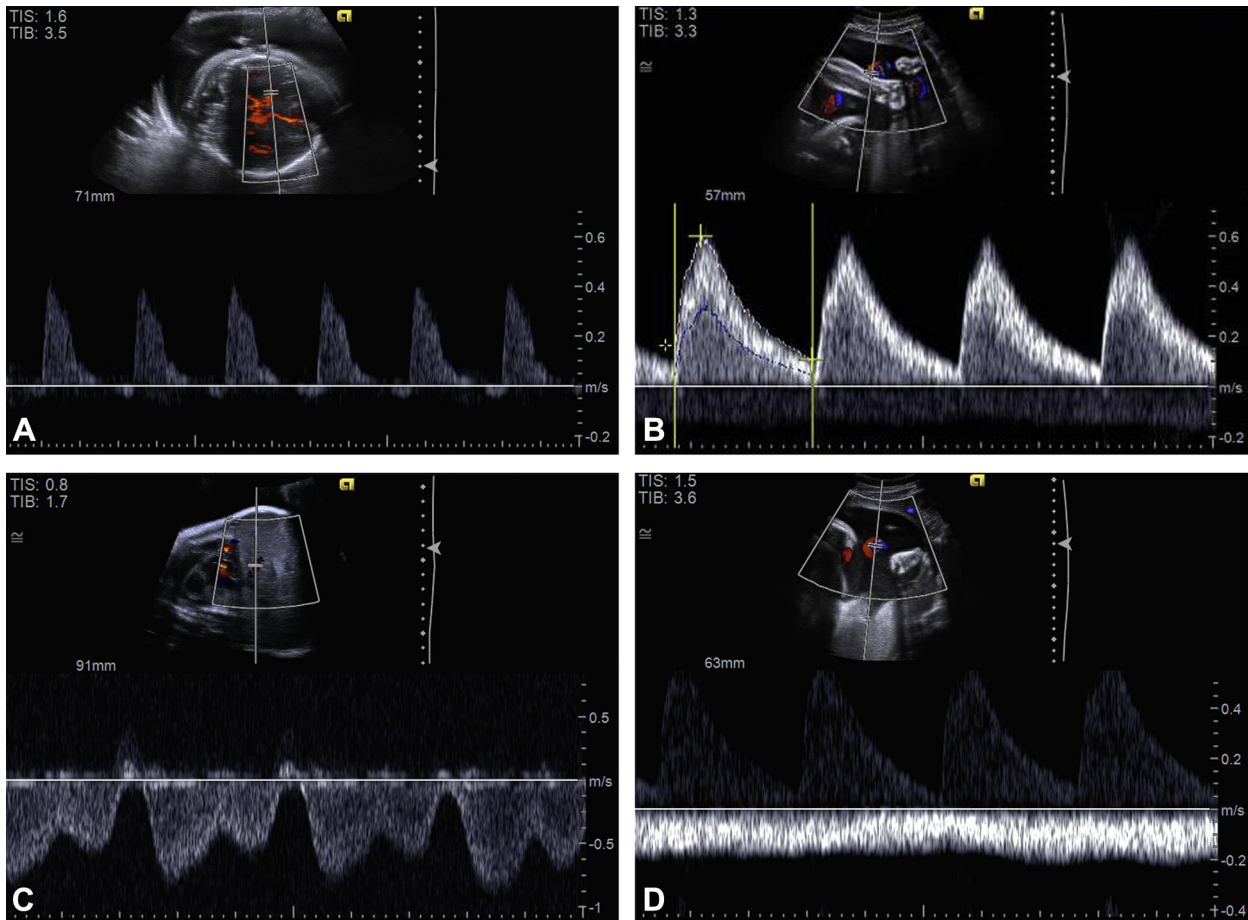
Figure 3 Pulsed-wave spectral Doppler tracings. **(A)** Middle cerebral artery. **(B)** Umbilical artery. **(C)** Ductus venosus. **(D)** Umbilical vein.
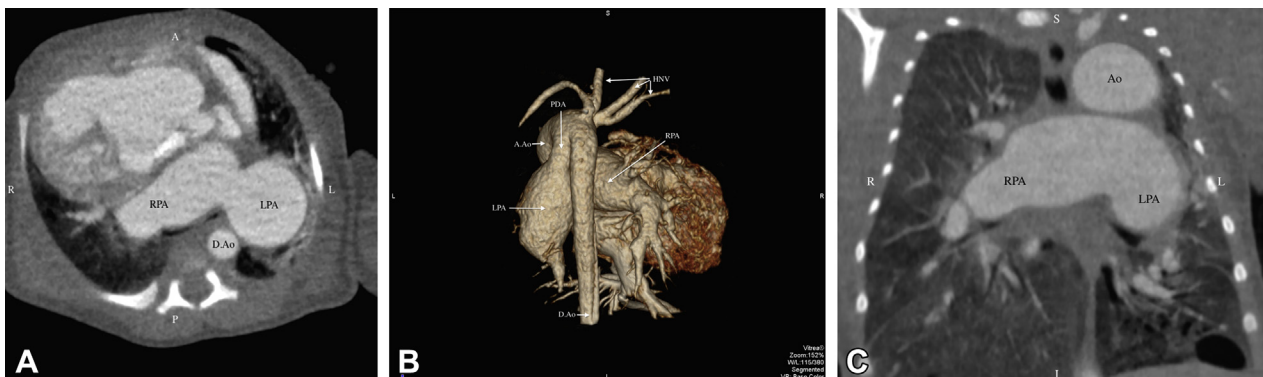

Figure 4 **(A)** Axial computed tomographic section. **(B)** Three-dimensional rendered computed tomographic image. **(C)** Coronal computed tomographic section. *A*, Anterior; *A.Ao*, ascending aorta; *Ao*, aorta; *D.Ao*, descending aorta; *HNV*, head and neck vessels; *I*, inferior; *L*, left; *LPA*, left pulmonary artery; *P*, posterior; *PDA*, patent ductus arteriosus; *R*, right; *RPA*, right pulmonary artery; *S*, superior.

tell us to balance our "beneficence based obligations" to the pregnant mother, fetus, and neonate. Although the neonate endured 3 days of intubated, sedated, and paralyzed existence with severely limited quality of life, these parents were thankful for this care, as it allowed them to be able to live their lives with the resolve that they gave their baby the best chance for survival, and for this, the sacrifice seemed justified.

CONCLUSION

We have described a rare and previously undescribed variation of APVS with superior-inferior ventricles with a double-outlet right ventricle, multiple VSDs, and PDA, resulting in a circular shunt physiology. Fetal echocardiography enabled us to accurately predict the anatomy and severity of disease, allowing optimal family counseling and management planning.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.case.2017.07.007.

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