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Original Articles

Prenatal diagnosis of absent pulmonary valve syndrome: results of a single-center experience in Beijing

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Summary

Objective: The purpose of this study was to analyze the fetal echocardiographic features of absent pulmonary valve syndrome (APVS). *Materials and Methods:* Echocardiographic findings were retrospectively analyzed and summarized in nine fetuses with APVS. *Results:* The right ventricle was dilated in six cases (66.7%). The cardiac axis was abnormally deviated to the left in four cases (44.4%). The pulmonary valve was either absent or rudimentary in all cases. The main pulmonary artery or its branches were significantly dilated. Color Doppler flow imaging showed severe pulmonary regurgitation. Spectral Doppler imaging showed stenosis of the pulmonary annulus in seven cases. Seven cases were associated with tetralogy of Fallot, two with right aortic arch, two with double outlet right ventricle, and one with mitral valve atresia and single ventricle of right ventricular type. *Conclusions:* Presence of a markedly dilated right ventricle and pulmonary arteries, combined with stenosis and severe regurgitation of the pulmonary annulus should be considered as APVS.

Key words: Fetal echocardiography; Absent pulmonary valve; Prenatal diagnosis.

Introduction

Absent pulmonary valve syndrome (APVS) is a rare cardiac truncus anomaly characterized by a dysplastic or rudimentary pulmonary valve. It is usually associated with tetralogy of Fallot (TOF) and agenesis of the ductus arteriosus (DA) [1]. Postnatal APVS occurs in approximately 3-6% of patients with TOF. Prenatal diagnosis of APVS is feasible and has been previously described [2, 3]. The overall outcome of APVS is less favorable than other forms of TOF, and is determined by the degree and severity of airway compression and lung disease [4]. Accurate prenatal diagnosis of APVS may be useful in assessing outcomes and providing consultations. The objective of this study was to describe the characteristics, associations, and outcomes of APVS diagnosed in fetuses in a single center.

Materials and Methods

Nine cases of prenatally diagnosed APVS were retrospectively analyzed from the database of fetal echocardiographies of 9,302 cases documented between December 2010 and August 2015. Maternal ages ranged from 27-35 years, with a median of 30 years. The gestational age at diagnosis ranged from 23-32 weeks, with a median of 26.6 weeks. Counseling was conducted in all cases. Autopsy of the fetuses was performed with the consent of the parents. The present study protocol was approved by the review board of the hospital and informed content was obtained in all cases.

All cases underwent fetal echocardiography. A detailed anatomical scan was performed with high-quality ultrasound equipment. A two-dimensional /three-dimensional (2D/3D) volume probe was used with a frequency range of 4-8 MHz. The common fetal biometry measurement included the biparietal diameter and Doppler recordings of the middle cerebral artery and the umbilical artery. The cardiac structure and hemodynamics of the fetuses were systematically observed by using sequential segmental analysis. The parameters of 2D imaging included the dimensions of the thoracic cavity, heart, left ventricle, right ventricle, left atrium, right atrium, aorta, main pulmonary artery (MPA), right and left pulmonary arteries, and the cardiac axis. Spectral Doppler recordings included the aorta, pulmonary artery, and ductus venosus. Color flow Doppler imaging was used to examine the cardiac valves. The final diagnosis for each case was determined when two experienced observers reached agreement. Necropsy reports and postnatal surgical and medical files were available for confirmation of the prenatal diagnosis in all cases.

Results

Of the nine cases examined, eight demonstrated situs solitus and concordant atrioventricular and ventriculoarterial connections. The remaining case was associated with a complex cardiac anomaly. The cardiac axis was abnormal and deviated to the left in four cases (44.4%). The right

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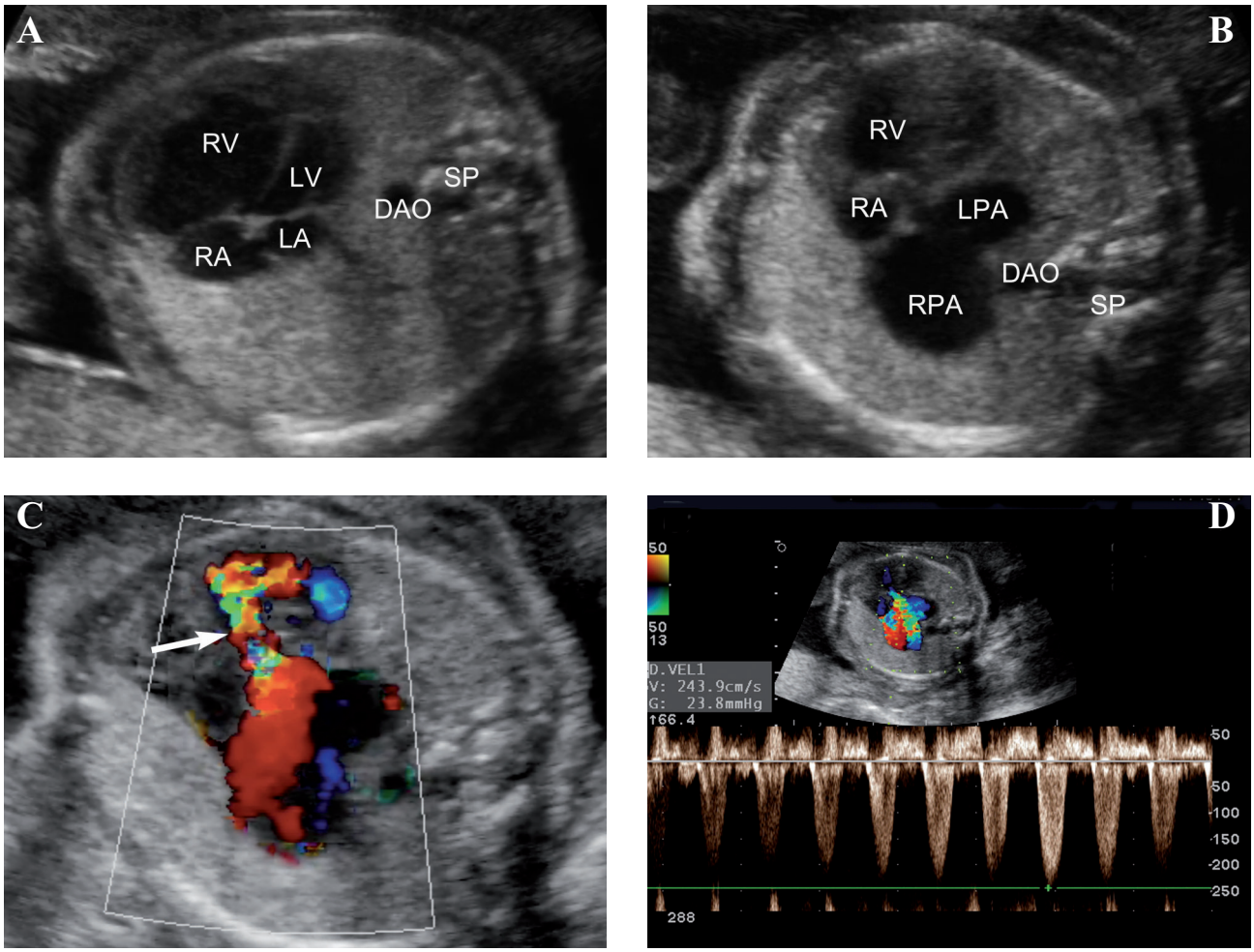

Figure 1. — APVS with tetralogy of Fallot.
A: The right ventricle (RV) is markedly dilated, and the axis of the heart is deviated to the left in a four-chamber view.
B: The left and right pulmonary arteries are characteristic of aneurysmal dilatation.
C: Color Doppler flow imaging demonstrates severe regurgitation from the pulmonary annuli without normal pulmonary valves during diastole (arrow).
D: Spectral Doppler imaging reveals high-turbulence flow originating from the pulmonary annulus. SP = spine, DAO = descending aorta, RA = right atrium, RV = right ventricle, LA = left atrium, LV = left ventricle, LPA = left pulmonary artery, RPA = right pulmonary artery.

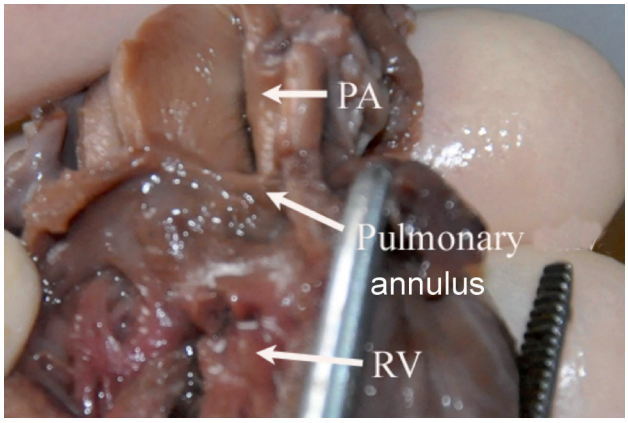

Figure 2. — Autopsy sample in a fetus with APVS. No normal pulmonary valve is noted in the region of pulmonary annulus. The dilated main pulmonary artery is apparent. RV = right ventricle, PA = pulmonary artery.

Table 1. — *General clinical and echocardiographic features of fetal APVS.*

Case	GA (weeks)	Gravida (G) and para (P) status	Thoracic cavity (mm)	Heart (mm)	Cardiac axis (°)	LV (mm)	RV (mm)	LA (mm)	RA (mm)	Aorta (mm)	MPA (mm)
1	23	G1P0	45.0	29.0	58	8.3	11.4	5.3	9.4	4.8	10.8
2	24	G1P0	46.0	30.0	70	8.0	12.8	8.2	12.0	5.2	13.0
3	30	G5P2	54.2	29.0	56	11.8	13.5	12.6	14.6	6.1	9.2
4	27	G2P1	66.5	50.5	135	14.0	19.9	11.0	24.5	7.0	6.3
5	26	G2P1	62.3	27.6	50	10.0	12.7	7.9	8.4	6.5	9.3
6	32	G3P2	60.8	30.1	44	4.2	26.5	9.2	12.9	6.3	15.9
7	24	G1P0	47.0	24.0	72	8.0	8.6	8.8	9.1	5.4	6.1
8	27	G2P0	57.0	33.0	95	8.5	17.0	9.9	13.0	5.7	7.2
9	26	G1P0	53.0	27.0	61	10.8	12.5	9.8	11.8	6.1	4.7

Case	LPA (mm)	RPA (mm)	Velocity of AV (cm/s)	Velocity of PV (cm/s)	PI	TR	DV	DA	PE	Combined anomalies
1	6.9	10	91.0	182.0	Severe	None	Normal	Agenesis	Mild	TOF, SUA
2	7.6	11	85.0	309.0	Severe	Moderate	Reversed a-wave	Agenesis	None	TOF
3	6.2	5.4	90.0	143.0	Severe	Mild	Normal	Normal	None	DORV
4	7.1	6.8	127.0	311.0	Severe	None	Normal	Agenesis	None	TOF
5	3.2	3.0	99.0	256.0	Severe	None	Normal	Normal	None	TOF
6	12.3	13.4	64.0	63.0	Severe	None	Normal	Agenesis	None	MA, SV, DORV, RAA
7	6.1	6.4	84	224	Severe	None	Normal	Agenesis	None	TOF, RAA
8	6.3	6.6	72	177	Severe	None	Normal	Normal	None	TOF
9	6.5	9.8	108	183	Severe	None	Normal	Agenesis	None	TOF

GA = gestation age, LV = left ventricle, RV= right ventricle, LA = left atrium, RA = right atrium, MPA = main pulmonary artery, LPA = left pulmonary artery, RPA = right pulmonary artery, AV = aortic valve, PV = pulmonary valve, PI = pulmonary insufficiency, TR = tricuspid regurgitation, DV = ductus venosus, DA = ductus arteriosus, PE = pericardial effusion, TOF = tetralogy of Fallot, SUA = single umbilical artery, DORV = double outlet right ventricle, MA = mitral atresia, SV = single ventricle, RAA = right aortic arch.

ventricle was dilated in six cases (66.7%) (Figure 1A). In the three-vessel view, the main pulmonary artery or its branches were markedly dilated in all cases (Figure 1B). No normal pulmonary valve leaflet tissue was observed in any case.

Color Doppler flow imaging across the MPA revealed turbulence in the flow of blood ejected during systole. However, during diastole, severe blood regurgitation back through the absent or dysplastic pulmonary valve into the dilated right ventricular outflow chamber was evident in all cases (Figure 1C). Spectral Doppler imaging revealed shuttle flow signals across the pulmonary valve annulus during both systole and diastole in all cases (Figure 1D). One case showed A-wave reversal in the ductus venosus during atrial contraction. Two cases had tricuspid regurgitation.

All APVS cases were combined with one or more of the following cardiovascular anomalies: TOF (seven cases, 77.8%), double outlet right ventricle (DORV) (two cases, 22.2%), right aortic arch (two cases, 22.2%), mitral atresia and single ventricle of right ventricular type (one case, 11.1%), single umbilical artery (one case, 11.1%), and agenesis of the DA (six cases, 66.7%).

Of the nine fetuses with APVS, seven cases were confirmed by autopsy (Figure 2), one case was not permitted for confirmation by autopsy, and one case was confirmed based on the echocardiography report at the local hospital by telephonic follow-up.

General clinical information and echocardiographic data from the nine fetuses with APVS are listed in Table 1.

Discussion

APVS is a very rare but fatal congenital heart defect. Early and accurate diagnosis provides helpful information to parents during consultation. Emmanoulides *et al.* [1] first described the significant association of TOF with an absent pulmonary valve and ductal agenesis.

Two variants of APVS are found in fetuses. An absent pulmonary valve associated with TOF and ductal agenesis is the most common variant [2]. The rarer variant is an absent pulmonary valve associated with an intact ventricular septum, mildly dilated pulmonary artery, and patent DA. This variant may also be associated with tricuspid atresia [5]. Of the nine cases in this study, seven were the more common variants associated with TOF and one was the rare variant associated with complex congenital heart disease.

The extent of pulmonary artery dilatation may result from the valve abnormality itself, which causes stenosis and re-

gurgitation [6], or it may be associated with the presence of DA, which would play a key role in the dilation of the pulmonary arteries [7, 8]. Volpe *et al.* [7] found that the mean diameters of the pulmonary trunk and its branches in cases of DA agenesis, are significantly greater than in the cases with a patent DA, which suggested that there may be a key role of DA agenesis in the dilated pulmonary artery seen with APVS. The present study was based on a limited number of cases and the association between the presence or absence of the DA and the severity of pulmonary artery dilatation needs to be determined using a larger sample size.

The echocardiographic appearance of APVS is very characteristic in the second trimester. The most significant feature of APVS is an absent or rudimentary pulmonary valve associated with a ventricular outlet defect. Cardiomegaly, especially of the right ventricle, can be distinguished and the cardiac axis appears to be positioned to the left. The main pulmonary artery and its branches are characterized by aneurysmal dilatation. 2D assessment of the pulmonary valve indicates the absence of the pulmonary valve or rudimentary leaflets, which do not have normal function. Color Doppler imaging reveals severe pulmonary regurgitation. Spectral Doppler imaging also shows that the peak velocity of flow is increased across the pulmonary annulus. Therefore, the diagnosis of APVS should be considered when aneurysmal dilatation of the pulmonary artery, along with severe regurgitation, is noted. In addition, APVS can be obviously detected during routine second-trimester ultrasound examinations when the four-chamber view appears clearly abnormal due to cardiomegaly and a significantly dilated pulmonary trunk. Of the nine APVS cases in this study, one had a-wave reversal of the ductus venosus, suggesting that the high pressure of the right atrium resulted from tricuspid regurgitation.

In comparison to diagnosis in the second trimester, accurate diagnosis of APVS during the first trimester is more difficult. Becker *et al.* [9] found no evidence of dilatation at the end of the first trimester and no right ventricular enlargement during the first trimester. The only characteristic of APVS that could be clearly identified was pulmonary valve insufficiency. Berg *et al.* [10] found that the reversed end-diastolic flow in the umbilical artery was associated with APVS.

APVS can occur as an isolated anomaly, usually associated with TOF. The condition may also occur in combination with other intracardiac anomalies such as a right aortic arch [11], absence of the aortic valve [12], and tricuspid atresia [5]. Of all APVS cases, 20-25% are associated with 22q11 microdeletion [7]. In the present study, intracardiac anomalies included TOF, DORV, and right aortic arch. However, the authors' analysis did not include any chromosomal examination.

Previous studies reported that the prognosis of APVS is poor [6, 7, 11, 13]. Heart failure and respiratory distress resulting from the compression of bronchi by the dilated pulmonary arteries are associated with a high mortality rate. However, recent reports suggest that postnatal outcomes continue to improve and that left ventricular dysfunction and a higher ratio of the pulmonary valve-to-aortic valve can accurately predict postnatal mortality [14, 15]. Intrauterine deaths occur in 14.3% of cases [7]. The presence of a patent DA may also be a cause of severe heart failure [16]. Acute intrapartum fetal demise with APVS has been reported [17]. Patients with an intact ventricular septum have a relatively improved prognosis [18].

With the development of ultrasound techniques, the stratification of prenatal diagnosis can help evaluate the prognosis of APVS. When prenatal consulting is sought, the specific progression of APVS and potential outcomes need to be explained explicitly to the parents [16].

In conclusion, the echocardiographic characteristics of APVS, including an absent or rudimentary pulmonary valve with pulmonary annulus stenosis, severe regurgitation, and aneurysmal dilatation of the pulmonary trunk or its branches, can be detected during the second trimester of fetal development.

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