

Image characteristics and main types of abnormal branching of fetal pulmonary artery in prenatal echocardiography — a retrospective study

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ABSTRACT

Objectives: To explore the image characteristics and main types of abnormal branching of fetal pulmonary artery in prenatal echocardiography.

Material and methods: A retrospective analysis of 41 cases diagnosed with abnormal branching of fetal pulmonary artery by prenatal echocardiography was made. The image characteristics of the abnormalities, their combination with intra- or extra-cardiac malformations and chromosomal anomalies were analyzed.

Results: The results of prenatal echocardiography showed that, among the 41 cases: 1) 4 cases were with anomalous origin of single pulmonary artery, 8 cases with pulmonary artery agenesis, 9 cases with pulmonary artery sling; 20 cases with crossed pulmonary arteries; 2) 11 cases were complicated with intracardiac malformations and 10 with extracardiac malformations; 3) only 7 case underwent chromosomal examination and 1 tested abnormal; 4) pregnancy outcomes: 25 fetuses were born and their abnormalities confirmed by echocardiography (MRI or surgery) to be consistent with prenatal ultrasound diagnosis; 16 cases had their pregnancy terminated due to their combination with other severe malformations, which were confirmed by pathological anatomy after induced abortion.

Conclusions: Prenatal echocardiography can provide detailed images for the diagnosis of abnormal branching of fetal pulmonary artery, which can be complicated by intra- and extracardiac malformations and chromosomal anomalies and should be alerted.

Keywords: prenatal diagnosis; echocardiography; abnormal branching of pulmonary artery

Ginekologia Polska 2024; 95, 6: 460–466

INTRODUCTION

The prevalence of abnormal branching of pulmonary artery is about 1.2‰ to 3‰ [1], which can be inherited in an autosomal dominant, autosomal recessive, or X-linked pattern, and are often combined with intra- or extracardiac abnormalities. Abnormal branching of pulmonary artery generally includes abnormal origin of single pulmonary artery, unilateral pulmonary artery agenesis (UPAA), pulmonary artery sling, crossed pulmonary arteries (CPAs), etc. and for the diagnosis of which prenatal echocardiography is the first choice. This study retrospectively analyzed the images of 41 abnormal branching of fetal pulmonary artery diagnosed by prenatal echocardiography, their combination with intra- or extracardiac malformations, and associated chromosomal anomalies, which are reported as follows.

MATERIAL AND METHODS

General data

41 fetuses with the diagnosis of abnormal branching of pulmonary artery by prenatal echocardiography at the Hospital of Chengdu University of Traditional Chinese Medicine and Sichuan Provincial Maternity and Child Health Care Hospital from January 2014 to December 2020 were retrospectively studied. The mothers aged between 20–40 years, with a mean age of (30 ± 10) years. The gestational age ranged between 20–34 weeks, with a mean of (27 ± 7) weeks. The inclusion criteria were pregnant women in good health, with no special past or family history, and who underwent routine prenatal ultrasound examination of the fetus between 22 to 32 weeks of pregnancy in two hospitals. Abnormal branching of fetal pulmonary artery in prenatal echocardiography.

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Received: 8.08.2023 Accepted: 10.12.2023 Early publication date: 19.01.2024

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The exclusion criteria were pregnant women who should not be originally suitable for pregnancy, but became pregnant. The excluded pregnant women are those with severe conditions including congenital heart disease and other diseases such as severe hyperthyroidism that would put the mother in grave danger, or with abdominal wall fat hypertrophy causing poor fetal image quality.

Apparatus and methods

Color Doppler ultrasound including GE Voluson E8, Samsung WS80A, Philips EPIQ 7 and Mindray Resona8S were used to perform a comprehensive screening of the fetus using a transabdominal probe (probe frequency 1–8 MHz). If evidence of abnormal branching of pulmonary artery were observed on the three-vessel and tracheal view or the three-finger view, a further inspection for signs of other intra- or extra-cardiac anomalies was conducted. All cases were engaged in follow-ups. This study followed standard medical ethics principles.

Observation

The image characteristics of abnormal branching of pulmonary artery on sections of the three-vessel and tracheal view or the three-finger view were observed, the condition's combination with intra- or extra-cardiac anomalies, and chromosomal anomalies investigated.

RESULTS

Image characteristics of abnormal branching of fetal pulmonary artery, their combination with intra- or extra-cardiac malformations, and chromosomal anomalies

Findings on the three-finger view

Normally ductus arteriosus, left pulmonary artery (LPA) and right pulmonary artery (RPA) can be seen from left to right on this view (Fig. 1).

Of the 41 fetuses studied, there were: 4 cases of anomalous origin of single pulmonary artery: 1 case with the LPA originating from the aortic arch (Fig. 2); 3 cases with the RPA originating from the ascending aorta (Fig. 3).

Eight cases with UPAA: 2 on the left and 6 on the right (Fig. 4).

Nine cases with pulmonary artery sling: 8 cases in the entire form (the LPA originated posterior to the RPA, passed between the trachea and esophagus, bypassed the right main bronchus and distal trachea, and traveled towards the left pulmonary hilar, as shown in Fig. 5) and 1 in a partial form (the left inferior and right pulmonary arteries originated from the MPA, the left upper pulmonary artery originated from the RPA, as shown in Fig. 6).



Figure 1. The normal three-finger view. Normally ductus arteriosus, left pulmonary artery (LPA) and right pulmonary artery (RPA) can be seen from left to right on this view; DA — ductus arteriosus; MPA — main pulmonary artery



Figure 2. Left pulmonary artery (LPA) originates from the aortic arch; AO — aorta; DA — ductus arteriosus

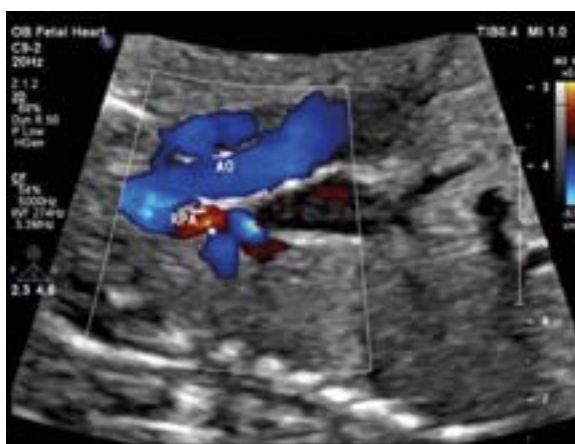


Figure 3. Right pulmonary artery (RPA) originates from the ascending aorta; AO — aorta

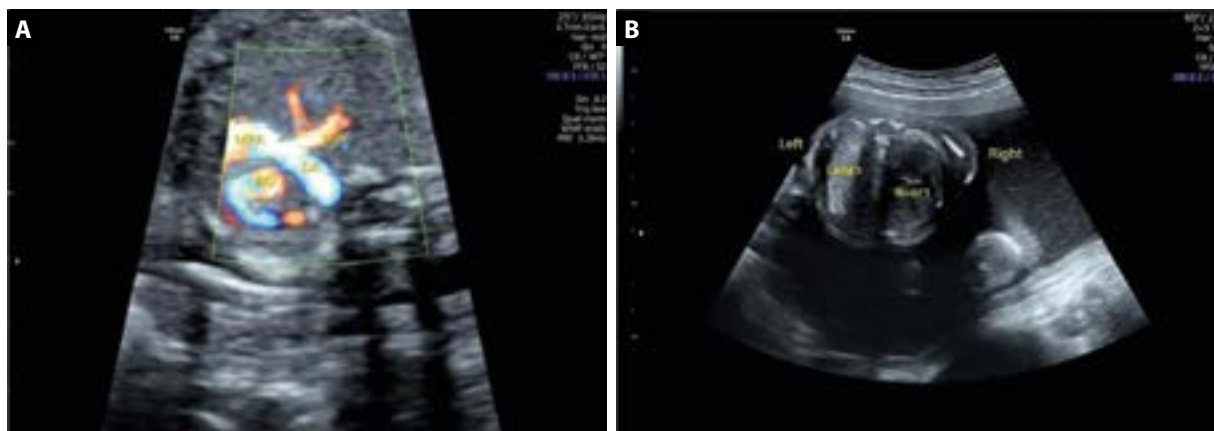


Figure 4. Right pulmonary artery (RPA) agenesis; **A.** Right pulmonary artery is not seen in the bifurcation section of the pulmonary artery; **B.** Right lung is not seen in the right chest cavity, dextral heart (the heart is located in the right chest cavity, the apex of the heart points to the right); AO — aorta; DA — ductus arteriosus; MPA — main pulmonary artery; LPA — left pulmonary artery



Figure 5. Pulmonary artery sling in an entire form. The left pulmonary artery (LPA) originated posterior to the right pulmonary artery (RPA), passed between the trachea and esophagus, bypassed the right main bronchus and distal trachea, and traveled towards the left pulmonary hilar; MPA — main pulmonary artery; DA — ductus arteriosus



Figure 6. Pulmonary artery sling in a partial form. The left inferior and right pulmonary arteries (RPA) originated from the main pulmonary artery (MPA), the left upper pulmonary artery originated from the RPA; LUPA — left upper pulmonary artery; LDPA — left lower pulmonary artery; L — left; R — right; SP — spine

Twenty cases with crossed pulmonary arteries (CPAs): the LPA originated from the right wall of the MPA and traveled towards the left to the left lung, and the RPA originated from the left wall of the MPA and traveled towards the right to the right lung, with the LPA and RPA crossing at their beginnings (Fig. 7).

Abnormal branching of fetal pulmonary artery and their combination with intra- or extracardiac malformations

Eleven of the 41 cases were combined with intracardiac malformations (2 with anomalous origin of single pulmonary artery, 1 with UPAA, 5 with pulmonary artery sling, and 3 with CPAs).

Ten of the 41 cases were combined with extracardiac malformations (1 with anomalous origin of single pulmo-

nary artery, 8 with UPAA, and 1 with pulmonary artery sling).

Chromosomal findings

Only 7 of the 41 fetuses were examined for chromosomes (1 case with the RPA originating from the ascending aorta, 2 cases with pulmonary artery sling and 4 cases with CPAs), of which 1 case had chromosomal anomalies (the case of CPAs: deletion of chromosome 22).

Pregnancy outcomes

Twenty-five fetuses were born, and their prenatal diagnoses were confirmed by echocardiography (MRI or surgery); 16 pregnancies were terminated due to their combination with other severe anomalies, which were confirmed by pathological anatomy after induced abortion (Tab. 1).



Figure 7. Crossed pulmonary arteries (CPAs); The left pulmonary artery (LPA) originated from the right wall of the main pulmonary artery (MPA) and traveled towards the left to the left lung, and the right pulmonary arteries (RPA) originated from the left wall of the MPA and traveled towards the right to the right lung, with the LPA and RPA crossing at their beginnings

DISCUSSION

Anomalous origin of unilateral pulmonary artery

It was found in the cases that pulmonary artery on one side normally originated from the MPA and pulmonary artery the other side anomalously originated from the aorta, ductus arteriosus or other sites, a condition that was suspected to be associated with abnormal embryonic development. The occurrence of unilateral pulmonary artery originating from the aorta is due to delayed migration of the sixth aortic arch on the affected side to the opposite side during embryonic stage and rest on the arterial side of the aortic sac, eventually leading to the origin of the affected pulmonary artery from the proximal aorta or other sites, with single pulmonary artery originating from the aortic arch or ascending aorta more commonly seen. Previous studies reported cases such as aberrant right pulmonary artery that originated from the right ductus arteriosus emanating from the brachiocephalic trunk [2], anomalous origin

Table 1. Profile of 41 cases with abnormal branching of fetal pulmonary artery

Type	No.	Intracardiac malformations	Extracardiac malformations	Outcome
Anomalous origin				
LPA originating from the aortic arch	1	None	None	Induction
RPA originating from the ascending aorta	1	None	None	Induction
	2	Coarctation of the aorta	None	Induction
	3	VSD, tricuspid atresia, pulmonary atresia	Visceral inversion, right isomerism	Induction
UPAA				
On the left	1	None	Absent left lung, intestinal atresia	Induction
	2	None	Absent left lung	Induction
On the right	1–5	None	Absent right lung	Induction
	6	dextroversion	Absent right lung, dysplasia of thoracic vertebrae	Induction
PA sling				
In the entire form	1–4	None	None	Born
	5	Tetralogy of Fallot	None	Induction
	6	PLSVC	None	Born
	7	Coarctation of the aorta, PLSVC	None	Born
	8	VSD, coarctation of the aorta, pulmonary valve stenosis, PFAA	None	Induction
In a partial form	1	VSD, pulmonary valve stenosis, ARSA, dextrocardia	Cleft lip and cleft palate, microtia of the right ear	Induction
CPAs				
	1	DORV, pulmonary valve stenosis	None	Induction
	2	ARSA	None	Born
	3–19	None	None	Born
	20	VSD	None	Born

LPA — left pulmonary artery; RPA — right pulmonary artery; VSD — ventricular septal defect; UPAA — unilateral pulmonary artery agenesis; PLSVC — persistent left superior vena cava; PFAA — persistent fifth aortic arch; ARSA — aberrant right subclavian artery; CPAs — crossed pulmonary arteries; DORV — double outlet right ventricle

of the LPA from the left ductus arteriosus emanating from the brachiocephalic trunk [3] or from the innominate artery [4]. The anomalous origin of a unilateral pulmonary artery from the ductus arteriosus was not found in this study. The reason might be the limited sample size and more samples shall be included in future studies. The anomalous origin of the pulmonary artery may exist alone or be complicated with other malformations, among which pulmonary atresia with ventricular septal defect (VSD) and pulmonary artery stenosis are the most common [5]. The anomalous origin of the RPA is often combined with aortopulmonary window (AP window), aortic arch dissection [6, 7], pulmonary aneurysm, pulmonary hypertension or heart failure [8]. In this study, for case with RPA originating from the ascending aorta, one case was combined with coarctation of the aorta, another one combined with VSD, tricuspid atresia, pulmonary valve atresia, visceral inversion and right isomerism, and the rest were not found to have been combined with other malformations. Studies have reported [9] that patients with anomalous origin of unilateral pulmonary artery from the ascending aorta might have a microdeletion of 22q11. In this study only one case underwent chromosomal examination, and the result was normal, therefore the correlation between anomalous origin of unilateral pulmonary artery and chromosomal anomalies could not be established yet.

Unilateral pulmonary artery agenesis (UPAA)

Normally during the embryonic period, the pulmonary artery trunk originates from the aortic sac, the distal MPA and the proximal pulmonary artery are formed by the sixth aortic arch, and the distal pulmonary artery develops into the pulmonary vascular plexus. In UPAA cases, the proximal sixth aortic arch would degenerate, the internal pulmonary artery would be persistently connected to the distal sixth aortic arch, a situation arises from which the pulmonary blood supply on the affected side would come from branches of the aberrant artery while the bronchial artery would originate from the descending aorta or the innominate artery, thus creating an aortopulmonary collateral circulation. In a fetus with UPAA combined with tetralogy of Fallot, the distal end of the existing single pulmonary artery is connected to the aortic arch via the ductus arteriosus. After birth, poor blood supply and collateral circulation from the aortic branches on the affected side would result in local ischemia and hypoxia, which in turn lead to vasoconstriction, hyperplasia, stenosis, increased pulmonary vascular resistance and eventually pulmonary hypertension [10]. Right pulmonary artery agenesis is often combined with coarctation of the aorta [11], left pulmonary artery agenesis is often associated with a right-sided aortic arch [12], and pulmonary artery agenesis or dysplasia is often combined with right isomer-

ism [13]. In this study, all cases of pulmonary artery agenesis were combined with pulmonary agenesis, including one case of right pulmonary artery agenesis combined with dextroversion and thoracic spine dysplasia; and one case of left pulmonary artery agenesis combined with intestinal atresia. Right pulmonary artery agenesis was found to be more frequent than left pulmonary artery agenesis, which is inconsistent with previous reports [14]. Right pulmonary artery agenesis was often associated with DiGeorge's syndrome [15]. All the eight cases of pulmonary artery agenesis in this study were not examined for chromosomes, and the relationship between pulmonary artery agenesis and chromosomal anomalies still needs to be explored.

Pulmonary artery sling

Normally, in the early embryonic stage, the left and right pulmonary arteries would emanate from both sides of the lung bud and connect to the sixth pair of aortic arches on both sides as the embryo develops. If the LPA failed to connect to the sixth arch on the left side, it would originate from the RPA, then pulmonary artery sling, also called aberrant left pulmonary artery, would occur. This anomaly can be present in an entire form or a partial form. In an entire form both LPAs originates from the RPA, while in a partial form either of the two LPAs originates from the RPA with the aberrant LPA passes through the trachea and the esophagus, resulting in a vascular ring and frequent compression of the lower trachea, the right main bronchus and the esophagus. Since the airway hasn't started its function during the fetal period, no relevant clinical symptoms would present. After birth, compression of the airway by the aberrant LPA may cause respiratory disturbances and recurrent respiratory infections in newborns; compression of the esophagus may cause swallowing disorders. In this study, there was one case of partial pulmonary sling: the left inferior PA and the RPA originated from the MPA, and the left superior PA originated from the RPA, a type that is rare [16]. Previous studies reported that pulmonary artery slings would often be combined with intra- or extracardiac malformations [17–19]. In this study, 55.5% (5/9) of the cases were combined with intracardiac malformations, mainly tetralogy of Fallot, VSD and permanent left superior vena cava (PLSVC), and only one case was combined cleft lip and cleft palate and right microtia, while the remaining cases did not have combined extracardiac malformations. Studies have reported [20, 21] that fetal pulmonary artery sling is often combined with chromosomal anomalies. In this study, chromosomal examination was performed for two cases and both results were normal. The current inadequate literature on this anomaly and the small sample yet cannot provide convincing explanations on the correlation between pulmonary artery sling and chromosomal anomalies.

Crossed pulmonary arteries (CPAs)

In this condition, both the left PA and right PA originate from the MPA and cross each other at their beginnings in front of the trachea and then travel to the right and left respectively. Despite the change in their spatial relationship, their course between the cross and the hila are normal. The cross would not result in any mechanical airway obstruction or hemodynamic abnormalities. It has been reported [22] that CPAs might be associated with abnormal differentiation of the MPA during embryonic development, resulting in a counterclockwise rotation at the MPA bifurcation. CPAs may occur alone or in combination with other intra- or extracardiac malformations and chromosomal anomalies. Studies have reported [23] that CPAs is susceptible to the combination of conotruncal defects and genetic syndromes, including VSD and double outlet right ventricle (DORV), and is associated with trisomy 18 and 22q11 deletion. In this study, 3 of the 19 CPAs cases were combined with intracardiac malformations: one with DORV and pulmonary valve stenosis, one with aberrant right subclavian artery (ARSA), and one with VSD; 4 of the 19 cases had chromosomal examinations, and one of them was found to have chromosome 22 deletion, with a 2.54 Mb deletion in the region of 22q11.21, demonstrating that CPAs would be combined with chromosomal anomalies. Chromosomal examination should be routinely performed when such abnormalities are encountered.

The treatment and follow-up results after birth

Follow-ups among the 25 newborns, 6 had pulmonary artery sling (Tab. 1, No. 1–4 without malformations, No. 6 with PLSVC, and No. 7 with aorta coarctation and PLSVC) and within one year after birth all received surgeries of pulmonary artery sling to correct the condition. Their follow-ups showed satisfactory patient outcomes. The other 19 cases had crossed pulmonary arteries (Tab. 1, No. 2 with ARSA, No. 3–19 without malformations, No. 20 with VSD). Case No. 2 didn't receive any surgeries for the aberrant right subclavian artery after birth and the follow-up found no signs of dyspnea or dysphagia for the patient. Cases No. 3–19 didn't receive any surgeries after birth and the follow-ups showed good results. Case No. 20 received VSD transcatheter repair at the age of 2 and the follow-ups showed satisfactory patient outcome. The follow-ups were conducted mainly through telemedicine communications or on-site visits.

Limitations

In this study, only seven cases underwent chromosomal examination. The sample was small and cannot provide adequate evidence to elucidate in detail the correlation

between the abnormal connection of pulmonary artery branches and chromosomal anomalies. The small portion of the cases screened with malformations to have further chromosomal and microarray examinations is mainly due to the socioeconomic factors. As society advances and the patient education improve, we hope more affected cases could have genetic consultations and chromosomal and microarray examinations. Investigations with larger samples and involving wider regions are required to cast light on the genetic changes of this anomaly.

CONCLUSIONS

In conclusion, prenatal echocardiography can clearly show that the image characteristics and the main types of abnormal branching of fetal pulmonary artery and the associated intra- or extracardiac malformations. The pregnancy of fetus who have anomalous origin of single pulmonary artery and unilateral pulmonary artery agenesis combined with severe deformity of pulmonary artery sling or crossed pulmonary arteries should be terminated while the pregnancy of fetuses with pulmonary artery sling or crossed pulmonary arteries without severe malformations can be born and closely followed up. Our results can provide a more comprehensive information for prenatal consultation and eugenics.

Article information and declarations

Data availability statement

All data generated or analyzed during this study are included in this published article. The data of this study is available upon request.

Ethics statement

This study protocol was reviewed and approved by the Ethics Committee of the hospital of Sichuan Provincial Maternity and Child Health Care Audit Committee, Written informed consent was obtained from participants prior to the study.

Authors contributions

HYY conceived the study and literature review and drafted the manuscript. CGZ analyzed the data and interpreted data. LHH revised the manuscript and supervised the whole study. All authors read and approved the final manuscript.

Funding

None.

Acknowledgements

None.

Conflict of interest

All the authors declare no conflicts of interest.

Supplementary material

None.

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