Prenatal diagnosis and postnatal course in four fetuses with very rare pulmonary artery anomalies

Çok nadir görülen pulmoner arter anomalilerinin prenatal tanısı ve postnatal seyri

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Abstract

Pulmonary artery (PA) anomalies are very rare congenital cardiac malformation, of which a significant number remain unrecognized or misdiagnosed during the prenatal period. We report the prenatal diagnosis and outcome of pregnancy with fetal pulmonary artery anomalies and discuss the related management issues. We identified four cases of prenatally diagnosed rare pulmonary artery anomalies that were seen and confirmed at the newborn period by echocardiography, and computed tomographic angiography at our center from 2018 to 2020. The course of the pregnancy, perinatal outcome, and the postnatal course in each case were analyzed. Three fetuses were born by repeat cesarean section approximately at 39 weeks of gestation and the other woman delivered vaginally. Of the abnormal origin of the left pulmonary artery two cases, the first one had right pulmonary artery abnormalities deriving from the ascending aorta, in the second one, the left pulmonary artery originating from the right pulmonary artery was seen. Two cases with agenesis of ductus arteriosus (DA), and the first one is accompanied with tetralogy of Fallot (TOF) and right aortic arch (RAA) with normal pulmonary valve, the second case presented with an absent pulmonary valve syndrome (APVS) with tetralogy of Fallot. Prenatal ultrasonography can correctly diagnose the abnormal origin of the pulmonary artery branches. Branching of pulmonary artery, presence of ductus arteriosus, location of the aortic, and ductal arch by the trachea should be routinely screened in the prenatal anatomic examination and 3 vessels trachea view determines the primary clues of pulmonary artery malformations.

Keywords: Agenesis of ductus arteriosus, left pulmonary artery originating from the ascending aorta, absent pulmonary valve syndrome, left pulmonary artery sling, right aortic arch, tetralogy of Fallot

Öz

Pulmoner arter anomalileri çok nadir görülen konjenital kalp hastalıklarından olup birçoğu prenatal dönemde farkedilmeyebilir veya yanlış tanımlanabilmektedir. Burada fetal pulmoner arter anomalilerinin prenatal tanısı ve sonuçlarını ve yönetimini tartışmayı amaçladık. 2018 ile 2020 arasında kliniğimize başvuran prenatal dönemde tanı konulan dört vaka tanımlandı ve postnatal yenidoğan döneminde ekokardiyografi ve bilgisayarlı tomografik anjiyografi ile tanımlanarak doğrulandı. Her olgunun gebelik seyrini, perinatal sonuçlarını ve postnatal takiplerini analiz ettik. Sezaryan öyküsü olan 3 hasta 39. gebelik haftasında sezaryen ile, 1 hasta normal vajinal yolla doğurtuldu. Vakaların ikisinde sol pulmoner arter anormal orjinli olup bu vakaların ilkinde sol pulmoner arter asendan aortadan çıkarken, ikinci vakada sol pulmoner arter sağ pulmoner arterden kaynaklanmakta idi. İki vakada duktus arteriosus yokluğu olup ilk olguda Fallot tetralojisi ve sağ aortik ark, ikinci olguda ise pulmoner kapak yokluğu ile birlikte Fallot Tetralojisi saptandı. Prenatal ultrasonografi ile anormal pulmoner arter dallanması doğru bir şekilde tanımlanabilir. Pulmoner arter dallanması, aort ve duktal arkın trakeaya göre yerleşimi prenatal ultrasonografik incelemede değerlendirilmeli ve 3 damar trakea kesiti pulmoner arter malformasyonlarında prenatal dönemde tanı konması için primer ipucu sağlamaktadır.

Anahtar Kelimeler: Duktus arteriosus yokluğu, sol pulmoner arterin asendan aortadan orijini, pulmoner kapak yokluğu sendromu, sol pulmoner arter askısı, sağ aortik ark, Fallot tetralojisi

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Introduction

Congenital pulmonary artery (PA) anomalies are extremely rare among cardiovascular anomalies⁽¹⁾. These pathologies usually present with other complex cardiac diseases, when these anomalies are isolated, they are often likely to be unrecognized during fetal life. Accurate prenatal diagnosis of congenital heart disease not only prevent neonatal morbidity and mortality but also provide appropriate preoperative conditions, and improve surgical outcomes⁽²⁾. We described four cases including left pulmonary artery sling, left pulmonary artery originating from the ascending aorta (AOLPA/hemitruncus), two cases with agenesis of ductus arteriosus (DA). Cases with ductus arteriosus agenesis were accompanied with tetralogy of Fallot (TOF) - absent pulmonary valve (APVS) and tetralogy of Fallot - right aortic arch (RAA), respectively. Left pulmonary artery sling, also known as aberrant left pulmonary artery, derives from the superior and posterior aspect of the right pulmonary artery instead of main pulmonary artery and then turns sharply leftward posterior to the trachea to enter the hilum of the left lung⁽³⁾. Left pulmonary artery originating from the ascending aorta is characterized by the anomalous origin of left pulmonary arteries from the posterolateral wall of the ascending aorta in the presence of two semilunar valves⁽⁴⁾. The ductus arteriosus is a unique vessel of fetal circulation that connects the pulmonary trunk and descending aorta. The underlying cause of ductus arteriosus agenesis is not well-known and it is associated with other cardiac anomalies such as tetralogy of Fallot, absent pulmonary valve, truncus arteriosus, ventricular septal defect⁽⁵⁾. The aim of this study to review our experience of prenatal ultrasonographic features of pulmonary artery abnormalities. We emphasized that the 3 vessels trachea (3VT) view which is the most important view in the diagnosis of pulmonary artery anomalies and in addition, left pulmonary artery originating from the ascending aorta should be taken into consideration in the differential diagnosis when the fourth vessel is detected in 3 vessels trachea view.

Materials and Methods

A total of 6752 women with singleton pregnancies from 18 to 30 weeks gestation were examined from September 2018 to February 2020 at the Department of Perinatology and Pediatric Cardiology, Istanbul Medeniyet University, Istanbul, Turkey. Fetal anatomic and echocardiographic examinations were performed by using Voluson E6 Expert machine, Samsung Ultrasound H60, Esaote MyLab™9 Platform. All cases underwent a complete fetal anatomic screening according to the ISUOG practice guideline. The standard four chambers and ventricular outflow tracts of the fetal heart were obtained routinely during the fetal anatomic screening for all patients by detailed two-dimensional, color Doppler echocardiography. After finding cardiac anomaly, detailed echocardiographic examination including 3 vessels trachea, aortic and ductal arch, pulmonary artery branches, aortic long axis, superior

vena cava, inferior vena cava inflow, pulmonary venous return were assessed. We used color Doppler blood flow to track the pulmonary artery branches and ductus arteriosus. Chromosome analysis and fluorescent in-situ hybridization (FISH) analysis for microdeletion 22q11.2 were recommended to all the patients. In addition to ultrasonography, demographic features and medical histories of all the mothers were reviewed and the perinatal outcomes were recorded. In the postnatal period, to verify the prenatal diagnosis of all pulmonary artery anomalies different imaging modalities, such as echocardiography, cardiac CT angiography, and angiography were used. The study was approved by the hospital ethics committee and all of the pregnant women with pulmonary artery anomalies provided written informed consent.

Results

All four cases with a prenatal diagnosis of pulmonary artery anomalies with or without cardiac malformations were reviewed for intrauterine course and outcome between 2018 and 2020. The mean gestational age at the time of admission was 24,8 weeks (range, 22-28 weeks) and the mean maternal age was 32,5 years (range, 30-35 years). Three of four patients were referred to our center for suspicious of congenital heart disease, while the remaining one case was detected during the routine ultrasonographic examination. All cases were singleton pregnancies and no extracardiac anomalies were identified. The four cases of the pulmonary artery anomalies were left pulmonary artery sling, left pulmonary artery originating from the ascending aorta, ductus arteriosus agenesis with right aortic arch - tetralogy of Fallot, and ductus arteriosus agenesis with absent pulmonary valve - tetralogy of Fallot, respectively. Only one of the four patients accepted invasive procedure and the results of chromosome analysis and fluorescent in-situ hybridization (FISH) analysis for microdeletion 22q11.2 were normal. 3/4 fetuses were delivered by cesarean section (CS) due to previous cesarean section at term. Physical examination of the other three infants was performed and dysmorphic findings were not found in the postnatal period. Three infants except for one case with ductus arteriosus agenesis accompanied with absent pulmonary valve - tetralogy of Fallot, were clinically stable and they don't require surgery at the time of writing. A summary of the data from all four patients is shown in Table and each clinical case report is described below and accompanied by supporting figures (Figs 1-9).

Case 1

A 33 years old woman gravida(G) 5, parity(P) 1, abortus (Ab) 3 with a non-consanguineous marriage, underwent routine ultrasound examination at 22 weeks gestation and fetal echocardiography (Samsung Ultrasound H60) was performed for suspected cardiovascular malformation. The family history was insignificant regarding congenital diseases or malformations. Prenatal echocardiography demonstrated that

Figure 1. The left pulmonary artery originates from the right pulmonary artery

Figure 2. Axial contrast enhanced computed tomography confirmed the aberrant left pulmonary artery

the left pulmonary artery originated from the right pulmonary artery and then turning left, crossed midline behind the trachea, anterior the esophagus and descending aorta towards the hilum of the left lung (Figure 1). In the 3 vessels trachea view, the trachea was encircled by aberrant left pulmonary artery and left-sided ductus arteriosus. The diameter of right and left

Figure 3. The aortic arch, and ductal arch were located on the right side of the trachea, and four vessels were seen on the 3VT view

P: Main pulmonary artery, A: Aorta, SVC: Superior vena cava, T: Trachea, *: Left pulmonary artery

Figure 4. The left pulmonary artery originated from the posterior aspect of ascending aorta and then turning left, crossed midline anterior the trachea towards the hilum of the left lung

Yellow arrow: Pulmonary artery, Red arrow: AoPa

pulmonary arteries was equal and the thymus size was in the normal range for 22 weeks gestation. Neither any congenital anomaly and polyhydramnios nor any genetic abnormalities including abnormal karyotype and Di George syndrome were detected by amniocentesis. Due to placenta previa totalis, a 3480 g female baby was delivered by cesarean section in a tertiary care center at 38 weeks of gestation. APGAR scores were 9 and 10 at 1 and 5 minutes, respectively. By postnatal echocardiography on the first day after birth, the diagnosis of left pulmonary artery sling was confirmed and peak systolic velocity of the left pulmonary was measured in the normal range, excluding the stenosis or hypoplasia of left pulmonary artery. Postnatal

Figure 5. The right aortic arch, malalignment ventricular septal defect, overriding aorta in the five-chamber view were shown

Figure 6. The diameters of pulmonary annulus, right and left pulmonary artery were seen on the 3VT view

axial contrast enhanced computed tomography confirmed the aberrant left pulmonary artery and normal appearing lungs and tracheobronchial anatomy (Figure 2). The asymptomatic baby was discharged from hospital on the third day after birth and she is still symptom-free for eight months during the time of the writing.

Case 2

A 32-year-old woman with a history of hyperthyroidism, G2P1 was referred to perinatology clinic for second trimester

Figure 7. Hypoplasia of the pulmonary annulus, subaortic ventricular septal defect with the overriding aorta, severe dilatation of the pulmonary trunk were seen on the outflow tract of the right ventricular view

Figure 8. Absent pulmonary valve cusps, absent ductus arteriosus, and right aortic arch were determined on the 3VT view

ultrasonographic and fetal echocardiographic screening at 26-weeks gestation. The family history was negative for congenital heart defects, chromosomal abnormalities, or unexpected newborn death shortly after birth. There were no other malformations outside the heart of the fetus (Samsung Ultrasound H60). Fetal echocardiography showed that viscerotransverse situs solitus with normal systemic and pulmonary venous connections and normal four-chamber view. Fetal cardiac findings were as follows: the aortic arch and ductal arch were located on the right side of the trachea and four vessels on the 3 vessels trachea view (Figure 3). Although the right pulmonary artery arised from the pulmonary trunk, the origin of the left pulmonary artery could not be seen clearly.

Figure 9. Increased peak flow velocity through the pulmonary valve annulus and a retrograde diastolic flow originating from the pulmonary valve annulus was revealed by Color Doppler ultrasound

To evaluate the anatomy in a transverse plane by Doppler ultrasonography, sweeping from inferior to superior, and tracking the left pulmonary artery from the hilum of the left lung, anterior the trachea revealed its origin from around the vicinity of the ascending aorta closed to the brachiocephalic artery (Figure 4). The thymus was seen normally behind sternum at the level of the 3 vessels trachea view. The parents were consulted for genetic diseases but cordocentesis for karyotyping and analysis of 22q11 deletion was refused by the patient. At 40 weeks of gestation, a female infant of 3565-g was born after an uncomplicated vaginal delivery with APGAR scores of 9 and 10 at 1 and 5 minutes, respectively. The physical examination of the baby was normal without any dysmorphic features and arterial oxygen saturation was normal. Neonatal echocardiography revealed left pulmonary artery origin in the posterior aspect of ascending aorta, midsegment stenosis in the left pulmonary artery with a peak pressure gradient of 30 mmHg. Right-sided aortic arch, right-sided patent ductal arteriosus, and mild tricuspid regurgitation were seen in the postnatal echocardiography. Two days after birth we performed CT angiography and confirmed the fetal diagnosis showing the described left pulmonary hemitruncus. The newborn was discharged at 3 days after birth without cardiac or respiratory symptoms. The baby was doing clinically well in her last clinic visit at 4 months of age.

Case 3

A 35-year-old G4P1Ab2 refugee woman was referred to perinatology clinic for suspected of a fetal heart defect. There was no family history of congenital heart disease or she did

not have any risk factors leading to congenital heart disease. The results of a fetal echocardiogram at 23 weeks of gestation lead to show the right aortic arch, malalignment ventricular septal defect, overriding aorta in five-chamber view (Figure 5); further ductus arteriosus could not be seen arising from the main pulmonary artery and connecting to the descending aorta at the 3 vessels trachea view and sagittal view, respectively (Samsung Ultrasound H60). Pulmonary valve, main pulmonary artery, and the branches of the pulmonary valve were in the normal range. The diameters of the pulmonary annulus, right and left pulmonary artery were 2,49mm, 1,55mm, and 1,87 mm, respectively (Figure 6). Color Doppler confirmed the presence of an overriding aorta with blood draining from both ventricles into the aorta. The antegrade flow was seen in the main and branch of the pulmonary artery but ductus arteriosus could not be demonstrated by Collor Doppler. After prenatal genetic consultation, amniocentesis for karyotyping and analysis of 22q11 deletion was declined by the parents. The female fetus was delivered by cesarean section due to previous cesarean section at 38 weeks gestation. The neonate did not need any cardiac or respiratory support and weighed 3175 g. No findings suggesting any genetic anomaly were found in the phenotype of the newborn baby. Postnatal transthoracic echocardiogram revealed that the four-chamber view appeared normal, however, aortic root slightly shifted the right ventricle and located to the right of the trachea, ductus arteriosus was absent as fetal findings. The diameters of pulmonary annulus, right and left pulmonary artery were 5,8mm, 4,5mm, and 4,8 mm, respectively. The peak pressure gradient at the level of the pulmonary valve was approximately 23 mmHg during the discharge from the hospital. She is still uneventual for two months during the time of the writing. Surgical correction is delayed until it reaches the appropriate age.

Case 4

A 30 years old woman, G2P1 was sent to our clinic for suspicious of congenital diaphragmatic hernia on obstetrical ultrasound at 28 weeks of gestation. The healthy pregnant women did not have any genetic disorders or fetal heart anomaly in her family history. The anatomic screening was in the normal range except the fetal heart (Samsung Ultrasound H60). The fetus presented with situs solitus, levocardia, and the atrioventricular connection were normal. A slightly larger right heart was shown on a four-chamber view; pulmonary valve annulus was hypoplastic (4,5 mm); subaortic ventricular septal defect with the overriding aorta, severe dilatation of the pulmonary trunk and its branches (right and left pulmonary artery were 1,2 mm and 13,8 mm, respectively) were seen on the outflow tract of the right ventricular view (Figure 7); absent pulmonary valve cusps, absent ductus arteriosus and right aortic arch were determined on the 3 vessels trachea view (Figure 8). Increased peak flow velocity through the pulmonary valve annulus and a retrograde diastolic flow originating from the

pulmonary valve annulus was revealed by Color Doppler ultrasound (Figure 9). Absent pulmonary valve with tetralogy of Fallot was diagnosed that based on the following findings: absent pulmonary valve, absent ductus arteriosus, right aortic arch, presence of malalignment ventricular septal defect, and overriding aorta. The main pulmonary artery diameter was 5.63 mm, left and right artery diameters were 3.37 mm and 3.33 mm respectively. The mother refused to undergo karyotype analysis and fluorescent in-situ hybridization analysis to detect the 22q11 microdeletion. Fetal hydrops did not develop with compensatory extension of the left and right pulmonary artery and with the shunt through a patent foramen ovale during the follow-up from the 28 weeks of gestation to the delivery. The male fetus was born by repeat cesarean section at 39 weeks of gestation. Postnatal a transthoracic echocardiographic findings were consistent with prenatal diagnosis. Cardiac results included tetralogy of Fallot, aneurysmal dilatation of pulmonary arteries branches, and the right ventricle was seen slightly larger. When the baby was presented early with airway compression from aneurysmal pulmonary arteries and early correction surgery was performed successfully at 2 months old.

Discussion

Reports of prenatal diagnosis of pulmonary artery malformations, including agenesis of the ductus arteriosus, absent pulmonary valve, abnormal branching of pulmonary vessels, and origin of pulmonary artery, are extremely rare anomalies^(1,6). Pulmonary artery anomalies may be isolated or accompanied by other complex cardiac and extracardiac anomalies. Since pathological anatomy is very different, surgical treatment and prognosis are also variables⁽²⁾. We described four cases of the pulmonary artery anomalies which were identified on fetal echocardiography and confirmed at the newborn period by echocardiography and CT angiography (Table 1).

The pulmonary artery derives from the right ventricle, courses towards the left of the more posterior ascending aorta, its branches after a short course in normal manner. The first branch is right pulmonary artery, left branch subsequently. The pulmonary artery continues distally towards the left side and into the ductus arteriosus that connects to the descending aorta in anatomically normal fetus. In healthy fetuses, ductal and transverse aortic arches merge together with a course to the left of the trachea and no vascular structures exist posterior or surround the trachea at the level of three-vessel tracheal view which is the most important view in the diagnosis of conotruncal abnormalities⁽⁷⁾. During the normal development of the cardiovascular system, the aortic arches develop from the aortic sac, with a pair of branches (right and left) and initially, six pairs of aortic arches are present and symmetrical. They develop and regress at different stages of development. In the process of normal embryogenesis, the sixth aortic arches separate into ventral and dorsal segments and the ventral part of the arches forms the proximal branch of the pulmonary arteries

bilaterally. The left ventral arch is responsible for the formation of the pulmonary trunk, the left dorsal sixth arch continues as the ductus arteriosus and connects the main pulmonary trunk with the left dorsal aorta⁽⁸⁾. The left pulmonary artery originates as a branch of the left ventral sixth aortic arch and capillaries that arise from the pulmonary postbranchial plexus surrounding the lung bud by the 8th week of embryonic development⁽⁹⁾.

The first prenatal diagnosis of left pulmonary artery sling was demonstrated in 2011 during the fetal ultrasound examination at 32 weeks gestation by Yorioka⁽¹⁰⁾. To date a few cases of prenatally diagnosed left pulmonary artery sling have been reported⁽¹⁾. The development of aberrant left pulmonary artery was purposed that if the connection between left lung bud ventrally and left six arches to fail, the connection occurs between right six aortic arch and the developing left lung bud dorsally, it results in a left pulmonary artery that forms from the right pulmonary artery, passing posterior to the trachea⁽¹¹⁾. We described one prenatal case with left pulmonary artery sling with follow up from 22 weeks gestation to the postnatal 2 years old. After birth, axial contrast computed tomography and postnatal echocardiography findings confirmed the prenatal diagnosis of left pulmonary artery sling. According to the Wells classification of left pulmonary artery sling, computed tomography demonstrated that the bronchial anatomy was type 1A, the left pulmonary artery (LPA) arises from the right pulmonary artery, and courses posteriorly between the trachea and esophagus⁽¹²⁾. The carina was typically located at the T4-T5 level and left aberrant pulmonary artery did not cause compression of the trachea, bronchus, and esophagus. Symptoms of this condition usually become clinically manifest in the neonatal period that in 50% of the patients, and in 65% they occurred before 1 month of age⁽¹³⁾. The most common symptom is about the respiratory system, causing dyspnea wheezing and stridor. The symptoms are produced by compression of the tracheobronchial tree and the esophagus, cause tracheobronchial stenosis, tracheomalacia, and airway compression in the postpartum period. In about half of the cases are associated with other cardiac and non -cardiac defects such as atrial septal defect, persistence left superior vena cava, ventricular septal defect, abnormal pulmonary lobulations, and tracheal bronchus⁽¹³⁾. Morbidity and mortality are often depended primarily on the presence of tracheobronchial tree anomaly and especially tracheal or bronchial stenosis more than left pulmonary artery sling, with mortality rates as high as 50% without surgical correction⁽¹¹⁾. Although half of the patients have symptoms, in our case left pulmonary artery sling is the isolated anomaly without symptoms at the time of writing.

Anomalous origin of unilateral pulmonary artery is a rare congenital pulmonary vascular malformation that one branch of pulmonary artery originates from the ascending aorta while the other one arises from the main pulmonary artery. The embryogenesis and development of ductus arteriosus and the aortic arch is still uncertain. Ductus arteriosus originates from the left sixth arch, presumably and ductus arteriosus is connected

Table 1. Summary of cases with pulmonary artery anomalies

Case	Type of PA Anomaly	Maternal Age(years)	G-P-Ab	Gestational week (GW) at diagnosis	Other Cardiac Anomalies	Time and mode of delivery	Postnatal Follow-up
1	LPAS	33	5-1-3	22	Retrotracheal LPA	38GW-CS	Perform MR Angiography. Asymptomatic
2	AOLPA	32	2-1	26	Right AA Right DA	40GW-VB	Perform Angiography Asymptomatic
3	Agenesis of DA	35	4-1-2	23	ToF Right AA	38GW-CS	Perform echocardiography Asymptomatic
4	Agenesis of DA	30	2-1	28	APVS ToF	39GW-CS	Perform echocardiography Correction surgery at 2 months old

PA: Pulmonary artery, G: Gravida, P: Parite, Ab: Abortus, LPAS: Left pulmonary artery sling, CS: Caesarean section, AOLPA: Abnormal origin of left pulmonary artery, AA: Aortic arch, DA: Ductus arteriosus, VB: Vaginal birth, TOF: Tetralogy of fallot, APVS: Absent pulmonary valve syndrome

with the first part of the left pulmonary artery. As the 6th arches do not develop partially or completely on the left side, the left pulmonary artery cannot be attached to the main pulmonary artery and persists the aortic sac from which the pulmonary artery originates⁽¹⁴⁾. Right hemitruncus is more frequent than left hemitruncus⁽¹⁵⁾, however, left hemitruncus is more associated with other cardiovascular anomalies with either tetralogy of Fallot or right aortic arch⁽¹⁶⁾. After birth, pulmonary vascular resistance decreases progressively in healthy babies however, excessive blood flow into the anomalous origin of unilateral pulmonary artery from the aortic arch leads to pulmonary over circulation and the affected lung is exposed to systemic pressure, while the other lung reaches entire of the blood from the right ventricle. As a result of pulmonary over circulation, pulmonary hypertension, subsequently, heart failure develops. In order to avoid irreversible pulmonary vascular damage and development of pulmonary hypertension, early diagnosis and surgical correction are crucial in hemitruncus⁽¹⁷⁾. It has been reported that mortality rates are very high in cases that are not surgically treated⁽¹⁸⁾. Prenatal detection of hemitruncus is crucial on fetal echocardiography because early surgical correction improves survival⁽¹⁹⁾. In this case, we report the prenatal diagnosis of a case with left hemitruncus, right-sided aortic arch, right-sided ductal arch in the 3 vessels trachea view. Postnatal echocardiography and axial contrast enhanced computed tomography confirmed the fetal diagnosis showing the described left pulmonary hemitruncus and midsegment stenosis in the left pulmonary artery with a peak pressure gradient of 30 mmHg was determined which was confirmed by cardiac catheterization. Detection of the fourth vessel in 3 vessels trachea view should lead to search for the differential diagnosis including abnormal pulmonary venous connections, persistent left superior vena cava, esophageal or bronchial tree anomalies, or cystic thoracic mass. We emphasized that left hemitruncus should be taken into consideration in differential diagnosis and the importance of demonstrating both pulmonary

artery branching.

In the normal fetal circulation, ductus arteriosus carries 78% of the right ventricular blood away from the lungs, joins the descending aorta to supply the lower part of the fetus. The underlying mechanism of ductus arteriosus agenesis is not yet clear. One of the mechanisms is that agenesis of ductus arteriosus occurs unless the left dorsal sixth arc continues as the ductus arteriosus. The secondary mechanism is that the blood in the right ventricle, which has high oxygen saturation, can not be transported to the lungs due to the severe obstruction of the pulmonary artery and the higher oxygen saturated aortic blood diverts from aorta to the ductus arteriosus, thereby inducing constriction⁽²⁰⁾. Embryologically, the right aortic arch occurs due to the persistence of the right dorsal aorta instead of the left dorsal aorta. The embryological process causing the development of tetralogy of Fallot is not clearly known, it is assumed that an anterior and cephalad deviation of the infundibular septum results in a malalignment ventricular septal defect, aortic root overrides the ventricular septal defect that cause a subsequent right ventricular outflow obstruction. Absent pulmonary valve syndrome may be accompanied by ventricular septal defect which is called as tetralogy of Fallot with absent pulmonary valve and this is generally associated with absence of the ductus arteriosus. However, if the ventricular septal defect does not occur, the ductus arteriosus is usually present. In the absence of ductus arteriosus, the main pulmonary trunk can not connect the left dorsal aorta, pulmonary artery blood pressure increases, severe pulmonary regurgitation develops, resulting in an enlarged pulmonary artery and this pathological process interferes with normal development of the pulmonary valve. Isolated agenesis or premature closure of the ductus arteriosus is an uncommon congenital cardiac malformation, they are usually associated with tetralogy of Fallot, absent pulmonary valve, truncus arteriosus, or maternal use of prostaglandin synthetase inhibitors. We demonstrated two cases with agenesis of ductus arteriosus and the first one is

accompanied with tetralogy of Fallot and right aortic arch with normal pulmonary valve at 23 weeks of gestation, the second case presented with absent pulmonary valve with tetralogy of Fallot. Although in the first one, ductus arteriosus did not develop, pulmonary valve and branches of pulmonary artery were seen in the normal range because blood from the right ventricle to the aorta exit via malalignment ventricular septal defect, and pulmonary valve and branches of pulmonary artery were not exposed to high pressure of right ventricle. In tetralogy of Fallot, the agenesis of a ductus arteriosus would probably occur at the beginning of the pregnancy, patent foramen ovale and large ventricular septal defect would be able to carry the blood from the right ventricle into the descending aorta, thus, the pulmonary valve, pulmonary vascular bed and pulmonary artery branches can develop normally⁽²¹⁾. The component of absent pulmonary valve syndrome includes the absence or rudimentary pulmonary valve, stenosis of the pulmonary valve annulus, dilatation of the pulmonary trunk, and left and right branches of pulmonary arteries. This condition is rarely isolated, it is most often associated with tetralogy of Fallot and agenesis of ductus arteriosus. The fetal echocardiographic diagnosis was confirmed for both cases. The first case is 4 months old at the time of writing and no therapeutic intervention was performed yet. In the second case, early successful correction was performed to due the significant airway compression when the baby was 2 months old.

Fetal echocardiography is considered to be an important, non-invasive, and safe diagnostic modality for assessing congenital heart anomalies. Our cases highlight the variability of abnormalities of pulmonary artery. Although outflow tract anomalies have a characteristic echocardiographic appearance in 3 vessels trachea view, prenatal diagnosis of these anomalies may be missed or anomalies may be misdiagnosed especially abnormal branching of pulmonary artery⁽²²⁾. Therefore, the detection of pulmonary anomalies prenatally may be challenging but is very important since postnatal careful follow-up of the neonate improves short and long-term outcomes. When the pulmonary branch can not be displayed as a Y shape, it is absolutely necessary tracing the course of left and right pulmonary artery branch to diagnose the anomaly.

In summary, branching of pulmonary artery, presence of ductus arteriosus, location of the aortic, and ductal arch should be routinely screened in the prenatal anatomic examination and 3 vessels trachea view determines primary clues of pulmonary artery malformations. Clinicians should increase their awareness in the prenatal diagnosis of pulmonary artery anomalies in order to avoid unfavorable outcomes and 3 vessels trachea view needs to be performed excellently during the routine fetal anatomic examination.

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References

1. Hirsig LE, Sharma PG, Verma N, Rajderkar DA. Congenital Pulmonary Artery Anomalies: A Review and Approach to Classification. *J Clin Imaging Sci*. 2018 Jul 31;8:29. Review.
2. Tworetzky W, McElhinney D.B, Reddy V.M, Brook M.M, Hanley F.L, Silverman N.H. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. *Circulation*. 2001; 103: 1269-1273
3. Zhong YM, Jaffe RB, Zhu M, et al. CT assessment of tracheobronchial anomaly in left pulmonary artery sling. *Pediatr Radiol* 2010;40 :1755-1762.
4. Abu-Sulaiman RM, Hashmi A, McCrindle BW, Williams WG, Freedom RM. Anomalous origin of one pulmonary artery from the ascending aorta: 36 years' experience from one centre. *Cardiol Young* 1998;8:449-54.
5. Han W1, Xie M1, Cheng TO2, Wang Y1, Zhang L1, Hu Y1, Cao H1, Hong L1, Yang Y1, Sun Z1, Yu L3. The vital role the ductus arteriosus plays in the fetal diagnosis of congenital heart disease: Evaluation by fetal echocardiography in combination with an innovative cardiovascular cast technology. *Int J Cardiol*. 2016 Jan 1;202:90-6.
6. Prenatal diagnosis of anomalous origin of pulmonary artery. Li X, Mu Z, Li X, Weng Z. *Prenat Diagn*. 2018 Apr;38(5):310-317. Epub 2018 Mar 23.
7. Carvalho JS, Allan LD, Chaoui R, Copel JA, DeVore GR, Hecher K, Lee W, Munoz H, Paladini D, Tutschek B, Yagel S. ISUOG Practice Guidelines (updated): sonographic screening examination of the fetal heart. *International Society of Ultrasound in Obstetrics and Gynecology, Ultrasound Obstet Gynecol*. 2013 Mar;41(3):348-59
8. Ryan D, Rosen; Bruno Bordoni. *Embryology, Aortic Arch Treasure Island (FL): StatPearls Publishing; 2020 Jan*
9. Yorioka H1, Kasamatsu A, Kanzaki H, Kawataki M, Yoo SJ. Prenatal diagnosis of fetal left pulmonary artery sling. *Ultrasound Obstet Gynecol*. 2011 Feb;37(2):245-6.
10. Yoichiro Ishii, Takashi Miyamoto, Kimiko Nakajima. et al. Abnormal cardiac axis as a prenatal marker of left pulmonary artery sling. *Pediatrics International*, 2016;58:158-161.
11. Yu JM1, Liao CP, Ge S, Weng ZC, Hsiung MC, Chang JK, Chen FL. The prevalence and clinical impact of pulmonary artery sling on school-aged children: a large-scale screening study. *Pediatr Pulmonol*. 2008 Jul;43(7):656-61.
12. Wells TR1, Gwinn JL, Landing BH, Stanley P. Reconsideration of the anatomy of sling left pulmonary artery: the association of one form with bridging bronchus and imperforate anus. *Anatomic and diagnostic aspects. J Pediatr Surg*. 1988 Oct;23(10):892-8.
13. Bouros D1, Pare P, Panagou P, Tsintiris K, Siafakas N. The varied manifestation of pulmonary artery agenesis in adulthood. *Chest*. 1995 Sep;108(3):670-6.
14. Kutsche LM, Van Mierop LHS. Anomalous origin of a pulmonary artery from the ascending aorta: associated anomalies and pathogenesis. *Am J Cardiol* 1988;61:850-6
15. Kutsche LM, Van Mierop LH. Anomalous origin of a pulmonary artery from the ascending aorta: associated anomalies and pathogenesis. *Am J Cardiol* 1988;61:850-6.
16. Carretero J, Rissech M, Mortera C, Mayol J, Caffarena J, Prada F. Aortic origin of the left pulmonary artery in an infant with Fallot's

- tetralogy. *Rev Esp Cardiol* 2005;58:1124–1126.
17. Prifti, E., Bonacchi, M., Murzi, B., Crucean, A., Leacche, M., Bernabei, M., ... Vanini, V. (2004). Anomalous Origin of the Right Pulmonary Artery from the Ascending Aorta. *Journal of Cardiac Surgery*, 19(2), 103–112.
 18. Abu-Sulaiman RM, Hashmi A, McCrindle BW, Williams WG, Freedom RM. Anomalous origin of one pulmonary artery from the ascending aorta: 36 years' experience from one centre. *Cardiol Young*. 1998 Oct;8(4):449-54.
 19. Fontana GP, Effman EL, Sabiston DC Jr (1987) Origin of the right pulmonary artery from the ascending aorta. *Ann Surg* 206:102–113
 20. Zach M, Beitzke A, Singer H, Höfler H, Schellmann B (1979) The syndrome of absent pulmonary valve and ventricular septal defect – anatomical features and embryological implications. *Basic Res Cardiol* 74:54–68
 21. Stern, S. J., Wadekar, N., Mertens, L., Manlhiot, C., McCrindle, B. W., Jaeggi, E. T., & Nield, L. E. (2014). The impact of not having a ductus arteriosus on clinical outcomes in fetuses diagnosed with tetralogy of Fallot. *Cardiology in the Young*, 25(04), 684–692.
 22. Farkas A, Steiner M, Giles H, Miller K. Arterial tortuosity syndrome: An extremely rare disease presenting as a mimic of pulmonary sling. *Radiol Case Rep*. 2017 Dec 13;13(1):295-298.