Case **report**

FIRST TRIMESTER DIAGNOSIS OF ABSENT PULMONARY VALVE (APV): A CASE REPORT OF PRENATAL TREATMENT WITH A REVIEW OF LITERATURE AND DATA FROM THE POLISH NATIONAL REGISTRY OF FETAL CARDIAC PATHOLOGY

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Abstract

Absent of pulmonary valve syndrome is a rare congenital heart defect, which is diagnosed prenataly in 0,8% of fetuses with congenital heart defect based on the data from National Polish Registry Of Fetal Cardiac Anomalies.

We present a case of pregnat woman and fetus with that heart defect, which was detected in the 1st trimester and treated prenatally with digoxin, amnioreduction, tocolysis and steroids following by the cardiac sugery in the neonatal period. Despite an intensive therapy, the infant died on the 3rd month of age.

We belive that the main reason of poor outcome was premature delivery at the 35th week of gestation.

We present unique cardiac images proving the changing characterists of this type anomay since 1 st trimester.

Key words: pregnancy, prevention of sponatenous preterm birth, cervical assessment

INTRODUCTION

Absent pulmonary valve is a rare congenital heart defect that may be diagnosed prenatally but is typically associated with poor prognosis. This anomaly was found in 0.8% of fetuses with heart defects in the Polish National Registry of Fetal Cardiac Pathology (ORPKP) between the years 2004-2013, (www.orpkp.pl). It is less commonly seen nowadays after birth due to the decision to terminate the pregnancy after prenatal diagnosis[1,2,3,4]. We present a case of this anomaly provisionally diagnosed at 12 weeks' gestation.

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CASE PRESENTATION

33-year-old patient, G3P1 underwent ultrasound screening at 12 weeks' gestation which showed normal nuchal translucency (1,2 mm) and normal heart size but with an abnormal heart axis of 95 degrees. On pulsed Doppler, there was a reversal of flow at the ductus venosus (DV) and pulmonary valve. A two-vessel umbilical cord was identified. The patient declined both biochemical marker and diagnostic genetic testing and would not consider termination of the pregnancy. Fetal echocardiography (FECHO) at 16 weeks showed cardiomegaly, right> left chamber size disproportion, severe heart axis deviation (90 degrees), a malalignment type ventricular septal defect with an overriding aorta and significantly dilated main pulmonary artery and branches of the pulmonary arteries (5mm). No ductus arteriosus was identified. Doppler examination, showed holosystolic regurgitation of the tricuspid valve and turbulent, accelerated flow across the pulmonary annulus (150cm/s) with reverse flow in diastole. The diagnosis of Tetralogy of Fallot (ToF) with absent pulmonary valve (APV) was made. Flow velocities in both the umbilical artery and the middle cerebral artery were normal. The circulatory system was assessed at 8/10 points in the Cardiovascular Profile Score (CVPS)[5]. Nuchal fold was 3 mm. Amniotic fluid index (AFI) was normal.

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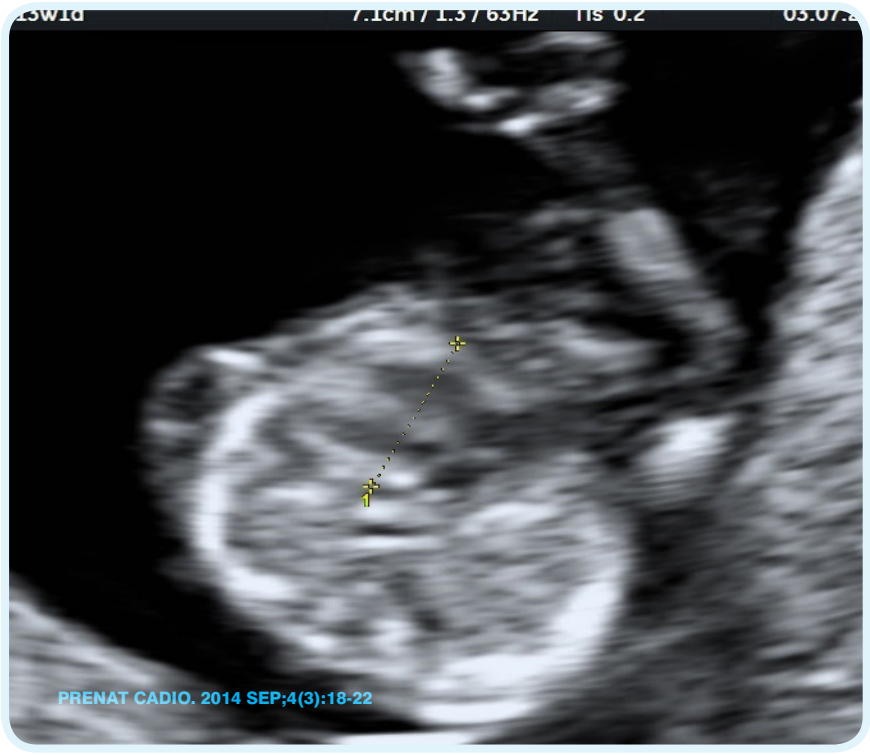

Figure 1. The four chamber view in 1st trimester, size of the heart 8mm.

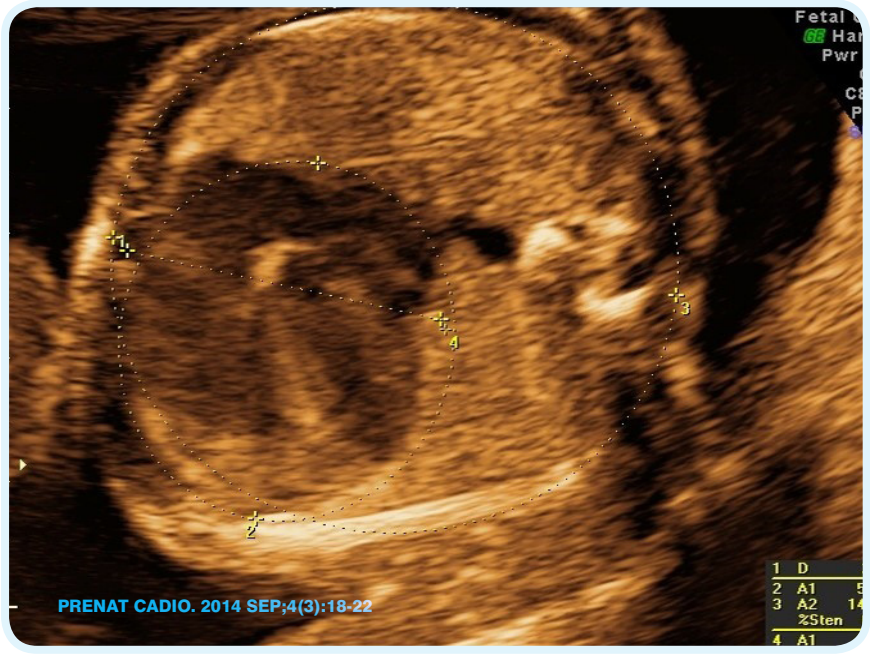

Figure 2. Fetal cardiomegaly at 22nd week of gestation and abnormal heart axis.

Parents received counseling from the fetal / pediatric cardiologist along with description of multi-stage heart surgery (in case of delivery at term) and potential complications. The patient was informed, relative to Polish law, that termination of pregnancy was possible.

The 22 week FECHO showed continued cardiomegaly, continued dilatation of the branch pulmonary arteries and increased main pulmonary artery velocity. The CVPS was set at 7 / 10 and AFI 16 cm. Transplacental digoxin treatment to prevent further cardiomegaly and in attempt to slow down further signs of circulatory insufficiency[6,7] was administered. At 25th week FECHO again showed cardiomegaly, with a double increase in the main and pulmonary artery branches diameter. The left lung appeared to be compressed by the heart. Pulmonary systolic velocity was 225 cm/s, diastolic reversal flow velocity was 200 cm/s. CVS= 9 points (Table 1).

Amnioreduction with tocolysis for decreasing AFI was performed and steroids were administered at 26 weeks. The condition of the fetus was good after amnioreduction, but in the following week, increasing cardiomegaly and dilatation of hepatic vessels were observed. Maternal hyperoxygenation test was performed at 34 weeks which showed normal pulmonary vascular reactivity.

Spontaneous birth occurred at 35 weeks' gestation following premature rupture of membranes. A female infant weighing 1970 g with Apgar scores of 5,6,6,8 at 1,3,5,10 minutes, respectively was delivered. Immediately after birth the newborn required intubation and mechanical ventilation and on the 2nd day was transferred in critical condition to the pediatric cardiology ward. In spite of intensive ventilation the child chronically manifested severe hypoxemia and hypercapnia. On day 30, a rescue heart surgery was performed: VSD was closed, pulmonary trunc was resected, the size of the proximal pulmonary arteries was reduced and the right ventricular outflow tract was reconstructed using a xenograft (Contegra). The distal pulmonary arteries were multiple and severely hypoplastic. After surgery the baby was 7 days on ECMO due to hypoxemia. Based on angiography and angio CT hypoplasia of left lung and left bronchus was confirmed, as well as severe hypoplasia of the distal pulmonary arteries. Artificial ventilation was continued, however despite intensive therapy the baby died in the fourth month of life.

DISCUSSION

According to Sauer[8] absent pulmonary valve (APV) for the first time described in 1847 by Chevers, constitutes about 0.9% of heart defects [2] and corresponds to the 0.8 % in the Polish National Registry of Fetal Cardiac Pathology (Table 3). This defect is characterized by the partial or complete absence of pulmonary valve leaflets. Various versions of this defect have been described. In all forms, the ring of the valve is narrowed and the pulmonary trunk

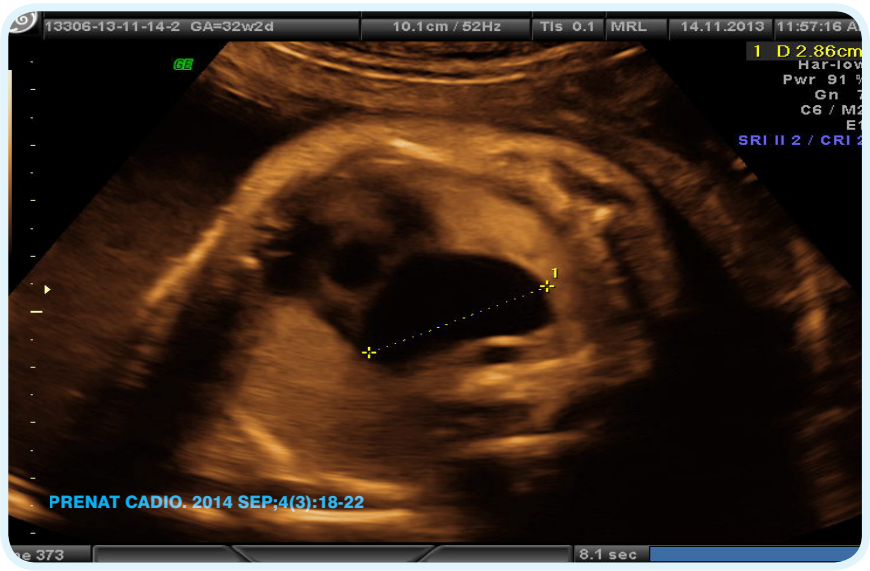

Figure 3. Dilatation of pulmonary branches up to 28 mm in fetus with APV at 32nd week of gestation

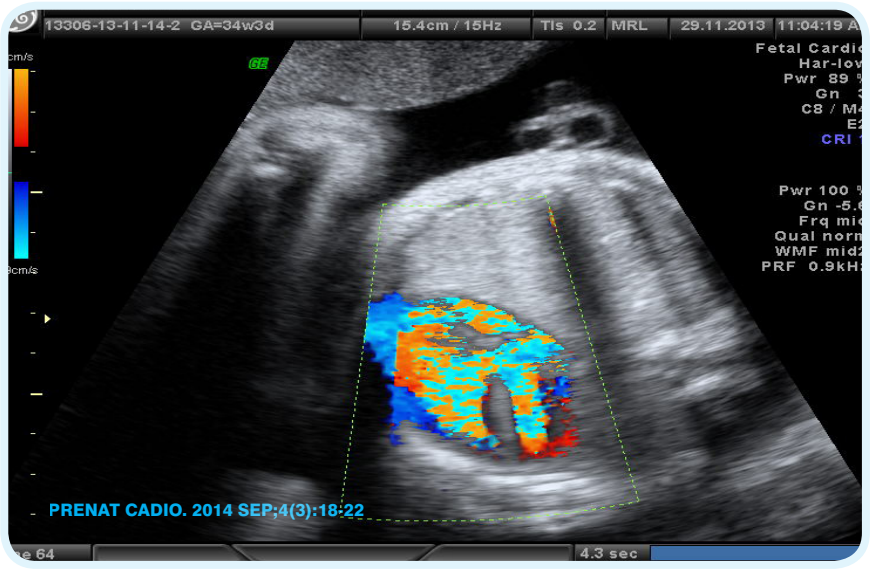

Figure 4. Fetal heart with APV at 34 week, heart size 37 mm, (power angio); 6 weeks on digoxin...compare the heart size in fig. 2 from 22nd week

and branches are aneurysmally dilated. This dilatation can exert pressure on the main stem bronchi and intrapulmonary branches already in fetal life which may result in necrotic changes in the lungs. APV most commonly occurs with tetralogy of Fallot (3 % of all ToF cases) and with intact ventricular septum[9]. APV with ToF may be associated with cardiomegaly, axis shift severely to the left or right (dextroposition). Agenesis of the ductus arteriosus has been implicated in the dilation of the pulmonary arteries. This version of APV is associated with chromosome 22q deletion in 20 to 25 % of affected fetuses[10]. Absent pulmonary valve with intact septum has been seen with tricuspid valve atresia and with double chambered right ventricle. The ductus arteriosus may be patent in this variant[11,12].

The etiology is unknown, however, association with genetic syndromes is common. APV with VSD (Fallot type) is linked to microdeletion of chromosome 22 (22q11.2)[10]. CATCH, a mutation in the *TBX1* gene which is responsible for the development of DG/VCFS, deletion of the long arm of chromosome 6. Some other cases of APV without VSD (non Fallot type) with deletion of the long arm of chromosome 18 have also been described.[13]

APV may be complicated by congestive heart failure, non-immunological hydrops fetalis, fetal hypotrophy and death in utero. The ORPKP shows more cases of APV diagnosed in utero than in live born newborns, due to termination of pregnancies and in utero demises (table 3).

GESTATIONAL AGE **PLACE OF EXAM** **DATE** **FETAL WEIGHT**	13 wks Kraków 3.VII	17 wks Kraków 5.VII 183g	22 wks Kraków 5.IX 422g	**25 wks** **Łódź** **11.IX** **527 g**	25wks Kraków 26.IX 655g	**27wks** **Łódź** **14.X** **1033g**	32 wks Łódź 14.XI 1590g	34 wks Łódź 29.XI 2297g
Ha/Ca **AP mm**	0,27 8	0,34 16	0,37 22	0,3 **42**	0,37 33	0,4 34	0,4 44	0,3 37
Disproportion RV>>LV	no	+	+	+	+	+	+	+
Heart axis		90	90	90	90	90		90
PV (mm)		5	6	3	6	4	3	3
RPA & LPA (mm)	No dilatation	5	6-7	13	9-12	16 - 23		
PA V max PA cm/s	30	150	150	270	225	240	250	250
PR cm/s	90	+	+		200	200		200
CVS		8	7	7	9	9	8	9
AFI (cm)	normal	normal	16	**35**	14	**27***	**24**	27

Table 1: Data from echocardiographic monitoring of the fetus with absent pulmonary valve in Kraków and Łódź, last exam at 34 wks and 10 days later premature rapture of membranes and spontaneous delivery in Kraków

The first prenatal diagnosis of APV was published by Fouron in 1989 [14]. The 4-chamber view shows cardiomegaly and aneurysmal dilatation of the pulmonary trunk and its branches (Mickey Mouse sign). Growth restriction, polyhydramnios and signs of hydrops fetalis may be present after the 2nd trimester. The leaflets of the pulmonary valve are difficult to visualize. The Doppler flow patterns in the

Author	Razavi[11]	Volpe P.[1]	Galindo A.[8]	Hajdu J.[9]	Wertaschnigg[12]
YEAR	2003	2004	2006	2007	2012
DATA FROM	1988-2000			1993-2005	2000-2010
NR OF CASES	20	21	14	10	10
DGN (WKS)	23 (18-36)	24 (18-31)	28 (16-38)	23 (18-33)	24 (20-37)
EXTRACARDIAC MALFORMATIONS		9 (42,8%) Tris 13, 18, 21		3 (30%)	7 (70%)
GENETIC SYNDROMES	22%	22q11 - 68%	22 q 11 3 (21%)		22q11 – 6 Del6q - 1
TERMINATION OF PREGNANCY	6 (30%)	9 (43%)	5 (35%)	6 (60%)	3 (30%)
DEATH IN UTERO	3 (15%)	3 (14%)	1 (7%)	2 (20%)	1 (10%)
LIVE BORN	11	9	8	2	5
DEATH IN 1st MONTH	5 (25%)	5 (55%)	5 (62%)	1 (50%)	1 (10%)
DEATH AFTER 1 MONTH	3 (15%)		1 (12,5%)		1 (10%)
SURVIVORS AFTER SURGERY	3/20 (15%)	3/21(14%)	2/14(14%)	1/10(10%)	4 /10 (40%)
PROGNOSIS	Bad	Bad	Bad	Bad	Better !!!

Table 2: Selected data from literature

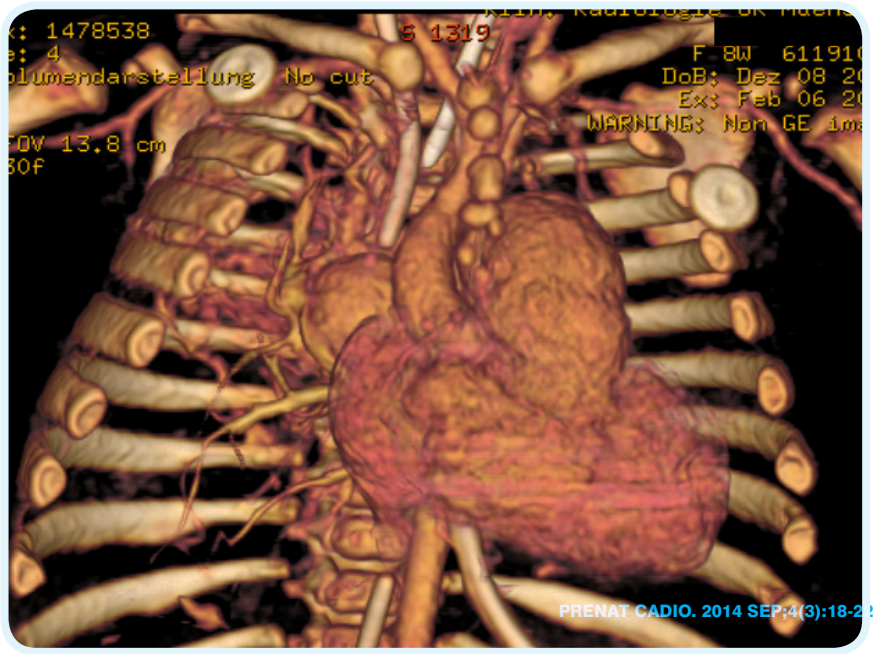

Figure 5. Angio CT beforfe cardiac surgery

right ventricular outflow display a bidirectional waveform and the sound of sawing wood.

In our case, the observed evolutionary changes of the heart were identified at the 12 week ultrasound study. The main pulmonary artery and its branches were enlarged and cardiomegaly increased with each examination. The velocities of pulmonic stenosis and regurgitation also accelerated over the course of the pregnancy, similar to Becker's, et al.observations.[15]

In this case, digoxin transplacental treatment was implemented at 23 weeks gestation based upon the fetal anti-congestive heart failure protocols at our institution. We observed that the cardiomegaly stabilized and returned to normal (Table 3). We believe that this therapy has not yet been reported in cases of APV.

The presence of regurgitation of the pulmonary valve, heart axis deviation and reversal in the DV at 12 weeks led to the diagnosis of TOF with ADV which was confirmed at 17 weeks by FECHO. Two previous publications described APV in the 1st trimester: regurgitation of the pulmonary artery valve at 13 (5/7) weeks but the diagnosis of TOF, later discovered at 21(5/7) weeks, was missed. Berg[16] reported that 3 out 5 fetuses with reversed umbilical artery flow had ToF with APV and aneuploidy (2=T18, 1=T13). Galindo, at al.[3] described APV at 16 weeks because of the reversed flow through ductus venosus and a slight regurgitation of the pulmonary trunk identified at 13 weeks. The data from our observations and a review of the literature suggests that, in the 1st trimester, APV manifests itself primarily by pulmonary valve regurgitation, heart axis deviation and diastolic flow in the umbilical artery. Our observations confirm the evolutionary character of TOF with APV and the presence of cardiomegaly which appears relatively late due to the gradual distention of pulmonary arteries and pulmonary valve regurgitation.

The prognosis for a newborn with this type of heart defect is mostly poor[1,2,3,4]. The survival rate varies between 25-33% in published literature (table 2), 30-60% of pregnancies are terminated and 90% when the diagnosis is made before the 24th week of pregnancy. *In utero* demise

1	Number of fetuses with selected anomaly	40
2	Mean number of US exams before detection of anomaly	2
3	Mean gestational age of fetuses at the time of anomaly detection (based on last menstrual period)	25
4	Mean gestational age at the time of anomaly detection at 25th week of gestation	25
5	In how many fetuses the follow-up was filed	13 (31%)
7	Mean birth weight of neonates	1600 g
8	Death after cardiac surgery	67%

Table 3: The selected data from National Registry of Cardiac Anomalies (www.orpkp.pl) related to Absent Pulmonary Valve Syndrome

occurs in 7-20% of cases with 25-62% deaths in the first month of life. In contrast, Wertaschnigg presented a different set of statistics, stating that survival rate of newborns can be as high as 86%[17]. Delivery before the 38th week is currently seen as a risk factor for heart surgery, irrespective of the type of heart defect [18].

CONCLUSIONS

1. Pulmonary valve regurgitation seen by ultrasound in the 1st trimester suggested a diagnosis of absent pulmonary valve leaflet syndrome and warranted targeted fetal echocardiography.

2. Dilatation of the main pulmonary artery and branches in TOF with APV was progressive during the course of pregnancy.

3. Absent pulmonary valve leaflet syndrome was an evolving defect that led to plyhydramnios to polyhydramnios that was amenable to transplacental anticongestive therapy.

References:

1. *Razavi RS, Sharland GK, Simpson JM. Prenatal diagnosis by echocardiogram and outcome of absent pulmonary valve syndrome. Am J Cardiol. 2003;91(4):429-32.*

2. *Volpe P, Paladini D, Marasini M, Buonadonna AL, Russo MG, Caruso G, Marzullo A, Arciprete P, Martinelli P, Gentile M. Characteristics, associations and outcome of absent pulmonary valve syndrome in the fetus. Ultrasound Obstet Gynecol. 2004;24(6):623-8*

3. *Galindo A, Gutiérrez-Larraya F, Martínez JM, Del Rio M, Grañeras A, Velasco JM, Puerto B, Gratacos E. Prenatal diagnosis and outcome for fetuses with congenital absence of the pulmonary valve. Ultrasound Obstet Gynecol. 2006;28(1):32-9.*

4. *Hajdú J, Pete B, Harmath A, Beke A, Papp C, Szigeti Z, Papp Z. Congenitally absent pulmonary valve--analysis of ten prenatally diagnosed cases and review of the literature. Orv Hetil. 2007;148(33):1557-61.*

5. *Huhta James C, Paul James J. Doppler in Fetal Heart Failure. Part I. Prenat Cardio. 2011;1(2):4-8.*

6. *Respondek-Liberska M, Wilczyński J, Maroszyńska I, Sysa A, Moll J, Moll J. Effective transplacental therapy in fetal cardiomegaly to prevent lung hypoplasia-case report. Ginekol Pol 2007;78(7):565-9*

7. *Sliwa J, Respondek-Liberska M, Maroszyńska I, Krasomski G. Ebstein's malformation in the fetus with cardiomegaly. To treat or to observe?--a case report]. Ginekol Pol. 2010;81(2):135-9.*

8. *Sauer U. Absence of the pulmonary valve. Orphanet Encyklopedia. December 2003.http://www.orpha.net/patho/GB/uk-AbsPulmoValve.pdf*

9. *Volpe P, De Robertis V. Absent pulmonary valve syndrome. Visual Encyclopedia for Ultrasound in Obstetrics and Gynecology (VISUOG)*

10. *Sleurs E, De Catte L, Benatar A. Prenatal diagnosis of absent pulmonary valve syndrome in association with 22q11 deletion. J Ultrasound Med 2004 23:417–422*

11. *Litovsky S, Choy M, Park J, et al. Absent pulmonary valve with tricuspid atresia or severe tricuspid stenosis: report of three cases and review of the literature. Pediatr Dev Pathol 2000 3: 353–366.*

12. *Lato K, Gembruch U, Geipel A, et al. Tricuspid atresia with absent pulmonary valve and intact ventricular septum: intrauterine course and outcome of an unusual congenital heart defect. Ultrasound Obstet Gynecol 2010 35: 243–245.*

13. *Versacci P, Digilio MC, Sauer U, Dallapiccola B, Marino B. Absent pulmonary valve with intact ventricular septum and patent ductus arteriosus: a specific cardiac phenotype associated with deletion 18q syndrome. Am J Med Genet A. 2005;138A(2):185-6. 4.*

14. *Fouron JC, Sahn DJ, Bender R, Block R, Schneider H, Fromberger P, Hagen-Ansert S, Daily PO. Prenatal diagnosis and circulatory characteristics in tetralogy of Fallot with absent pulmonary valve. Am J Cardiol. 1989; 64(8):547-9.*

15. *Becker R, Schmitz L, Guschmann M, Wegner RD, Stiemer B, Entezami M. Prenatal diagnosis of familial absent pulmonary valve syndrome: case report and review of the literature. Ultrasound Obstet Gynecol. 2001;17(3):263-7*

16. *Berg C, Thomsen Y, Geipel A, Germer U, Gembruch U. Reversed end-diastolic flow in the umbilical artery at 10-14 weeks of gestation is associated with absent pulmonary valve syndrome. Ultrasound Obstet Gynecol. 2007; 30(3):254-8.*

17. *Wertaschnigg D, Jaeggi M, Chitayat D, Shannon P, Ryan G, Thompson M, Yoo SJ, Jaeggi E. Prenatal diagnosis and outcome of absent pulmonary valve syndrome: contemporary single-center experience and review of the literature. Ultrasound Obstet Gynecol. 2013; 41(2):162-7.*

18. *Costello JM, Pasquali SK, Jacobs JP, He X, Hill KD, Cooper DS, Backer CL, Jacobs ML. Gestational age at birth and outcomes after neonatal cardiac surgery: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. Circulation. 2014; 129(24):2511-7.*