

Prostaglandin E1 on Infradiaphragmatic Type of Total Anomalous Pulmonary Venous Connection – a Case Report

Catalin CIRSTOVEANU, MD^{a,e}; Eliza CİNTEZA, MD, PhD^{b,e}; Veronica MARCU, MD^c;
Mihaela BIZUBAC, MD^a; Alina BALOMIR, MD^a; Ileana BARASCU, MD^a;
Mariana COMAN, MD, PhD^c; Mihaela BALGRADEAN, MD, PhD^{d,e}

^aNeonatal Intensive Care Unit, “MS Curie” Emergency Children’s Hospital,
Bucharest, Romania

^bPediatric Cardiology Department, “MS Curie” Emergency Children’s Hospital,
Bucharest, Romania

^cRadiology Department, “MS Curie” Emergency Children’s Hospital,
Bucharest, Romania

^d2nd Pediatric Department, “MS Curie” Emergency Children’s Hospital,
Bucharest, Romania

^eUniversity of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania

ABSTRACT

We present the case of a newborn with severe pulmonary hypertension, diagnosed with infradiaphragmatic type of total anomalous pulmonary venous connection (TAPVC). The onset was in the first 10 days of life. Diagnosis was made by echocardiography and AngioCT. The pulmonary venous collector was surgically implanted into the left atrium in Germany, but the next month after surgery he developed cardiopulmonary insufficiency and died several days later. We would like to emphasize the importance of prostaglandin E1 administration in this particular case of infradiaphragmatic type of TAPVC and its usefulness in patient’s stabilization until surgery. The prognosis in TAPVC, infradiaphragmatic type, is poor and is related mainly to the existence of pulmonary venous obstruction.

Address for correspondence:

Eliza Cinteza, Pediatric Cardiology Department, “MS Curie” Emergency Children’s Hospital, 20, Constantin Brancoveanu Boulevard, 4th District, Bucharest, Romania
E-mail: elizacinteza@yahoo.com

Article received on the 21st February 2012. Article accepted on the 8th May 2012.

INTRODUCTION

Total anomalous pulmonary venous connection (TAPVC) is a very rare congenital heart disease (CHD), reported in 1-2.6% of all congenital heart disease (1-3). The onset can be abrupt with cardiopulmonary insufficiency or mild, and it has no specific clinical picture. An important step in diagnosis of this entity is to differentiate it from pulmonary disease in a newborn or from persistent fetal circulation with pulmonary hypertension, and, of course, from other CHD. There are three sites of anomalous drainage: supracardiac (50% of the cases), cardiac and infracardiac (25% each). Infracardiac TAPVR is also called infradiaphragmatic. Defects of mixed type are also possible. Evaluation of cardiac structures is very important because in 30% of the cases some associated anomalies may occur.

In many cases of TAPVC, the four pulmonary veins (PV) join together behind the left atrium, where they form a collector. This collector can drain into the right atrium directly, by way of the innominate vein into the superior vena cava (SVC), into the coronary sinus (CS), or through the diaphragm to the venous structures of the abdomen. In the infradiaphragmatic type, the four veins form a descending vertical collector that crosses the diaphragm in front of the esophagus, running parallel to the inferior vena cava (IVC), and drains into the hepatic-portal system (hepatic veins, portal vein or *ductus venosus*).

The infradiaphragmatic type is associated frequently with pulmonary hypertension due to pulmonary venous obstruction. The presence of an atrial septal defect or patent foramen

ovale is extremely important to maintain systemic flow. Pulmonary venous obstruction may occur in any of the forms but is almost always present in the infradiaphragmatic type. Not long ago, administration of prostaglandin E1 in TAPVC was regarded with great reluctance, sometimes even forbidden. Now, there are specific indications. In obstructive forms, the vasodilator effects of prostaglandin E1 may be the benefit or the detriment of the patient. Vasodilating action of prostaglandin E1 includes *ducti arteriosus* and *venosus* and systemic or pulmonary vascular muscles (4). □

CASE REPORT

A male newborn, 10 days old, born at 37 weeks by Cesarean section and weighing 3220g at birth, was admitted in our hospital with respiratory failure and persistent generalized cyanosis.

Clinical picture on admission: weight 3300 g, generalized cyanosis, respiratory distress, receiving high-frequency mechanical ventilation, oxygen saturation 89-90% with FiO2 1.0 and inhaled nitric administration, no pulmonary rales, heart rate 127 beats/min, grade-2/6 left parasternal systolic cardiac murmur, BP 60/45 mmHg, enlarged abdomen with hepatosplenomegaly, normal diuresis.

Laboratory results: Hb 13 g/dl , Ht 36.9%, platelet count 419,000/mm³, WBC 6,520/mm³, neutrophils 50%, basophils 1%, lymphocytes 41%, monocytes 5%, eosinophils 1%. Creatine kinase 111 U/L, AST 42 U/L, ALT 14 U/L, GGT 89 U/L, serum urea 12 mg/dl, serum creatinine 0.4 mg/dl, serum total bilirubin 5.3 mg/dl, CRP 0.20 mg/l, procalcitonin <0.5 µg/l.

Chest x-rays showed a normal cardiothoracic ratio, normal pulmonary transparency with increased interstitial markings, and a discrete right basal opacity.

Echocardiography showed situs solitus, levocardia, enlarged right atrium (RA) and right ventricle (RV) (16.5 mm), small left atrium (LA), small left ventricle (LV) (9 mm) (Figure 1), pulmonary artery (PA) 11 mm, aorta (Ao) 7 mm, atrioventricular and ventriculoarterial concordant connections, small patent foramen ovale patent (PFO) of 2.5 mm with right-to-left shunt, intact interventricular septum (IVS) with paradoxical motion, and patent *ductus arteriosus* (PDA). In the RA area, there were 3 vessels, all apparently connected to the RA (Figure 2). No

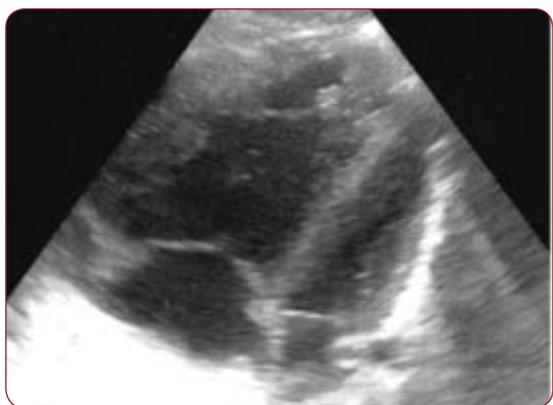


FIGURE 1. Four-chamber view with enlarged right atrium and ventricle and small left atrium and ventricle

pulmonary veins were seen. Also noted were moderate tricuspid and pulmonary regurgitation with normal valve morphology. The velocity of flow in the descending aorta was 0.6 m/sec, and flow velocity in the pulmonary artery was normal. Small pericardial and pleural effusions were present.

The hepatic venous system was dilated and had high resistance flow, suggesting patent ductus venosus (Figure 3).

Prostaglandin E1 was administered, 0.005-0.02 $\mu\text{g}/\text{kg}\cdot\text{min}$, with good response. The inhaled nitric oxide was stopped, and the oxygen saturation remained between 85 and 95% with FiO_2 0.8-1.0. Dopamine (15 $\mu\text{g}/\text{kg}/\text{min}$), furosemide, piperacillin-tazobactam, and gentamicin were administered.

Angiographic computerized tomography (angioCT) examination revealed total anomalous pulmonary venous connection with all four pulmonary veins draining into a common collector vein which communicated with the portal circulation below the diaphragm (Figure 4, Figure 5).

The child was transferred and operated at the Herz Zentrum in Bad Oeynhausen, Germany.

Two weeks after discharge from the Herz Zentrum, he presented with fever (38.6C), cough, increased respiratory effort, and anorexia, and he was admitted to "M.S Curie" Emergency Children's Hospital. Echocardiography showed enlarged RA and RV, small left chambers, hypertrophy of the RV, and turbulent flow in the collector vein. The flow velocity in the collector vein was 2.6 m/sec. The flow velocities in the great arteries were normal, and there was minimal pulmonary regurgitation.

He was diagnosed with right lobar pneumonia and cardiac failure and treated accordingly, but he died. The pathological examination confirmed the pneumonia and, regarding the heart, one of the pulmonary veins was occluded and another one was severe stenotic. These appeared above the collector anastomosis and at distance from surgical anastomosis. □

DISCUSSION

Since 1798 when Wilson described TAPVC as a "monstrous formation of the heart," numerous variants have been described (2,5). The incidence of this condition varies from 1-2.6% among children with CHD (2). The



FIGURE 2. Three vessels are seen connected to the right atrium

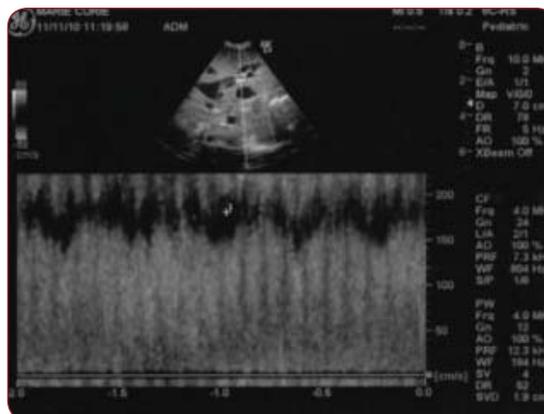


FIGURE 3. High resistance flow in the liver at the connection between the vein collector and the portal system, suggesting patent ductus venosus



FIGURE 4. Angio CT examination with coronal MIP reformat and 3D reconstruction. Infradiaphragmatic type of total anomalous pulmonary venous connection. The four pulmonary veins join together and drain downwards, connecting to the liver's portal vein system

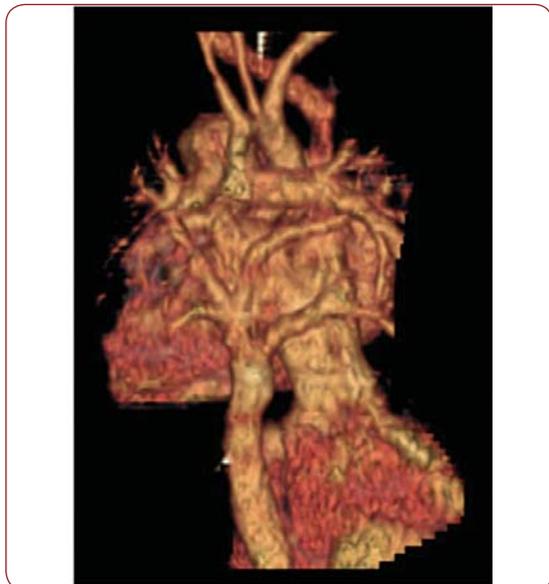


FIGURE 5. Angio CT examination. Infradiaphragmatic type of total anomalous pulmonary venous connection (reconstruction)

mortality in the first year of life is very high, over 80 % in the absence of surgery and less than 30% with surgery. 19% before 1995 to 5% after 1995 mortality was reported in a study on TAPVC (6). Mortality is higher in the infradiaphragmatic type due to some particularities related to pulmonary venous obstruction and pulmonary hypertension. Obstruction may result from connection of the collector vein to the portal circulation (resistance to blood flow), or at the ductus venosus, which usually suffers constriction postnatally, or from the presence of a long and narrow descendent collector vein or from compression as the collector passes through the diaphragm hiatus. A small ASD or PFO and intrinsic or extrinsic narrowing of the pulmonary veins are risk factors for obstructive pulmonary vascular disease (7) and are predictors for long-term survival.

In some cases, autosomal dominant inheritance has been suspected, but the number of families in whom this has been suspected is very few – 11 families (2). Exposure in the first three months of pregnancy to painting or paint stripper, lead, and pesticides has been associated with TAPVC in the Baltimore – Washington Infant Study (8). Syndromes like Holt-Oram, Klippel-Feil, and phocomelia may be associated with TAPVC (2).

TAPVC is explained by atresia of the common pulmonary vein while a communication between the venous splanchnic and pulmonary plexus still exists. Collaterals persist in the

primitive form, and their presence can generate TAPVC through abnormal myocardialization and smooth muscle cell formation (9).

The case presented was an infradiaphragmatic type of TAPVC. The patient presented with respiratory failure and persistent generalized cyanosis. He had pulmonary hypertension and small left chambers. The suspicion of infradiaphragmatic type of TAPVC was raised by echocardiography and established by angioCT. Associated PFO and PDA were present.

Generally with TAPVC, echocardiography shows absence of pulmonary veins (PVs) connecting to the LA, the LA is very small, and there is a right-to-left shunt at the level of the ostium secundum (atrial septum defect or patent foramen ovale). It is mandatory to find the connection of the PVs to the systemic circulation (10). Color Doppler is very helpful in evaluating the direction and velocity of flow in abnormal structures (11). Indirect echocardiographic findings are important, such as right-to-left shunt at the atrial level or paradoxical motion of the interventricular septum. The connection of the PVs to the superior vena cava, coronary sinus, or inferior vena cava is associated with dilatation of these structures (10). The RA, RV, and PA are enlarged. The anterior RV wall is thickened, and the septum is immobile (flat) or moves paradoxically (10-12). Transesophageal echocardiography can be used for visualization of the posterior PVs and their sites of drainage (10). Partially abnormal pulmonary venous connection (PAPVC) must be differentiated from TAPVC because it may have similar echocardiographic features (liquid dark space posterior to the left atrium, abnormal vertical vein, dilatation of the superior vena cava, dilatation of the coronary sinus, abnormal blood flow signal in the right atrium) (13). Postoperatively, flow velocity above 2 m/sec in the PVs, in the collector, or at the anastomosis level suggests obstruction (10).

We achieved stabilization of the patient initially when we started the prostaglandin E1 administration. Prostaglandin E1 has special indication in TAPVC: in newborn with obstructive total anomalous pulmonary venous connection, all types, for patency of PDA, but its effects in the complex circulation must be strictly controlled (3,4) and in the infradiaphragmatic type of TAPVC for opening the *ductus venosus* (4,14,15). Prostaglandin E1 favored a dilation of both *ducti arteriosus* and *venosus*. In the

PDA, the shunt was from right to the left. The dilatation was followed by decompression of the pulmonary vasculature. This resulted in increased oxygenation of the blood by reducing ventilation-perfusion mismatch. By increasing the shunt from right to left at the PDA level, we also increased the systemic blood flow and therefore systemic oxygenation but only for systemic circulation starting at the aortic arch and descending aorta level. The flux in coronary arteries remained reduced (small PFO). At the *ductus venosus* level, prostaglandin E1 administration diminished pulmonary venous obstruction.

Our patient presented pulmonary hypertension. Pulmonary hypertension in TAPVC with pulmonary venous obstruction is mixed: arterial, by increased pulmonary blood flow, and venous due to pulmonary venous stasis. Sildenafil was not considered due to mixed type of pulmonary hypertension and to residual postoperative pulmonary venous stenosis. In our case the pulmonary venous stenosis caused by intimal proliferation was progressive until obstruction followed in one of the veins and severe stenosis in another.

Early- and long-term prognosis depends on the existence of pulmonary venous obstruction and the patency of the anastomosis between the venous pulmonary collector and the left atrium. Associated anomalies, especially single ventricle and heterotaxy also influence prognosis (6, 16). Some data suggest that pulmonary venous obstruction develops in the first 6 months following primary repair (17). Late death is mostly associated with progressive intrapulmonary vein fibrosis (fibrous intimal hy-

perplasia associated with some medial hypertrophy) in the first year following surgery (17, 18). Early presentation (<6 months) from intervention and persistence of pulmonary hypertension after reintervention are risk factors for death (17). In a study on TAPVC, the survival at 15 years after repair was 84% and freedom from late death or reintervention was 85% (6). Multiple surgical reintervention or stenting interventional procedures are associated with a higher mortality and a recurrence of the restenosis (19). The sutureless repair technique (1996) and resection of the pulmonary vein scar tissue are very important and provides better midterm results (16). In some centers, heart-lung transplantation is a solution for PV stenosis. □

CONCLUSION

This case illustrates a rare congenital heart disease, an infradiaphragmatic type of total anomalous pulmonary venous connection with drainage into the portal system, which was accompanied by pulmonary venous obstruction. In this case, the patient died despite surgery. Prostaglandin E1 together with mechanical ventilation and nitric oxide administration were helpful in initial stabilization of the patient. Prostaglandin E1 has special indication in the infradiaphragmatic type of total anomalous pulmonary venous connection to open not only the ductus arteriosus but also the ductus venosus. Pulmonary vein stenosis and occlusion by intimal proliferation have dictated the evolution of the patient to cardiopulmonary insufficiency and exitus.

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