Journal of Cardiology Cases 17 (2018) 159–162

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Case Report

# The histological findings in transposition of the great artery with severe persistent pulmonary hypertension of the newborn

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ARTICLE INFO

*Article history:*
Received 14 April 2017
Received in revised form 1 December 2017
Accepted 4 January 2018

*Keywords:*
Transposition of the great arteries/intact ventricular septum
Persistent pulmonary hypertension of the newborn
Histological findings

ABSTRACT

The combination of persistent pulmonary hypertension of the newborn (PPHN) and transposition of the great arteries (TGA) has serious impacts on treatment and prognosis, often with adverse outcomes. We report the case of a male full-term newborn with TGA with intact ventricular septum and severe PPHN who died 2 h after birth; further, we examined his vascular histology. On autopsy, lung histology showed mild fibrous hypertrophy in the intima and moderate medial hypertrophy of the minimal pulmonary artery. Hypoplasia of the pulmonary artery was not detected. Pulmonary congestion was detected and pneumatization was poor. Debris was present in the alveoli. Hemosiderin deposition was detected, suggesting prenatal hemostasis or hemorrhage. Severe PPHN may have occurred because of pulmonary arterial spasm accompanying pulmonary congestion which had been in the fetal stage. A wide range of lesions can be present in the pulmonary vascular bed in TGA. The pathologies of pulmonary vascular tissues with TGA and PPHN are not uniform.

<**Learning objective:** Neonates with transposition of the great arteries with intact ventricular septum (TGA/IVS) may have severe pulmonary hypertension. The progression of pulmonary vascular disease in TGA/IVS is unpredictable; therefore, the delivery of a fetus diagnosed with TGA/IVS should be performed at an institution in which catheterization and balloon atrial septostomy can be performed.>



## Introduction

Transposition of the great arteries (TGA) is one of the most common cyanotic congenital heart diseases (CHDs) and accounts for 5–7% of all patients with CHD [1]. TGA is reportedly associated with persistent pulmonary hypertension of the newborn (PPHN) in 1–3% of cases [1]. The combination of PPHN and TGA has serious implications for treatment and prognosis [1,2], often with fatal outcomes. Data concerning the incidence and prognosis of the combination of TGA and PPHN are limited. In infants aged <6 months with TGA, an intact ventricular septum (TGA/IVS), and a closed patent ductus arteriosus (PDA), pulmonary vascular changes of more than Heath-Edwards grade 2 are unusual [3]. Grade 2 lesions have been reported more often in infants aged <6 months [3]. PPHN results from failure of the pulmonary vasculature to relax at birth. We report a case of a newborn with TGA/IVS and severe PPHN who died at 2 h after birth and examine the patient's vascular histology.

## Case report

A 37-year-old woman was referred to us at 30 weeks' gestation due to inadequate visualization of three vessels at another institution. Detailed scanning demonstrated normal growth, no anomalies, and a normal four-chamber view; however, the great vessels were inadequately evaluated. The patient returned at 32 weeks' gestation for targeted fetal echocardiography. Two-dimensional (2D) and color Doppler ultrasound revealed TGA (with D-loop). A patent foramen ovale (PFO) was detected but was not restrictive or aneurysmal (Fig. 1A). We performed 2D ultrasound on the day before delivery, but the shunt through the PFO was only right-to-left, and the flow through the PDA was pulsatile, with a flow rate of 0.9 m/s.

The patient (a male) was born in our hospital at 37 weeks' gestation through cesarean section (performed due to the mother's

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https://doi.org/10.1016/j.jccase.2018.01.003
1878-5409/

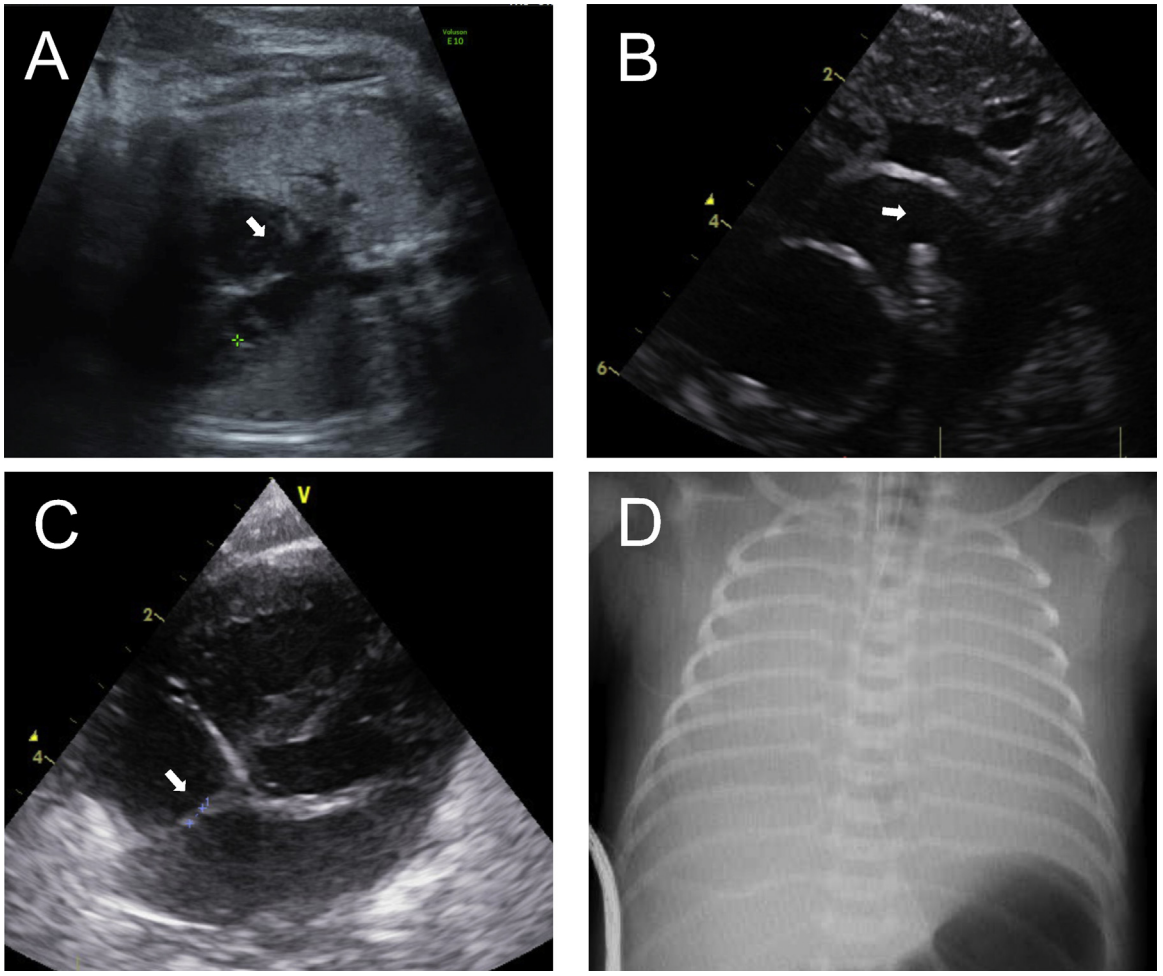


**Fig. 1.** (A) Transabdominal ultrasound at 37 weeks' gestation (the day before delivery). PFO (arrow) was not restrictive or aneurysmal. Color Doppler detected only right-to-left flow. (B, C) Postnatal echocardiography. (B) The PDA was not closed and not constricted. The diameter of the PDA was 3.3 mm. The flow was mainly right-to-left. (C) PFO was only a small orifice on imaging (arrow) and Doppler. (D) There was hardly any lung pneumatization on chest X-ray, suggesting respiratory problems. PDA, patent ductus arteriosus; PFO, patent foramen ovale.

prior history of cesarean section) with a birth weight of 3081 g and Apgar scores of 4 and 5. The amniotic fluid was clean. There were no findings of premature placental abruption. He was intubated soon after birth because of increasing respiratory distress and cyanosis. Despite a high ventilatory setting, he remained severely hypoxic and acidotic.

On the neonate's arrival at the neonatal intensive care unit, severe cyanosis was observed with a preductal oxygen saturation ($SpO_2$) of 50% and a postductal $SpO_2$ of 60%. Owing to severe persistent hypoxemia, progressive signs of end-organ deterioration (lactate 20 mmol/L) and severe acidosis (pH 6.425; $pCO_2$, 139 mmHg; BE, −27.5 mmol/l) persisted. Intravenous infusion of prostaglandin E1 was initiated to maintain ductal patency. Postnatal echocardiography confirmed prenatal findings, but a restrictive PFO and the flow at the ductal level were mainly right-to-left (Fig. 1B and C), suggesting elevated pulmonary vascular resistance. Chest X-ray hardly revealed any lung pneumatization, suggesting respiratory problems (Fig. 1D). After initial medical treatment, the patient remained severely hypoxemic despite mechanical ventilation, 100% inspired oxygen, moderate hyperventilation, inhaled nitric oxide therapy (30 ppm), inotropic support with dopamine, and volume expansion. The neonate's $SpO_2$ worsened gradually, with preductal $SpO_2$ as low as 30% and postductal $SpO_2$ as low as 40% at 1.5 h of birth. Sinus bradycardia and ventricular dysfunction gradually progressed, and the neonate suffered cardiac arrest and died while we planned and prepared for balloon atrial septostomy (BAS).

At autopsy, airway abnormality was not detected macroscopically. Lung histology showed mild fibrous hypertrophy in the intima and moderate medial hypertrophy of the pulmonary artery (Heath-Edwards grade 3) but hypoplasia of the pulmonary artery was not detected. In the pulmonary vein system, characteristic findings of pulmonary vein obstruction, such as intimal hyperplasia and media thickening, were not detected. Pulmonary congestion was detected and pneumatization was poor. Debris was present in the alveoli. Hemosiderin deposition was detected, suggesting prenatal hemostasis or hemorrhage. Anatomical abnormalities, such as alveolar capillary dysplasia, which is observed in PPHN, were not observed (Fig. 2).

## Discussion

PPHN affects 0.4–6.8 per 10,000 live births and is a common cause of hypoxia in neonates, with a mortality rate of 10–50% [4,5]. The combination of TGA/IVS and PPHN early in life is often fatal [1,2,4–6]. The mechanism of TGA/IVS complicated with PPHN is not well described and is complicated. There is a general consensus that effective pulmonary blood flow decreases after