Cardiology in the Young

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Effective control of refractory pulmonary hypertension with iloprost inhalation in an infant with congenital absence of the right pulmonary artery: a case report

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Brief Report

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Abstract

Unilateral absence of the pulmonary artery is a rare congenital cardiovascular anomaly that can lead to pulmonary hypertension and poor outcomes. We report the case of a 1-month-old infant with isolated unilateral absence of the pulmonary artery and severe pulmonary hypertension on the right and left sides, respectively. The patient was unresponsive to multiple medications for pulmonary hypertension, and surgical revascularisation was unfeasible. However, iloprost inhalation was effective.

Case report

A 1-month-old female infant presented to the emergency department with poor appetite and non-bilious projectile emesis for 3 days. She had prior histories of neonatal jaundice and glucose-6-phosphate dehydrogenase deficiency. She weighed 4.2 kg, which placed her in the 50th percentile for her age.

On admission, occasional episodes of shortness of breath and cyanosis were observed. Chest radiography revealed increased heart size. Transthoracic echocardiography revealed right ventricular hypertrophy and dilation (Fig. 1*a*), severe pulmonary hypertension, severe tricuspid regurgitation with a pressure gradient of 86 mmHg (Fig. 1*b*), and an absent right pulmonary artery. CT angiography confirmed right pulmonary artery absence without lung hypoplasia (Fig. 1*c*). Electrocardiography revealed a sinus rhythm of 130 BPM and right ventricular hypertrophy with a strain pattern (Fig. 1*d*). All laboratory test results were within the normal range, except for an elevated N-terminal prohormone of brain natriuretic peptide level of 23881.5 pg/mL.

Intubation and mechanical ventilation were initiated to manage severe pulmonary hypertension and impending respiratory failure. Sildenafil, bosentan, and nitric oxide inhalation for pulmonary hypertension were further performed without benefit. Nitric oxide inhalation was then discontinued owing to a poor response. The worsening of left lung infiltration, believed to be caused by bacterial infections, prompted the administration of empirical antibiotics. Severe hypoxaemia (partial pressure of oxygen, 40–60 mmHg; fraction of inspired oxygen, 100%), worsening of pulmonary hypertension, and severe tricuspid regurgitation with a pressure gradient of up to 120 mmHg during lung infection were observed. Iloprost inhalation was administered as a concomitant therapy for pulmonary hypertension. During the treatment, the patient's blood pressure decreased slightly while her oxygen levels increased. After a 6-week treatment course, the patient's echocardiogram demonstrated trivial tricuspid regurgitation with a pressure gradient of 42 mmHg, while her N-terminal prohormone of brain natriuretic peptide level decreased to 3056 pg/mL. Finally, the patient was extubated.

Cardiac catheterisation was performed after 6 weeks of medical treatment, showing pulmonary arterial hypertension and the absence of the right pulmonary artery (mean pulmonary arterial pressure, 40 mmHg; pulmonary arterial systolic pressure, 62 mmHg; pulmonary-systemic pressure ratio, 0.48). Aortography demonstrated three major aortopulmonary collateral arteries in the right lung: one had a diameter of 2.3 mm, arising from the internal thoracic artery, and two had diameters of 2.5 mm, arising from the thoracic aorta and the abdominal aorta (Fig. 2).

Currently, no clear consensus exists regarding optimal therapeutic strategies for the unilateral absence of the pulmonary artery. Nevertheless, a previous study indicated the potential benefits of revascularisation of the large hilar arteries.[1] However, in this case, severe pulmonary hypertension and unstable haemodynamics occurred; thus, medical management seemed less risky than surgical intervention at that time. Immediate surgery was not advised by

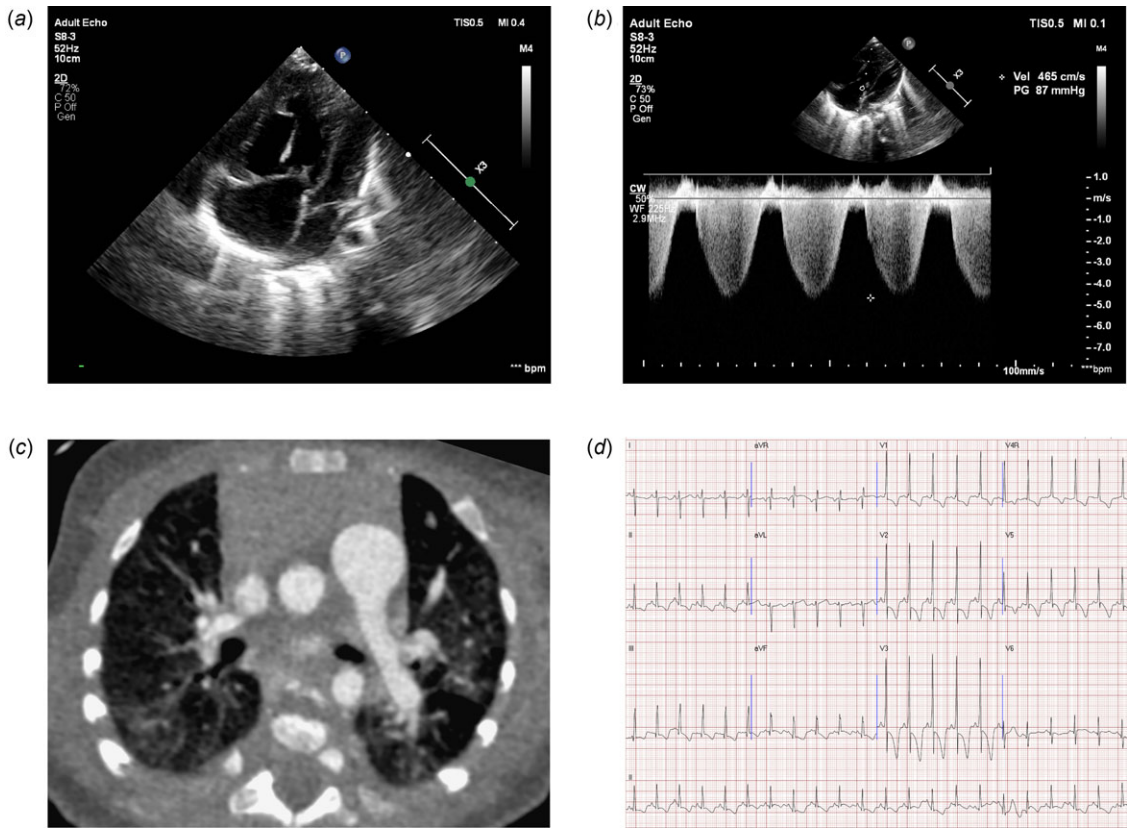

Figure 1. (***a***) Apical four-chamber view showing right ventricular and right atrial hypertrophy and dilation. (***b***) A severe tricuspid regurgitation and pressure gradient of 86 mmHg can be observed. (***c***) Contrast-enhanced CT showing the absence of the right pulmonary artery; no lung hypoplasia can be observed. (***d***) Electrocardiogram upon admission demonstrating a sinus rhythm of 130 bpm and right ventricle hypertrophy with a strain pattern.

the paediatric cardiac surgeon who was the only specialist in our region, and systemic collaterals from different origins supplied distinct areas of the right lung; Therefore, we decided to continue medical therapy for pulmonary hypertension and arranged outpatient visits.

Poor adherence to iloprost inhalation was observed during a follow-up visit a few weeks after discharge. Echocardiography showed moderate-to-severe tricuspid regurgitation with a pressure gradient up to 100 mmHg. After the patient resumed regular inhalation of iloprost 3–4 times daily, follow-up echocardiography revealed trivial-to-mild tricuspid regurgitation, with a decreased pressure gradient of 40–45 mmHg.

Discussion

Unilateral absence of the pulmonary artery is a rare congenital cardiovascular malformation with an incidence of 1/300,000 adults.[2] This condition results from the regression of the proximal sixth aortic arch coupled with the persistence of the intra-pulmonary pulmonary artery connection to the distal sixth aortic arch.[3] Unilateral absence of the pulmonary artery commonly affects the right pulmonary artery, as it is typically located contralateral to the aortic arch. In a prior study, the right pulmonary artery was absent in 109 (60%) of 182 patients with isolated unilateral absence of the pulmonary artery.[4] Left pulmonary artery interruption is frequently observed in other congenital heart defects such as tetralogy of Fallot, patent ductus arteriosus, septal defects, coarctation of the aorta, right aortic arch, truncus arteriosus, and pulmonary atresia.[2,3] Collateral vessels arising from bronchial arteries are common blood suppliers to the affected lung; however, other sources, including the intercostal, subdiaphragmatic, subclavian, and coronary arteries, may also act as collateral vessels.[3]

Unilateral absence of the pulmonary artery often leads to pulmonary hypertension in infants.[3] In patients with isolated absence of the right pulmonary artery, pulmonary hypertension develops due to insufficient elasticity of the left pulmonary vascular bed for coping with increased blood flow. Pulmonary hypertension is associated with poor prognosis.[5]

No consensus exists regarding the optimal therapeutic strategy to address the isolated absence of a pulmonary artery. The treatment of unilateral absence of the pulmonary artery-related complications includes interventional revascularisation, vaso-dilator therapy for pulmonary hypertension, and management of pulmonary haemorrhage.[1] In most prior cases, revascularisation resulted in a significant improvement in outcomes provided sufficiently large hilar arteries were present.[1] Early intervention to restore pulmonary blood flow may contribute to normal lung development and reduce pulmonary hypertension severity.[3] Nonetheless, the risk of imbalanced blood flow in pulmonary arteries and subsequent occlusion of the affected pulmonary artery after surgery remains a concern.[6]

In situations in which revascularisation is not feasible, alternative therapeutic measures should be considered such as long-term administration of vasodilators. However, responses to sildenafil, calcium channel blockers, and continuous intravenous

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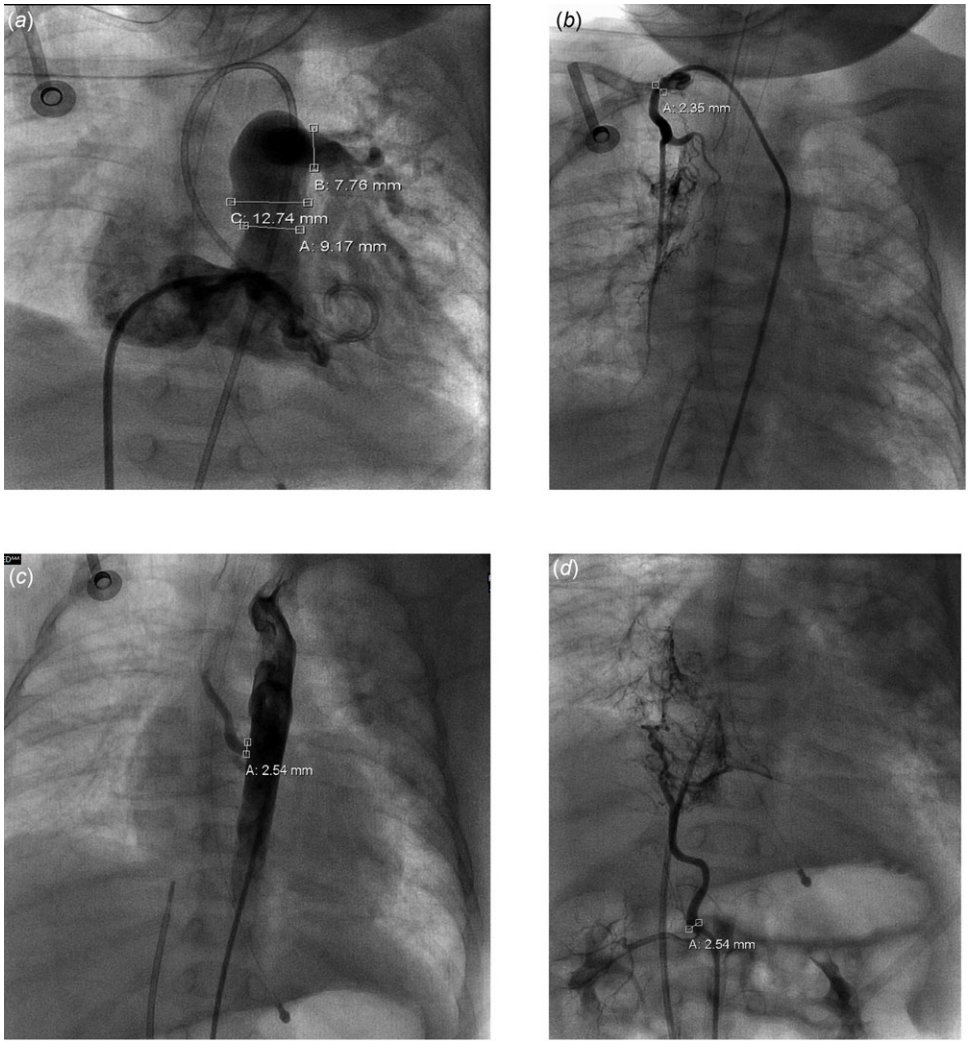

Figure 2. (***a***) Aortography showing the absence of the right pulmonary artery. Systemic collaterals that supply the right lung originate from three sources in this patient; (***b***) the internal thoracic artery; (***c***) the descending aorta; and (***d***) the abdominal aorta.

infusion of prostacyclin vary.[1] No paper has reported the use of iloprost as pulmonary vasodilator therapy in unilateral absence of the pulmonary artery.

Iloprost, a synthetic prostacyclin analog, can promote pulmonary vasodilation. This drug has a relatively short half-life of 20–25 minutes. In adult patients, iloprost inhalation has been reported to cause side effects such as flushing, jaw pain, and headaches; however, data regarding side effects in children are limited. Additionally, the efficacy of iloprost inhalation in children with pulmonary hypertension is poorly understood. Nevertheless, some studies have shown that iloprost may be effective in neonates with persistent pulmonary hypertension refractory to other agents for alleviating pulmonary hypertension.[7,8]

Our case highlights the unique challenge of managing extremely severe pulmonary hypertension, which is one of the reasons for contraindications to surgical intervention. Although multiple medications were attempted in the present case, iloprost inhalation was more effective than other agents, including nitric oxide. Discontinuation of iloprost worsened pulmonary hypertension despite continuous use of sildenafil and bosentan. To our knowledge, this is the first documented case of an infant with unilateral absence of the pulmonary artery and severe pulmonary hypertension effectively treated with iloprost inhalation. Continued monitoring for long-term effects and potential harm is essential, and the timing of surgical intervention should be carefully considered.

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Competing interests. The authors have no relevant financial or non-financial interests to disclose.

Ethical standard. The parents of the patient provided informed consent for the publication of this case report.

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