Novel diagnostic and therapeutic approaches to pulmonary hypertension due to the unilateral absence of a pulmonary artery

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Abstract

We report the case of a 64-year-old female diagnosed with severe pulmonary hypertension due to the unilateral absence of a pulmonary artery. The four-dimensional computed tomography scan is a useful modality for revealing detailed anatomical findings for differential diagnoses and surgical decision-making. The patient had severe pulmonary hypertension with a mean pulmonary artery pressure (PAP) of 74 mmHg and was treated with triple upfront combination therapy, leading to significant improvement in pulmonary haemodynamics (to 27 mmHg in mean PAP) and functional capacity (WHO functional class, from III to II; 6-min walk distance, from 211 to 276 m).

Keywords Unilateral absence of a pulmonary artery; Pulmonary hypertension; 4D computed tomography; Upfront triple combination therapy

Received: 30 January 2021; Revised: 28 April 2021; Accepted: 26 May 2021

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Introduction

Unilateral absence of a pulmonary artery (UAPA) is a rare congenital anomaly that is caused by the failure connection of the sixth aortic arch with the pulmonary trunk during embryologic development and is usually discovered in childhood. It is often associated with other cardiovascular abnormalities such as tetralogy of Fallot, septal defects, right aortic arch, and persistence of ductus arteriosus. In adulthood, therapeutic options include surgical resection of lung lobe/tissue and medical therapy with pulmonary arterial hypertension (PAH)-specific drugs. Despite evidence surrounding therapeutic options, there has been no published data describing upfront combination therapy, which was recently established in patients with idiopathic PAH. We describe the case of a 64-year-old female diagnosed with severe pulmonary hypertension and right heart failure due to the unilateral absence of a pulmonary artery and treated with upfront combination therapy.

Case Report

A 64-year-old female with no previous medical history, who was referred to our hospital for suspected pulmonary hypertension, presented with exertional dyspnoea and bilateral lower extremity oedema for 1.5 years. Initial examination revealed right-sided heart failure (jugular venous distension and lower extremity oedema) and pulmonary hypertension (accentuated pulmonic component of the second heart sound). Chest radiography revealed decreased right pulmonary volume, a shrunken right hilum, and left lung hyperinflation. Echocardiography revealed right ventricular enlargement with impaired function. Lung perfusion scintigraphy revealed no perfusion or normal perfusion in the right and left lungs, respectively (Figure 1A). Right heart catheterization revealed a mean right atrial pressure of 14 mmHg, right ventricular pressure of 119/22 mmHg, pulmonary artery (PA) pressure of 130/42 mmHg, mean PA pressure (mPAP) of 74 mmHg, and PA wedge pressure...
of 12 mmHg. The pulmonary vascular resistance was 35.4 Wood units, and the cardiac index was 1.3 L/min/m². The patient was high-risk according to the 2015 ESC/ERS guidelines on pulmonary hypertension management risk algorithm since the patient presented with right heart failure and a low cardiac index.

Pulmonary angiography (PAG) revealed an absent right PA and diffuse dilation without pouch defects, intimal irregularities, and abrupt vessel narrowing in the left PA (Figure 1B). Four-dimensional computed tomography (4DCT), acquired by the reconstruction of two dynamic scans in the upper and lower lungs, revealed an absent right PA from the main trunk in the PA phase. In the aortic phase, the right lateral thoracic and lower phrenic arteries flowed into an underdeveloped artery within the right lung (Figure 2, Supporting Information, Video S1).

Figure 1 (A) Lung perfusion scintigraphy demonstrated no perfusion in the right lung. (B) Pulmonary angiography demonstrated the absence of the right pulmonary artery and diffuse dilation without pouch defects, intimal irregularities, and abrupt narrowing of the vessel in the left pulmonary artery.

Figure 2 Four-dimensional computed tomography (4DCT) revealed the absent right pulmonary artery from the main trunk in the pulmonary artery phase. Dynamic scans were performed using a 320-row multi-detector CT (Aquilion ONE VISION, Canon Medical Systems, Otawara, Tochigi, Japan). We obtained two sets of 4DCT (upper lung region and lower region) covering the whole lung. These volume sets were connected using a dedicated workstation (ZioStation2, Ziosoft Inc., Tokyo, Japan). In the aortic phase, 4DCT showed collaterals, which developed from the right lateral thoracic artery and right inferior phrenic artery within the right lung (arrows).
The differential diagnoses of an absent right PA included acquired pulmonary vascular diseases involving the proximal PA [e.g. chronic thromboembolic pulmonary hypertension (CTEPH) and isolated Takayasu’s arteritis] and UAPA. CTEPH and Takayasu’s arteritis were ruled out from the 4DCT and PAG findings, and the patient was diagnosed with UAPA.

In addition to the treatment regimen of intravenous infusion of dobutamine and diuretics, upfront oral triple combination therapy, including riociguat, ambrisentan, and selexipag, was initiated. Because the patient was at high risk, continuous intravenous epoprostenol (EPO) was considered. However, intravenous therapy was not started in this case because (i) the patient had severe hypoxemia, and hypoxic pulmonary vasoconstriction was suspected as a component of PAH; (ii) unlike typical PAH, the patient was elderly and had a mildly high PA wedge pressure (12 mmHg), so the involvement of pulmonary hypertension associated with left heart failure (Group 2) could not be ruled out; (iii) the effect on intravenous EPO was unknown in PAH associated with UAPA. For these reasons, we decided to start safe oral therapy rather than intravenous therapy and to evaluate the effect of oral treatment within 2 months. Treatment with riociguat was started at a dose of 3 mg once daily, then increased every 1 week to 7.5 mg once daily. After successful titration of riociguat, ambrisentan was started at a dose of 2.5 mg once daily and then increased every 1 week. After 4 weeks, the dose was increased to 10 mg once daily. After successfully titration of ambrisentan, selexipag was started at a dose of 0.2 mg twice daily and subsequently increased to 0.8 mg twice daily (Figure 3). Each drug was started sequentially, without any side effects. Dobutamine and diuretics were discontinued on days 23 and 10, respectively.

By the 25th week of treatment, mPAP improved to 27 mmHg in association with an improvement in functional capacity (WHO functional class, from III to II; 6-min walk distance, from 211 to 276 m). During the 2-year follow-up period, no deterioration was observed.

**Discussion**

Unilateral absence of a pulmonary artery is a rare congenital anomaly caused by failure of the sixth aortic arch to connect with the pulmonary trunk during embryologic development.1

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**Figure 3** Clinical course after treatment with upfront triple combination therapy.

| 0 | 1 | 4 | 8 | 25 | 48 | weeks |
|---|---|---|---|----|----|-------|
| ![Dobutamine](3y) | ![Riociguat 7.5mg/day](7.5) | ![Ambrisentan 10mg/day](10) | ![Selexipag 1.6mg/day](1.6) |
| Cardiac Index (L/min/m²) | 1.3 | 3.1 | 3.6 | 4.3 |
| Pulmonary vascular resistance (Wood units) | 35.4 | 6.8 | 3.4 | 3.7 |
| Mean Pulmonary arterial pressure (mmHg) | 35 | 27 | 27 |
| 6-minute walk distance (m) | 211 | 280 | 276 | 305 |

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It is often associated with other cardiovascular abnormalities and is usually diagnosed during childhood. Patients with UAPA were divided into three groups. Generally, Group 3 patients present with haemoptysis and/or pulmonary hypertension in adulthood without overt pulmonary hypertension in childhood. Surgical treatment (e.g. PA anastomosis) is indicated in most childhood cases, where PA development can be expected postoperatively. In this case, the absence of right PA was confirmed accurately on 4DCT, revealing no surgical indication. Compared to pulmonary arteriography, we believe that 4DCT, in addition to being a non-invasive test, is a useful imaging modality to assess lung volume and to confirm detailed vascular anatomy, especially collateral supply, such as pulmonary vascular bed on the healthy side compensates for increased blood flow. UAPA does not always induce pulmonary hypertension, and the frequency of pulmonary hypertension is 19–25%. Notably, mild medial hypertrophy of the pulmonary arterioles in the unaffected lung, possibly caused by long-term exposure to high blood flow, was found on autopsy. Reports of PAH-specific drug efficacy in UAPA suggest that the disturbed pulmonary vascular bed in the unaffected lung is a possible therapeutic target.

This is the first case of UAPA with severe pulmonary hypertension treated with novel approach strategies, including diagnosis with 4DCT and early treatment with upfront combination therapy.

Acknowledgements

The authors acknowledge Takehiro Nakai, radiology technician (RT), and Takahiro Arai, RT, for the reconstruction of the 4DCT.

Conflict of interest

The authors have no potential conflicts of interest related to any company or organization whose products or services are discussed in this article.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Video S1. Supporting information.

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DOI: 10.1002/ehf2.13459