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An unexpected and unusual cause of pulmonary hypertension in a patient with hypersensitivity pneumonitis: a partial anomalous pulmonary venous connection causing pulmonary artery hypertension

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Key words: partial anomalous pulmonary venous connection, non-fibrotic hypersensitivity pneumonitis, pulmonary hypertension.

Contributions: SG, PU, JA, NDP, AW, resources, data curation, investigation, writing - original draft; SG, PU, writing - review and editing, visualization; PU, supervision.

Conflict of interest: the authors declare that they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: no Ethical Committee approval was required for this case report by the Department. Informed consent was obtained from the patient included in the study.

Patient consent for publication: the patient gave his written permission to use his data to publish this case report and any accompanying images.

Funding: none.

Availability of data and materials: all data underlying the findings are fully available.

Received: 1 December 2022.
Accepted: 24 February 2023.
Early view: 3 March 2023.

Monaldi Archives for Chest Disease 2024; 94:2497
doi: 10.4081/monaldi.2023.2497

Abstract

Partial anomalous pulmonary venous connection (PAPVC) occurs when any pulmonary vein, but not all, drains directly into the right atrium or its venous tributaries. PAPVC can very rarely present as an individual cause of pulmonary artery hypertension. Here we are presenting the case of a 41-year-old farmer with a history of exertional dyspnea for the past 3 years, which increased over 6 months. Chest high-resolution computed tomography was suggestive of non-fibrotic hypersensitivity pneumonitis. Hence, the patient was started on systemic steroids, with which the patient's oxygen saturation improved. On 2D echocardiography, the right ventricle systolic pressure was 48 + right atrial pressure. Right heart catheterization showed a mean pulmonary artery pressure of 73 mmHg and pulmonary vascular resistance of 8.7. On further evaluation, a computed tomography pulmonary angiogram was done, which surprisingly revealed the left superior pulmonary vein draining into the left brachiocephalic vein.

Introduction

Partial anomalous pulmonary venous connection (PAPVC) is a rare cardiac congenital anomaly that occurs when any pulmonary vein, but not all, drains directly into the right atrium or its venous tributaries [1]. PAPVC can rarely present as a cause of pulmonary artery hypertension (PAH). Here we describe a case of non-fibrotic hypersensitivity pneumonitis (HP), suspected to have hypoxia-related Class III pulmonary hypertension, which, on further evaluation, was found to have PAPVC-causing PAH.

Case Report

A 41-year-old male farmer with a history of occupational exposure to moldy hay presented with exertional dyspnea, modified Medical Research Council (mMRC) functional class II, and dry cough for 3 years, which exacerbated over 6 months (mMRC class IV). There was no history of wheezing, chest pain, or any inhaler use. He did not give any history of joint pain, skin rash, skin tightening, or proximal muscle weakness. There was no history of fever or weight loss. He denied any history of alcohol consumption or smoking. His medical history was significant for systemic hypertension, and at the time of presentation, his blood pressure was 142/80 mmHg (systolic/diastolic). The general examination was unremarkable except for elevated jugular venous pressure. Although there

was no history of wheezing, bilateral diffuse polyphonic wheeze was present with occasional end-inspiratory fine crepitations on chest auscultation in all areas.

Cardiac auscultation revealed splitting of the second heart sound with a loud P2 in the pulmonary area. Room air oxygen saturation at presentation was 88%, and arterial blood gas analysis: pH=7.45, partial pressure of oxygen (PaO_2)=48 mmHg, partial pressure of carbon dioxide (pCO_2)=33 mmHg, HCO_3=22. A complete hemogram revealed normal parameters, viz. hemoglobin (15.0 g/dL), total leucocyte counts (9280 per microliter), and platelet count (161,000 per microliter). Hepatic, renal, and thyroid function tests were also reported as normal. The electrocardiogram revealed the presence of a right axis deviation with the presence of 'P' pulmonale. Chest high-resolution computed tomography (HRCT) showed bilateral upper lobe predominant centrilobular nodules and patchy ground glass opacities with mosaic perfusion involving all lobes (Figure 1). Fiber-optic bronchoscopy was done; a cellular examination of bronchoalveolar lavage (BAL) fluid from the right upper lobe anterior segment revealed lymphocytosis (35%). Given his occupational history, clinical presentation, HRCT findings, and BAL reports, a diagnosis of non-fibrotic HP was made [2]. He was started on systemic steroids: oral prednisolone 30 mg once daily (0.5 mg/kg once daily), tablet furosemide 40 mg twice a day, and nebulization with salbutamol 2.5 mg four times a day, which improved his oxygen saturation and arterial blood gas PaO_2 in 5 days. Repeat arterial blood gas analysis showed pH=7.40, PaO_2=64 mmHg, pCO_2=39 mmHg, and HCO_3=25. Spirometry and diffusion capacity of the lung for carbon monoxide were performed following the improvement in arterial blood oxygen saturation levels, and the results were normal. His 6-minute walk test showed a drop in peripheral oxygen saturation from 94% to 86%, and his 6-min walk distance was 264 m. His N-terminal pro-brain natriuretic peptide (NT-proBNP) assay was 880 ng/L. Transthoracic echocardiography showed right atrial and ventricular dilatation and moderate tricuspid regurgitation with a right ventricular systolic pressure of 48 mmHg + right atrial pressure with a normal left ventricular ejection fraction.

In view of disproportionate pulmonary hypertension and normalization of room air arterial PaO_2 following systemic corticosteroid therapy, a bubble study was done to rule out intracardiac shunt, which revealed an intact interatrial septum. Right heart catheterization (RHC) was done by the cardiology team, which showed pulmonary artery pressure of 120/50/73 mmHg (systolic/diastolic/mean), pulmonary capillary wedge pressure of 11 mmHg, pulmonary vascular resistance of 8.7 wood units, and Qp/Qs of 1.6 (*Supplementary Table 1*). A computed tomography pulmonary angiogram (CTPA) did not show any filling defect in the pulmonary artery, thus excluding pulmonary thromboembolism, but unexpectedly revealed the left superior pulmonary vein draining into the left brachiocephalic vein (Figure 2).

The patient deferred surgery due to his stable symptoms and was started on combination pharmacotherapy (ambrisentan and tadalafil) [3]. On the 3-month follow-up, the patient's dyspnea improved to mMRC functional class I, and his repeat 6-minute walk distance was 452 m.

Discussion

In utero, the pulmonary veins and the left atrium arise separately. The foregut gives rise to the lung buds, which drain into the systemic circulation (the cardinal and umbilicovitelline veins). The common pulmonary vein, which arises as a sacculation from the primitive atrium, communicates with the pulmonary vascular bed [4]. The connections between the pulmonary vasculature and the systemic venous system regress over time. A persistent partial or total anomalous pulmonary vascular connection develops when this fails to occur, resulting in drainage into the systemic venous circulation [4]. PAPVC, being asymptomatic, often goes undiagnosed in most cases. More often than not, such patients are misdiagnosed as suffering from idiopathic PAH. The anomalous pulmonary veins arise mostly from the right lung and drain primarily to the superior vena cava, fol-

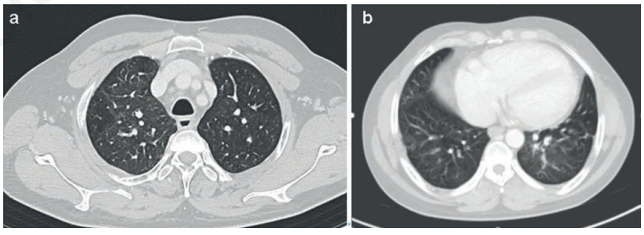

Figure 1. a) High-resolution computed tomography chest scan showing bilateral upper lobe ground glass opacity with few centrilobular nodules and mosaic attenuation; b) high-resolution computed tomography chest showing patchy ground glass opacity in the lower lobe.

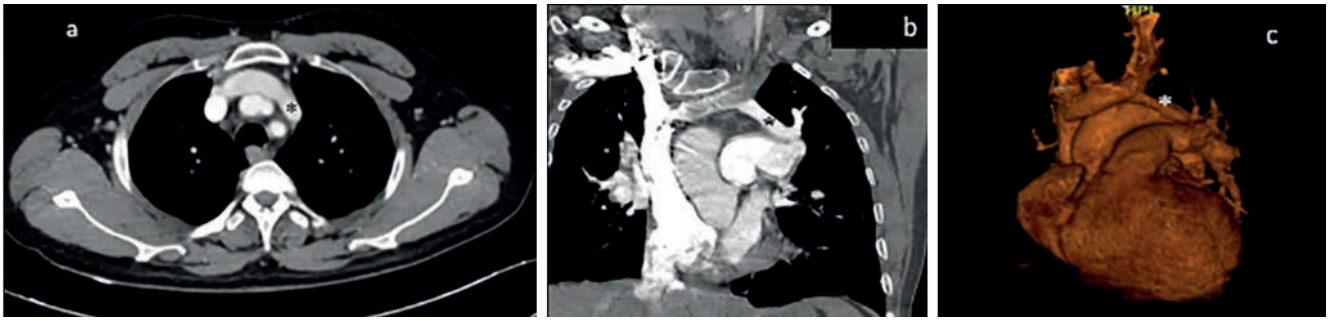

Figure 2. a) Computed tomography pulmonary angiogram axial section showing left superior pulmonary vein (black asterisks) draining into the left brachiocephalic vein; b) computed tomography pulmonary angiogram coronal section showing left superior pulmonary vein (black asterisks) draining into the left brachiocephalic vein; c) the volume rendering technique image shows the left superior pulmonary vein (white asterisks) draining into the left brachiocephalic vein.

lowed by the right atrium or the inferior vena cava. Only 3-8% of the anomalous pulmonary veins come from the left lung and connect primarily to the left brachiocephalic vein [5]. Our patient was found to have an anomalous left superior pulmonary vein draining into the left brachiocephalic vein.

In PAPVC, the persistent systemic venous connection acts similar to a left-to-right shunt: a portion of the right ventricular output, after oxygenation in the lungs, does not participate in systemic circulation but is rather returned to the right atrium. This causes an increase in pulmonary vascular resistance due to the remodeling of the pulmonary vasculature with time, leading to pulmonary arterial hypertension [6]. In turn, pulmonary hypertension may lead to severe tricuspid regurgitation, atrial arrhythmias, and decompensated heart failure. Over time, right heart failure may worsen, leading to Eisenmenger's syndrome. In our case, as the NT-proBNP value was elevated, the patient was suspected to have right heart failure. Hence, diuretics were given [7]. The possibility of left ventricle dysfunction secondary to right ventricle overload or systemic hypertension was also considered. However, trans-thoracic echocardiography did not show any evidence of left ventricle dysfunction.

The diagnosis of PAPVC can be quite challenging, especially in patients with abnormalities in the lung parenchyma, as pulmonary hypertension (PH) is usually attributed to parenchymal lung disease without further evaluation. Therefore, patients may be initially misdiagnosed with Class III pulmonary hypertension and deferred PAH-specific therapy such as vasodilators. In our patient, based on his occupational history, clinical presentation, HRCT findings, and BAL reports, a diagnosis of non-fibrotic HP was made, but as moderate PH was unexplained, he was evaluated further, leading to the recognition of PAPVC-associated PAH.

Recognition earlier can lead to a successful surgical correction, underlining the importance of awareness of this condition. However, our patient was not willing to undergo surgery. Catheter embolization of the anomalous connection was not viable in our patient due to the lack of a co-existent connection from the anomalous vein to the left atrium to accommodate the increased flow post-embolization. Hence, medical therapy was resorted to; he was started on combination pharmacotherapy (ambrisentan and tadalafil) with a 3-month follow-up.

Prior studies on patients with pulmonary arterial hypertension secondary to congenital cardiac disorders, including PAPVC, showed clinical and hemodynamic improvements with endothelin receptor antagonists, phosphodiesterase inhibitors, and prostaglandins [8]. After the initiation of pharmacotherapy, the patient needs to be closely monitored for disease progression.

Conclusions

In conclusion, pulmonary hypertension in a patient with initial hypoxemia secondary to lung disease should not always be classified as Class-III PH, especially when hypoxemia resolves with treatment, but should rather be evaluated with RHC and CTPA as it might change the approach to treatment.

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Online supplementary material:

Supplementary Table 1. Hemodynamic measures obtained during right heart catheterization.