The Unclassified Phenotype: Severe Pulmonary Hypertension with Low DLCO Challenging Diagnostic Boundaries - A Case Report

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Introduction

World Health Organization groups categorize Pulmonary hypertension (PH) into five groups based on the underlying causes or pathophysiology. Patients with rare phenotypes, such as those with a smoking history and low DLCO (diffusing capacity of the lungs for carbon monoxide), may be incorrectly classified as IPAH (idiopathic pulmonary arterial hypertension), even though they exhibit traits more commonly associated with other groups, like Group 3 PH (pulmonary hypertension due to lung disease). While these patients may show signs of pulmonary vascular remodeling and PH, their underlying lung pathology might not be apparent or could represent a more complex phenotype. Our case indicates that there is a need for the emergence of distinct pulmonary vasculopathy, especially related to smoking and lung injury characterized by a low diffusion capacity for carbon monoxide without overt signs of parenchymal lung disease involving atypical vascular changes or capillary remodeling.

Case Presentation

We present a 63-year-old male with a past medical history significant for chronic hypoxic respiratory failure secondary to COPD on 4 L of oxygen, diastolic heart failure, tobacco use disorder, hyperlipidemia, and obstructive sleep apnea who came to the hospital due to concerns of shortness of breath. The patient was noted to be tachypneic and hypoxic with hypoxemia on arrival and was initiated on BiPAP for increased work of breathing. Physical examination was notable for diminished breath sounds bilaterally and grade 2 pedal edema. Chest x-ray was concerning central vascular congestion, and a CT angiogram of the chest revealed mild-moderate emphysema with mild bronchial wall thickening. He was initiated on IV steroids, DuoNebs, budesonide, and albuterol nebulizations, along with IV diureses. Laboratory studies from admission revealed significantly elevated BNP 4400 with a baseline at 1300. The respiratory viral panel was negative, and ABG revealed hypoxemia with 7.44/42/40/28. 2D echo showed an ejection fraction of 50-55%, abnormal septal motion consistent with right ventricular volume overload, elevated right ventricular end-diastolic pressure, moderately enlarged right ventricular size, and dilated IVC (>1.7cm). Pulmonary function testing a month prior revealed FEV1 at 50%, total lung capacity at 74%, and diffusion capacity markedly reduced at 31%. Cardiac catheterization revealed severe PH with pulmonary arterial pressure at 60, wedge pressure at 15, cardiac index

of 1.7, and output at 3.2. Pulmonary vascular resistance was 1123, with right atrial pressure at 23. The patient was aggressively diuresed and was initiated on inhaled Flolan therapy. Given the severity of his PH with reduced cardiac index and severely elevated pulmonary vascular resistance, the patient was then transferred to a tertiary care center for IV Epoprostenol therapy and evaluation for a lung transplant. 301

Discussion

Considering rare phenotypes in classifying PH is essential for accurate diagnosis and treatment. The current classification system, primarily based on the WHO groups, categorizes PH into five groups based on the underlying causes or pathophysiology. However, rare or atypical phenotypes, such as those with a low DLCO or specific lung parenchymal changes, can sometimes complicate this classification. Our patient was hospitalized multiple times in the past for worsening PH and was classified as an IPAH group as his FEV1 was only mildly diminished. Still, given his rapid decrease in DLCO and Smoking history, he might have been misclassified despite sharing features more characteristic of other groups like Group 3 PH. These patients might present with pulmonary vascular remodeling and PH, but their underlying lung pathology might not be immediately evident or fit a more complex phenotype. The classification system may need to be refined to account for these exceptions. This could involve recognizing atypical vascular changes, endothelial dysfunction, or capillary remodeling patterns that don't fit into traditional IPAH or Group 3 categories.

Conclusion

This case report highlights the diagnostic challenges and the importance of considering capillary remodeling in patients with rapidly progressing severe pulmonary hypertension with low DLCO and smoking history. Given the rarity, a high index of suspicion and comprehensive evaluation are essential for accurate diagnosis and management. The classification system may need to be refined to account for these exceptions.