The Unclassified Phenotype: Severe Pulmonary Hypertension with Low DLCO and Capillary Remodeling Challenging Diagnostic Boundaries

Vaishnavi Parchuri, Nikita Chintam, Von Patrick Dela Rosa, Deepika Davalath, Mamun Ahmed, Parth Patel, Mashal Salam, Ugonna Ononuju, John Kern

AtlantiCare Regional Medical Center, Pomona, N.J.

Introduction

- World Health Organization groups categorize Pulmonary hypertension (PH) into 5 groups based on the pathophysiology. Patients with rare phenotypes, such as those with a smoking history and low DLCO, may be incorrectly classified as Group 3 (PH due to lung disease) based on pulmonary function tests even with the presence of atypical vascular changes and share more characteristics with Group 1 (Pulmonary arterial Hypertension).
- Our case indicates that there is a need for the emergence of distinct pulmonary vasculopathy characterized by a low DLCO involving atypical vascular changes, especially in cases with severely elevated pulmonary vascular resistance (PVR) and a potential early referral to lung transplant.

Presentation

We present a 63-year-old male with a PMH of moderate emphysema, diastolic heart failure, tobacco use disorder, and hyperlipidemia who presented with shortness of breath.

- He was noted to be tachypneic and hypoxic on arrival and was initiated on BiPAP.
- Physical exam was notable for diminished breath sounds bilaterally and grade 2 pedal edema.
- Chest x-ray was concerning for central vascular congestion, and a CTA chest reve revealed mild- moderate emphysema.

Hospital Course

- Upon presentation, the patient was initiated on methylprednisolone, bumetanide diuresis, and nebulized bronchodilators (DuoNeb and budesonide).
- Laboratory evaluation - **markedly elevated proBNP of 4400 pg/mL** (baseline 1300), consistent with cardiac strain, while the viral panel was negative. Arterial blood gas showed pH 7.44 / pCO_2 42/pO_2 40 / HCO_3 28, indicating compensated hypoxemia.
- The autoimmune panel was negative for C-ANCA, PR-3, P-ANCA, and C-ANCA excluding secondary vasculitis etiologies.
- 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 tests obtained one month earlier showed FEV_1 50% predicted, TLC 74% predicted, and a **markedly reduced DLCO of 31%**, suggesting a pulmonary vascular component disproportionate to the degree of airflow limitation.
- Cardiac catheterization confirmed **severe pulmonary hypertension** with mean pulmonary artery pressure PAP 60 mmHg, PCWP 15 mmHg, cardiac index 1.7 L/min/m^2, and PVR 1123, along with elevated RA pressure (23 mmHg).
- The patient was aggressively diuresed and started on inhaled epoprostenol (Flolan), resulting in transient hemodynamic improvement. Given the severely elevated PVR, low cardiac output, and refractory pulmonary hypertension, he was subsequently transferred to a tertiary center for continuous IV prostacyclin therapy and evaluation for lung transplant.

Discussion

- Rare or atypical phenotypes, such as those with a low DLCO or specific lung parenchymal changes, can sometimes complicate WHO PH classification.
- Our patient was classified as Group 3 PH, given the history of smoking and emphysema, despite having only a mild reduction of FEV1, markedly elevated PVR, and rapid progression of PH.
- A markedly low DLCO in the setting of only moderate obstructive disease should raise suspicion for pulmonary vascular remodeling beyond classic COPD-related group 3 PH.
- These patients might present with pulmonary vascular remodeling and PH, but their underlying lung pathology might not be evident. This could involve recognizing endothelial dysfunction and capillary remodeling patterns that don't fit traditional PH groups.

Conclusion

This case report highlights the diagnostic challenges and the importance of considering capillary remodeling in patients with rapidly progressing severe PH with low DLCO and smoking history and a need for early referral to lung transplant. Advanced imaging, genetic studies, and more detailed clinical profiles can aid in refining diagnostic criteria and potentially lead to new subcategories in PH classification that are more inclusive of these phenotypes.

References