VARIED ETIOLOGY OF PULMONARY HYPERTENSION: A CASE-SERIES

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Abstract

Pulmonary Hypertension is a haemodynamic and pathophysiological condition that has diverse clinical presentation and variable prognosis. There are currently five categories of pulmonary hypertension. Here we present series of pulmonary hypertension cases with varied etiology.Evaluation includes series of investigations to confirm the diagnosis and specify the etiology. It is imperative to make correct diagnosis as target therapy with phosphodiesterase inhibitors and endothelin-1 receptor antagonists effectively controls the disease progression in certain groups of patients.

Keywords: pulmonary hypertension, chronic thromboembolism, phosphodiesterase inhibitors, endothelin-1 receptor antagonists

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1. Introduction

Pulmonary hypertension (PH) is defined as mean pulmonary artery pressure (PAP) of >25 mm Hg at rest and >30 mm Hg during exercise and pulmonary arterial hypertension (PAH) is diagnosed when pulmonary capillary wedge pressure (PCWP) or left atrial pressure is <15 mm Hg in presence of PH. It is typically diagnosed via right heart cardiac catheterisation[1].

There are currently five categories of pulmonary hypertension (PH)[2]. These include: pulmonary arterial hypertension (PAH) (group 1), PH due to left sided heart disease (group 2), PH secondary to chronic hypoxic lung disease (group 3), PH secondary to chronic thromboembolism (CTEPH) (group 4) and PH secondary to unclear or multifactorial pathogenesis (group 5).

PH remains a serious disease with variable prognosis, depending on etiology, functional class and hemodynamic parameters[3]. Elaborate history, meticulous examination, electrocardiogram, detailed echocardiography radiological imaging and serology all aid in diagnosis of PH, while confirmation is with cardiac catheterisation.

The case series discussed here demasquerades the various clinical categories with markedly differing prognosis under a common label of PH in the patients admitted to our institute.

Case series:

Case 1:

A 32-year-old female, presented with breathlessness of 1 month and swelling of both feet for 3 days. Physical examination revealed bilateral pitting pedal edema, elevated jugular venous pressure and loud second heart sound (P2). Electrocardiogram (ECG) showed right axis deviation, right atrial enlargement and right ventricular hypertrophy (RVH) with strain. Echocardiography revealed dilated right atrium (RA), right ventricle (RV) with D-shaped left ventricle, severe tricuspid regurgitation (TR) and severely elevated pulmonary artery systolic pressure (Figure 1). Lab parameters including serology markers were normal. She was diagnosed as IPAH, initiated on treatment with calcium channel blocker, phosphodiesterase inhibitor and oral anticoagulation with which she was discharged in an improved condition.

Case 2:

A known chronic obstructive pulmonary disease (COPD) patient, 65-year-old male, presented with breathlessness for two weeks. Initial vital signs were pulse rate-118 beats per minute, BP 124/86 mmHg, respiratory rate- 35/min, SpO2 61 % on room air. Laboratory reports showed significant acidosis and hypercarbia (pH 7.28 and CO2 >115 respectively) while other parameters were unremarkable. Computed tomography chest (Figure 2) revealed hyperinflation of the lungs with left upper zone opacity and marked dilation of the pulmonary trunk. He was diagnosed as PAH secondary to COPD, left upper-lobe pneumonia and treated with non-invasive ventilation, antibiotics and bronchodilators with which patient improved and was discharged in three weeks on home oxygen therapy.

Case 3:

A known patient of deep vein thrombosis (DVT), 47-years-old male presented with gradual onset and progression of dyspnea over one month with anasarca. Patient was irregular on his anticoagulant therapy for DVT. Physical exam findings included anasarca, jugular venous distention and a prominent S2 on cardiac auscultation. ECG showed right axis deviation and right ventricular hypertrophy with strain. Transthoracic echocardiogram (Figure 3) showed dilated RA/RV, mild RV dysfunction, organised small thrombus in RA, severe TR and severe pulmonary artery hypertension. Labs reports except for markedly elevated D-Dimer value were within normal limits. Computed tomography pulmonary angiography showed complete filling defect with non-opacification seen involving the right pulmonary artery and its branches and left upper pulmonary artery – suggestive of complete thrombus with features of pulmonary hypertension. He was diagnosed as CTEPH and treatment with intense anticoagulation and decongestive therapy clinically improved him over next 2 weeks to be discharged in a stable condition.

2. Discussion

Pulmonary circulation has an extensive surface area of about 50–70 sq.m at rest. It is normally a high flow, low pressure and low resistance system which can accommodate marked increase in cardiac output without any significant increase in pressure. However, with abnormal pulmonary vasculature, pressure rise can approach up to systemic levels.

While-not being a very common disease, PH remains a serious disorder. The etio-pathogenesis is varied, forming basis for categorising in various groups[2,3]. Depending on the underlying cause, the precise pathophysiology differs. The mechanism is believed to be secondary to endothelial dysfunction with an imbalance between endogenous vasodilators (like prostacyclin) and vasoconstrictors (like endothelin-1) resulting in a net effect of vasoconstriction and thrombus formation. In the case of PAH, it is characterised by vascular remodelling and is accompanied by

fibrosis, inflammation, and abnormal proliferation of endothelial and vascular smooth muscle cells. Nitric oxide, endothelin, and prostacyclin are the three main routes that contribute to the emergence and spread of PAH.[4] The proliferation and hypertrophy of pulmonary vascular smooth muscle cells, which typically have a low rate of multiplication, causes intimal constriction and increases blood flow resistance. Additionally, in individuals with PAH, circulating platelets remain perpetually activated and support the prothrombotic condition by aggregating at the level of the damaged endothelial cells.

Our case1 is IPAH, belongs to Group1, which is rare but fatal disease with high mortality having mean survival of 2-3 years from diagnosis. Adult female predominance is seen three times higher in IPAH and prognosis is better in the same gender[2,6]. Management is based on NYHA classification with a goal of positive impact on quality of life as well as survival. These include oral calcium channel blockers (in patients with vasoreactivity) and endothelin receptor antagonists, phosphodiesterase inhibitors and prostanoids.

Case 2 patient, belongs to Group 3 PH and it is the outcome of pulmonary vasoconstriction brought on by persistent hypoxemia. Treatment of the underlying lung disease and providing long term oxygen therapy to those who are hypoxic are the cornerstones of therapy for this condition. The efficacy of pulmonary vasodilators in this group is unclear. Dyspnea and PAH disease progression are best assessed by cardiopulmonary exercise testing and the six-minute walk test.[5]

Case3 is a patient of chronic thromboembolism (CTE) belongs to Group 4 class of PH, as CTE restricts regular blood flow in pulmonary vessels. It is important to rule out CTEPH in every PAH patient as it is a potentially curable disease. The gold standard test to diagnose CTEPH is a pulmonary angiogram.[7] Adempas (drug name: Riociguat) is an oral soluble guanylate cyclase(sGC) stimulator and only approved drug by FDA for the treatment of CTEPH.[8] However it can be used for selected patients of CTEPH only. While patients are treated with traditional therapy for PH, the curative therapy is pulmonary thromboendarterectomy (PTE) surgery.[7,8] Additionally all CTEPH patients are required to be treated with anticoagulants through-out their life to prevent formation of new blood clots. CTEPH is the only potentially curable form of PH.

3. Conclusion

Pulmonary hypertension often arises as a complication of an underlying disease. This can be true for most groups of PH. While patients in all of the groups present commonly with dyspnea, each form of pulmonary hypertension is different in its Pathophysiology, prognosis and therapy. Once diagnosis is made accurately, therapy is individualised optimally, improvements in survival and quality of life are possible even with this serious condition.

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Legends:

1. Figure1: Echocardiography showing dilated RA and RV with D-shaped LV and severe tricuspid regurgitation with markedly elevated PASP.
2. Figure2: CT scan showing features of COPD with hyperinflation of lungs with left upper zone hazy opacity suggestive of LRTI.
3. Figure 3: ECG showing RBBB, right ventricular enlargement with strain.

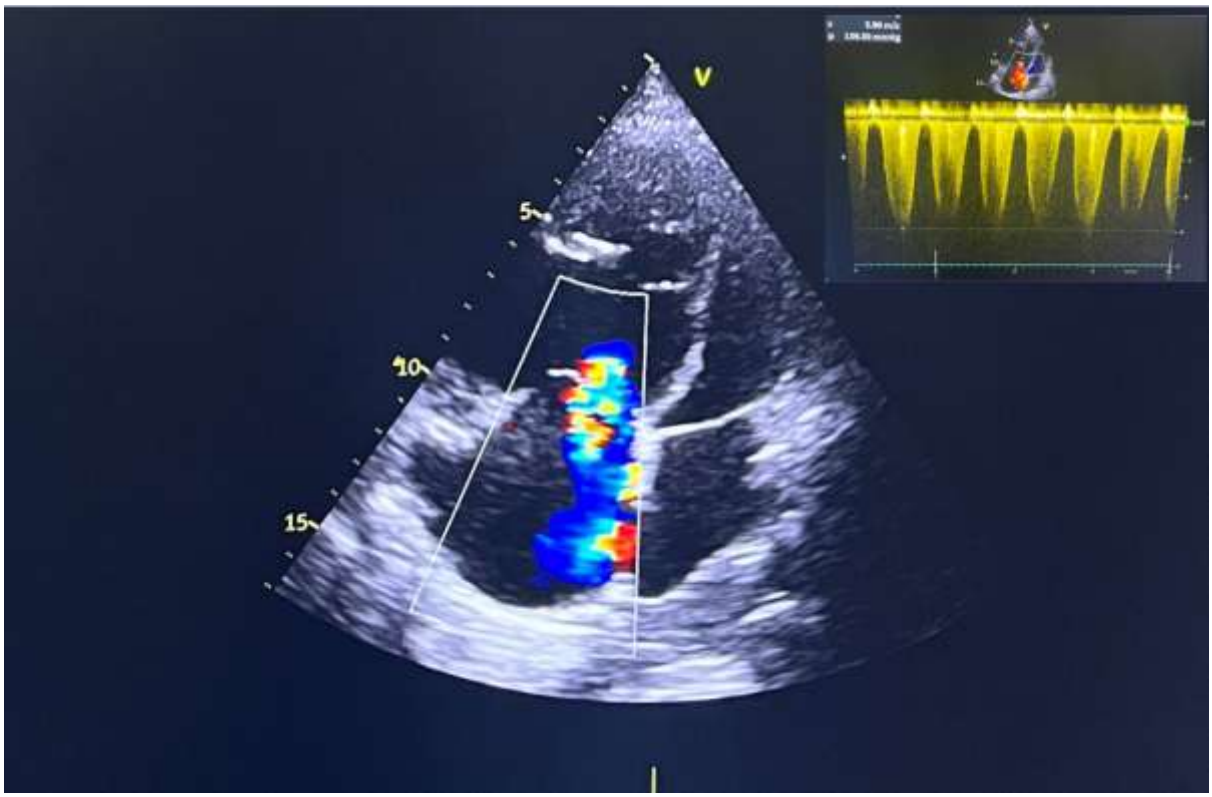

Figure1:

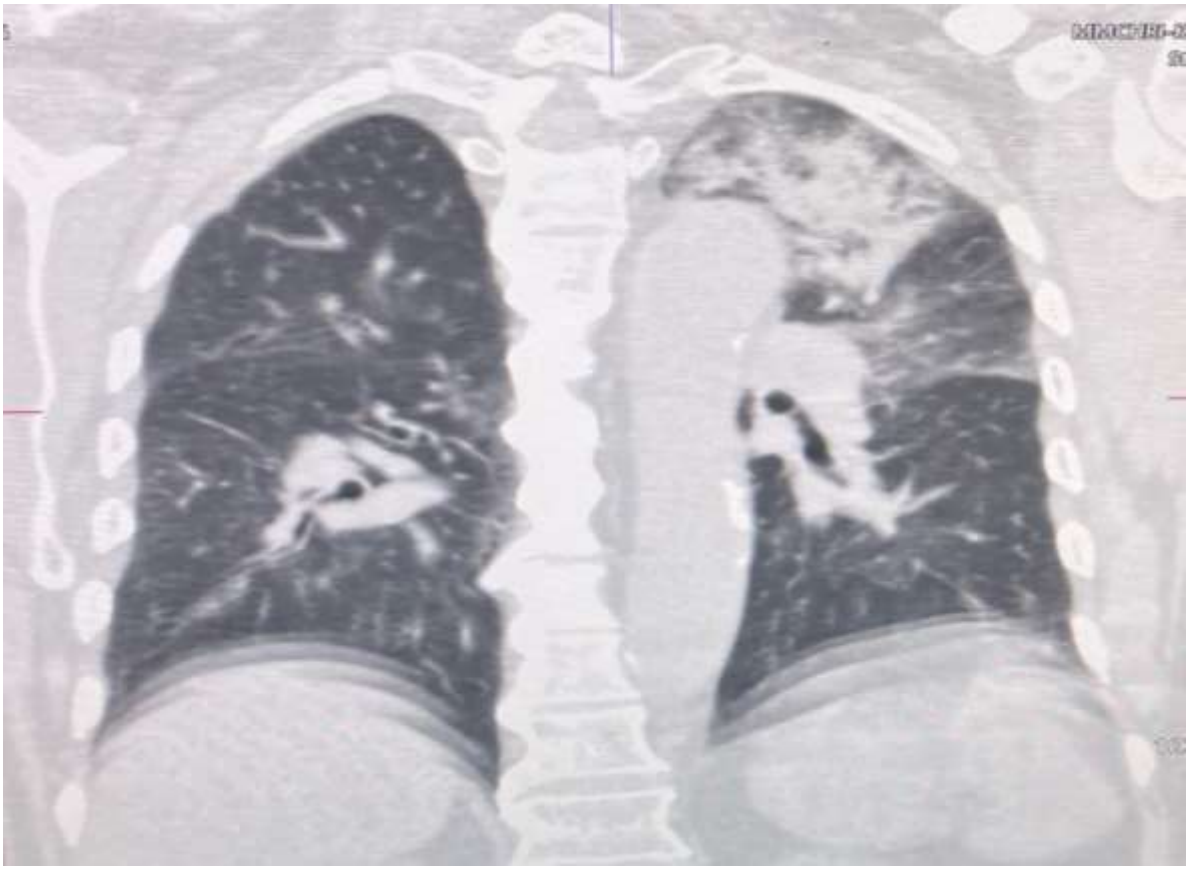

Figure2: