Pulmonary veno-occlusive disease as a cause of pulmonary arterial hypertension

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Pulmonary veno-occlusive disease (PVOD) represents a rare form of precapillary pulmonary arterial hypertension. We present a young patient hospitalized with progressive dyspnea, with initial workup suggestive of pulmonary hypertension and unexplained noncardiogenic pulmonary edema. His subsequent clinical course was consistent with the diagnosis of PVOD.

Pulmonary veno-occlusive disease (PVOD) represents an uncommon form of pulmonary arterial hypertension (PAH) characterized by progressive obliteration of the pulmonary venules, elevation of pulmonary arterial pressures, and increased pulmonary vascular resistance, leading to right ventricular failure and death (1–3). PVOD shares similar characteristics with idiopathic PAH, which can easily lead to misdiagnosis among these two entities. Based on data from the French pulmonary hypertension registry, the annual incidence of PVOD is low (4). A less-invasive diagnostic approach utilizing high-resolution computed tomography (CT) of the chest, arterial blood gases, pulmonary function tests, and appropriate hemodynamic interpretation of right-sided heart catheterization could be useful for the detection of PVOD (2).

CASE PRESENTATION

A 19-year-old man was brought to the hospital by his mother in an acute confusional state after being found lying on the floor and responding slowly to verbal and tactile stimuli. According to his mother, the patient had smoked spice (herbal mixtures of synthetic cannabinoid compounds) and complained of progressive dyspnea for the past 3 months. He smoked cigarettes, weed, and spice and drank alcohol. On admission he was hypoxic, with an oxygen saturation of 84% on room air. He had clubbing of fingernails and an accentuated second pulmonic heart sound. A chest radiograph showed enlarged pulmonary arteries and mild interstitial prominence (early pulmonary edema). A 12-lead electrocardiogram showed right axis deviation, incomplete right bundle branch block, and right ventricular hypertrophy. A CT scan of the chest with contrast showed diffuse bilateral confluent ground-glass opacities, septal line thickening with bilateral small pleural effusions, a mildly enlarged right atrium, mildly enlarged mediastinal and hilar lymphadenopathies, and

a dilated pulmonary trunk (*Figure 1*). A transthoracic echocardiogram showed a severely dilated right atrium and ventricle, a flattened ventricular septum, and an estimated right ventricular systolic peak pressure of 79 mm Hg. A ventilation/perfusion lung scan was negative for chronic thromboembolic pulmonary hypertension. Right-sided heart catheterization showed severe PAH with a mean pulmonary artery pressure of 56 mm Hg, pulmonary arterial occlusion pressure measured in different lung zones at 3 to 4 mm Hg, cardiac output of 4.2 L/min, and calculated pulmonary vascular resistance of 13.32 Wood units (*Figure 2*). The patient was discharged on oral diuretics, home oxygen, and low-dose warfarin.

DISCUSSION

The annual incidence of PVOD is approximately 0.1 to 0.2 cases per million in the general population per year. However, since 5% to 10% of PVOD cases are misdiagnosed as idiopathic PAH, the actual incidence rate may be higher (1). PVOD poses a diagnostic challenge given the overlapping features and similarities with idiopathic PAH (*Table 1*).

Hemodynamic evaluation is necessary to differentiate between suspected cases of PAH and PVOD. Both of these conditions show evidence of severe PAH with an elevated resting mean pulmonary artery pressure ≥ 25 mm Hg and pulmonary artery occlusion pressure ≤ 15 mm Hg (2). While the right atrial pressure is higher in idiopathic PAH, it is lower in PVOD. Another distinguishing finding in PVOD is normal or low pulmonary artery occlusion pressure (5, 6).

The use of pulmonary vasodilators does not appear to help in the management of PVOD or in predicting the risk

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Figure 1. CT scan of the thorax with intravenous contrast showing confluent ground-glass opacities (white arrow), thickened septal lines (top black arrow), and mild bilateral pleural effusion (bottom black arrow), which are highly suggestive of PVOD.

of pulmonary edema in the long term (7). One exception to this may be the use of intravenous epoprostenol, which led to significant improvements in symptoms, exercise capacity, quality of life, cardiopulmonary hemodynamics, and survival without

significant development of pulmonary edema in a few studies of patients with PVOD (8).

Histological analysis of lung biopsy is the “gold standard” for definitive diagnosis of PVOD (1). However, since this invasive procedure poses many risks, it is important to seek alternative, less-invasive tools, such as high-resolution CT and right-sided heart catheterization, which may be utilized to make an accurate diagnosis and distinguish PVOD from PAH. High-resolution CT of the chest in PVOD is characterized by 1) centrilobular ground-glass opacities, 2) septal lines, and 3) mediastinal lymphadenopathy. In contrast, normal lung parenchyma is noted among patients with idiopathic PAH (2, 5). The combination of these three CT findings is present in up to 75% of histologically proven cases, with a sensitivity of 75% and specificity of 84.6% (1). Hence, CT represents an important diagnostic tool.

PVOD is a progressive condition that is managed symptomatically. The prognosis appears to be more dismal than for idiopathic PAH, with a 1-year mortality rate as high as 75% (2). Studies have shown that the average time from first symptom onset to death or lung transplantation was significantly

Figure 2. Hemodynamic tracings during right heart catheterization. (a) Pulmonary arterial occlusion pressure of 1 to 2 mm Hg. (b) Mean pulmonary arterial pressure of 56 mm Hg.

Table 1. A comparison of selected characteristics of idiopathic pulmonary arterial hypertension and pulmonary veno-occlusive disease

Characteristic	Idiopathic pulmonary arterial hypertension	Pulmonary veno-occlusive disease
Anatomic site affected	Precapillary arteriolar vascular remodeling	Postcapillary venular proliferation
Gender predominance	Female predominance	Female:Male $\approx$ 1:1
Tobacco exposure	Unrelated	More frequent/higher exposure
High-resolution chest computed tomography	Normal findings	Ground-glass opacities, thickening of septal lines, mediastinal lymphadenopathies, bilateral pleural effusions
Hemodynamics	RAP is usually high (≥ 10 mm Hg), PAOP is usually low (≤ 15 mm Hg)	RAP is usually lower (< 5 mm Hg), as is PAOP (≤ 5 mm Hg)
Response to pulmonary vasodilators	Improves hemodynamics, functional status, and survival	Increased risk of pulmonary edema

RAP indicates right atrial pressure; PAOP, pulmonary artery occlusion pressure.

lower in severe PVOD cases than in idiopathic PAH cases, indicating that PVOD is more severe and progressive. Therapy is primarily focused on symptomatic management due to limited definitive treatment options for PVOD. Lung transplantation represents the treatment of choice and is the only therapeutic option capable of improving survival in patients with PVOD. Single- and double-lung transplantation procedures have both been used. Therefore, early diagnosis and lung transplantation are key prognostic factors in PVOD.

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