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Pulmonary Vascular Diseases

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INTRODUCTION

Pulmonary vascular diseases are a heterogenous group of disorders with multiple causes that directly affect the pulmonary vessels, as in idiopathic pulmonary arterial hypertension (PAH), or are caused by other disorders, as in pulmonary hypertension associated with lung disease and hypoxemia. This chapter considers diseases of the pulmonary circulation characterized by vascular remodeling and pulmonary hypertension, followed by pulmonary thromboembolism.

The World Health Organization (WHO) classification of pulmonary hypertensive disorders is presented in Table 18-1. The hallmark of these disorders is pulmonary hypertension, defined by a mean pulmonary artery pressure greater than 25 mm Hg at rest. Factors that increase pulmonary arterial pressure include increases in cardiac output, left atrial pressure, or blood viscosity, and most importantly, loss of cross-sectional area of the vascular bed, which increases vascular resistance. Loss of cross-sectional area may result from mechanical occlusion, loss of vessels, vascular remodeling, or vasoconstriction.

Clinical manifestations of pulmonary hypertension may not be exhibited until late in the course of the disease because the normal pulmonary vasculature is a high-flow, low-resistance, highly compliant system with very high capacitance. The normal pulmonary circulation can accept the entire output of the right ventricle with only slight increases in pressure.

For a deeper discussion on this topic, please see Chapter 68, "Pulmonary Hypertension," in Goldman-Cecil Medicine, *25th Edition.*

IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

Definition and Epidemiology

Idiopathic PAH is an uncommon disorder that is progressive and usually fatal without treatment. The median survival time after diagnosis of the disease is about 3 years without treatment (level 1 evidence). Variables associated with poor survival include heart failure, Raynaud's phenomenon, elevated right atrial pressure, significantly elevated mean pulmonary arterial pressure, and decreased cardiac index.

The peak incidence of idiopathic PAH occurs between the ages of 20 and 45 years, and it affects women more frequently than men. The cause of idiopathic PAH is unknown. However, some cases occur in families, called *heritable pulmonary arterial hypertension*. Heritable PAH is caused by mutations in the genes for bone morphogenetic protein receptor type 2 *(BMPR2)* and related receptors in the transforming growth factor-β family. PAH may also be associated with other disorders, such as human immunodeficiency virus (HIV) infection, scleroderma, hepatic cirrhosis, and anorectic drug use (see Table 18-1).

Pathology

The histologic characteristics of PAH include changes in the arterial and venous systems. The arteries are more commonly affected, with changes in the intima, media, and adventitia. There is medial vascular smooth muscle hypertrophy, adventitial thickening, and in situ thromboses of small pulmonary arteries. Plexogenic pulmonary arteriopathy is the classic pathologic finding in PAH, consisting of medial hypertrophy, intimal proliferation and fibroelastosis, and necrotizing arteritis. The plexiform lesion is an abnormal proliferation of pulmonary endothelial cells with slit-like channels seen only in PAH (E-Fig. 18-1).

Clinical Presentation

The clinical presentation of idopathic PAH can be subtle. The usual symptoms are dyspnea on exertion or chest pains that are not typical of angina pectoris. In more severe cases, patients may have syncope on exertion caused by the inability of the restricted pulmonary circulation to accommodate increased cardiac output with exercise. The WHO has classified the severity of symptoms in PAH (i.e., dyspnea, fatigue, chest pain, and syncope) in terms of functional ability: class I (symptoms with strenuous activity only), class II (symptoms with normal activity), class III (symptoms with activities of daily living), and class IV (symptoms with any physical activity; right heart failure, dyspnea, or fatigue may occur at rest).

Chest radiographs may reveal prominent pulmonary arteries or right ventricular enlargement (E-Fig. 18-2). Pulmonary function test results are usually normal, with the exception of diffusing capacity, which is usually decreased, reflecting the restricted circulation and decreased surface area available for gas exchange.

Diagnosis and Differential Diagnosis

The diagnosis of PAH depends on exclusion of other underlying heart or lung diseases that might cause pulmonary hypertension (see Table 18-1). In cases of PAH (group 1), the echocardiogram may reveal enlarged right atrial and right ventricular cavity size and encroachment of the interventricular septum on the left ventricle (E-Fig. 18-3). The echocardiogram also may be used to