HEPATOPULMONARY SYNDROME AND PORTOPULMONARY HYPERTENSION

The effects of cirrhosis and portal hypertension on the pulmonary circulation manifest as two distinct disorders, hepatopulmonary syndrome (HPS) and portopulmonary hypertension (PoPH).

Hepatopulmonary Syndrome

HPS occurs in 5% to 30% of patients with cirrhosis and is a progressive disease. It is characterized by gas exchange abnormalities (increased alveolar-arterial gradient and hypoxemia) resulting from intrapulmonary vascular dilation. The vascular dilation leads to vascular remodeling and angiogenesis, resulting in impaired oxygen transfer from the alveoli to the central stream of red blood cells within capillaries. Usually, this functional intrapulmonary right-to-left shunt significantly improves with the administration of 100% oxygen. HPS also has been reported in cases of hepatic venous outflow obstruction without cirrhosis.

Diagnosis

HPS is diagnosed based on high clinical suspicion and measurement of a widened alveolar-arterial oxygen gradient on room air in the presence or absence of hypoxemia. The gradient is calculated by analyzing arterial blood gases. HPS is graded from mild, in which the arterial partial pressure of oxygen (PaO_2) is greater than 80 mm Hg) to very severe (PaO_2 <50 mm Hg). Intrapulmonary shunting is demonstrated by contrast echocardiography, in which agitated saline is injected into a peripheral vein during the performance of two-dimensional echocardiography. Delayed appearance of microbubbles in the left cardiac chambers (more than three to six cardiac cycles after injection) indicates intrapulmonary vasodilation. Early visualization of microbubbles in the left cardiac chambers indicates intracardiac shunting. Other tests, including chest radiography, computed tomography, and pulmonary function tests, are performed to exclude intrinsic cardiopulmonary disorders.

Clinical Presentation

Clinical features range from subclinical abnormalities in gas exchange to profound hypoxemia causing significant dyspnea. Classically in HPS, the dyspnea is worse on standing and improves when the patient lies down (orthodeoxia and platypnea, respectively). Patients may also have marked nocturnal hypoxemia.

Screening and Treatment

Screening by pulse oximetry typically targets patients with values lower than 96% at rest on room air for further evaluation. However, no generally accepted guidelines exist. Currently, there is no established medical therapy for HPS. Liver transplantation remains the only option and reverses HPS in most patients. The use of TIPS to treat HPS is not established.

Prognosis

HPS carries a mortality rate of up to 40% in 2.5 years.

PORTOPULMONARY HYPERTENSION

PoPH is defined as the presence of pulmonary arterial hypertension in the setting of portal hypertension.

Diagnosis and Pathology

The diagnosis of PoPH is based entirely on results of right heart catheterization. The diagnostic values include a mean pulmonary arterial pressure greater than 25 mm Hg at rest or 30 mm Hg with exercise, a pulmonary capillary wedge pressure lower than 15 mm Hg, and a pulmonary vascular resistance greater than 240 dynes, all in the presence of portal hypertension or liver disease or both. PoPH is graded according to the mean pulmonary artery pressure, from mild (>25 to 35 mm Hg) to moderate (35 to 50 mm Hg) to severe (>50 mm Hg). Patients with mild PoPH do not appear to have increased operative risk. Moderate PoPH carries a high intraoperative risk and should be medically managed before transplantation. Severe PoPH is generally considered a contraindication to surgery. The exact mechanisms of PoPH are poorly understood. Histologically, it has characteristics similar to those of pulmonary hypertension.

Clinical Presentation

The most common symptom of PoPH is dyspnea on exertion, but many cirrhotic patients with PoPH are asymptomatic.

Treatment

In addition to symptomatic treatment (oxygen for dyspnea and diuretics for volume overload), the medical management of PoPH is similar to that for pulmonary arterial hypertension. Small studies have shown benefit for the use of intravenous vasodilator (prostacyclin) therapy, oral treatments including phosphodiesterase inhibitors, and endothelin receptor antagonist.

If moderate PoPH responds to therapy, liver transplantation may be considered. However, it has not been established whether successful liver transplantation reliably reverses PoPH. Liver transplantation is contraindicated in severe PoPH because of high transplant-related morbidity and mortality.

Prognosis

Untreated PoPH carries high rates of morbidity and mortality; the mean survival time from diagnosis is 15 months. A study on the U.S.-based Registry to Evaluate Early and Long-term Pulmonary Arterial Hypertension Disease Management (REVEAL) showed a 5-year survival rate of 40% from the time of diagnosis in patients with PoPH.

HEPATOCELLULAR CARCINOMA

Epidemiology

Liver cancer is the fifth most common cancer in men and the seventh most common in women worldwide; HCC is the most common type of liver cancer. In the United States, approximately 90% of liver cancers are HCC, and cholangiocarcinomas account for most of the rest. In other areas of the world, including sub-Saharan Africa, China, Japan, and Southeast Asia, HCC is one of the most frequent malignancies and is an important cause of mortality, particularly among middle-aged men.

Etiology

HCC often arises from a cirrhotic liver, and it is closely associated with chronic viral hepatitis. Hepatitis B virus DNA has been shown to integrate into the host cell genome, where it may