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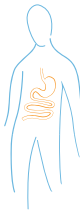

Cirrhosis of the Liver and Its Complications

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LIVER CIRRHOSIS

Definition

Cirrhosis is a slowly progressive disease that is characterized by formation in the liver of fibrous and scar tissue which eventually replaces normal hepatocytes and impairs portal blood flow. Fibrosis can be a self-perpetuating result of many initial processes, including infectious, inflammatory, toxic, metabolic, genetic, and vascular insults that lead to liver damage. Most of the clinical features of cirrhosis develop as a result of portal hypertension, hepatocellular dysfunction, or altered cellular differentiation.

Etiology

Nonalcoholic fatty liver disease (NAFLD), alcoholic liver disease, and hepatitis C virus infection are the most common causes of cirrhosis in industrialized nations; hepatitis B virus is the major cause in Asia and in most of Africa. There are many other significant causes of cirrhosis, including biliary cirrhosis (primary and secondary), autoimmune hepatitis, inherited diseases (e.g., α_1-antitrypsin deficiency), and drug-induced injury, that require specific evaluation. However, a significant number of patients with cirrhosis at presentation have no readily identifiable cause. These cases are referred to as idiopathic or cryptogenic in origin, and it remains a diagnosis of exclusion. Common and uncommon conditions that may lead to cirrhosis are listed in Table 43-1. Chronic active hepatitis, NAFLD, and α_1-antitrypsin deficiency are discussed in Chapter 41.

Pathology

The typical sequence of events that leads to development of cirrhosis involves significant hepatocyte injury followed by ineffective repair that results in hepatic fibrosis. The injury can be acute or chronic in nature, depending on the mechanism. The fibrotic response to injury leads to development of nodules surrounded by fibrous tissue that consist of foci of regenerating hepatocytes, formation of fibrovascular membranes, rearrangement of blood vessels, and finally cirrhosis. This disruption of the normal hepatic lobular architecture distorts the vascular bed and contributes to development of portal hypertension and intrahepatic shunting. On gross morphology, cirrhosis can be referred to as macronodular (>3 mm), commonly seen as a result of chronic active hepatitis, or micronodular (<3 mm) a typical feature of alcoholic cirrhosis or cirrhosis of mixed origin.

TABLE 43-1 COMMON CAUSES OF CIRRHOSIS

Alcohol abuse	Drug-induced liver injury (DILI)
Nonalcoholic steatohepatitis	Autoimmune hepatitis
Viral hepatitis (chronic hepatitis B, C, and D)	Primary biliary cirrhosis
Cardiac cirrhosis	Hemochromatosis (primary and secondary)
Chronic right-sided heart failure	Wilson's disease
Constrictive pericarditis	α_1-antitrypsin deficiency

Clinical Presentation

Symptoms of liver cirrhosis are often nonspecific in the early stages and include fatigue, malaise, weakness, weight change, anorexia, and nausea. With progression of portal hypertension or loss of hepatocytes, increased abdominal girth, sexual dysfunction, altered mental status, and gastrointestinal bleeding may be noted. Physical findings depend on the stage at presentation. Table 43-2 highlights the pathogenetic mechanisms underlying these diverse signs and symptoms.

Diagnosis

Owing to significant reserves of liver function, patients with cirrhosis are often asymptomatic and the diagnosis is established incidentally at the time of physical examination or laboratory testing. Alternatively, patients abruptly experience specific life-threatening complications of cirrhosis, most notably variceal bleeding, ascites, spontaneous bacterial peritonitis, and hepatic encephalopathy (HE). If cirrhosis is suspected on clinical grounds, the diagnosis can be made reliably by a combination of clinical, laboratory, and radiologic findings in most cases. However, liver biopsy is still considered the "gold standard" for accurate diagnosis. With advances in imaging, biopsy is now done more often to assess the stage and severity of disease, assign prognosis, and monitor the response to treatment.

Laboratory Findings

Hepatocellular dysfunction leads to impaired protein synthesis (hypoalbuminemia), hyperbilirubinemia, low levels of blood urea nitrogen (BUN), and elevated serum ammonia levels. Portal hypertension causes hypersplenism, which results in anemia, thrombocytopenia, and leukopenia. Patients with ascites often develop dilutional hyponatremia as a result of avid renal retention of sodium (Na^+) and water. The liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are good markers of active hepatocyte necrosis, whereas elevations of alkaline phosphatase and bilirubin out of proportion to