3 FIBROSIS AND CIRRHOSIS

When hepatic injury persists, liver regeneration may fail to restore the lost tissue. Fibrosis is a wound healing process leading to excessive accumulation of extra-cellular matrix (ECM) proteins. Hepatic stellate cells give rise to myofibroblasts upon activation, which are the major source of excess ECM during fibrogenesis. In the normal liver, collagen types I and III are concentrated in portal tracts and around central veins and can be stained by trichrome. Type IV collagen is present in the space of Disse, as highlighted by the reticulin stain (1). When chronic liver disease persists, excess collagen types I and III deposit in portal tracts and along individual liver cell plates within the space of Disse. This creates fibrous septa and severe alterations to sinusoidal ultrastructure (2). Cell death, deposition of aberrant extracellular matrix (fibrosis) and vascular reorganization are three major contributors to cirrhosis. Obliteration of small hepatic and portal vein thrombosis occurs and creates parenchymal extinction.

Parenchymal extinction (Figure 3-1) is defined as areas of contiguous hepatocyte loss and plays a critical role in the pathogenesis of cirrhosis (3). Loss of parenchyma causes vascular remodeling and connection between afferent and efferent liver vessels (shunt formation), leading to a profound imbalance of blood flow and further hepatocyte necrosis. Areas of parenchymal extinction are progressively replaced by fibrotic scars. Numerous, independent, and discrete areas of parenchymal extinction throughout the liver contribute to cirrhosis. If a fragment of parenchymal extinction is present in a small biopsy, it is indicative of cirrhosis in the absence of nodule formation in the biopsy.

CIRRHOSIS

It is defined by the presence of fibrous septa throughout the liver that subdivide the parenchyma into nodules (Figure 3-2). Common causes of cirrhosis include viral hepatitis, alcoholic and non-alcoholic steatohepatitis, biliary disease, metabolic disorders, hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency, venous outflow obstruction, and autoimmune disease. Cirrhosis is a risk factor for hepatocellular carcinoma. As such, we should evaluate for this possibility regardless of the underlying disease process.

Micronodular cirrhosis is a term traditionally used when cirrhotic nodules are smaller than 3 mm; alcohol abuse is the most frequent cause in North America. When nodules are greater than 3mm, the term macronodular cirrhosis is utilized by some. In reality, cirrhotic livers often present a mix of both micro and macronodular features, and these are non-specific findings that offer little diagnostic value.

FIBROSIS

It can start from the portal triads or central veins. The majority of the disease process is portal

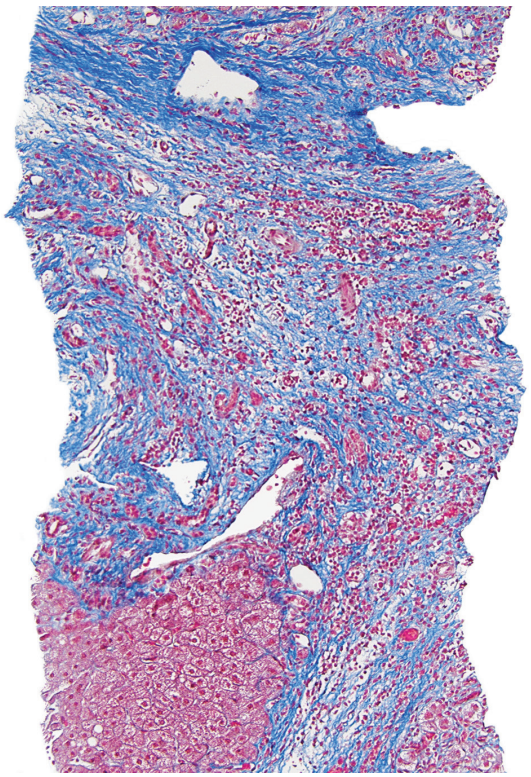

Fig. 3-1. Parenchymal extinction. It is defined as areas of loss of contiguous hepatocytes.

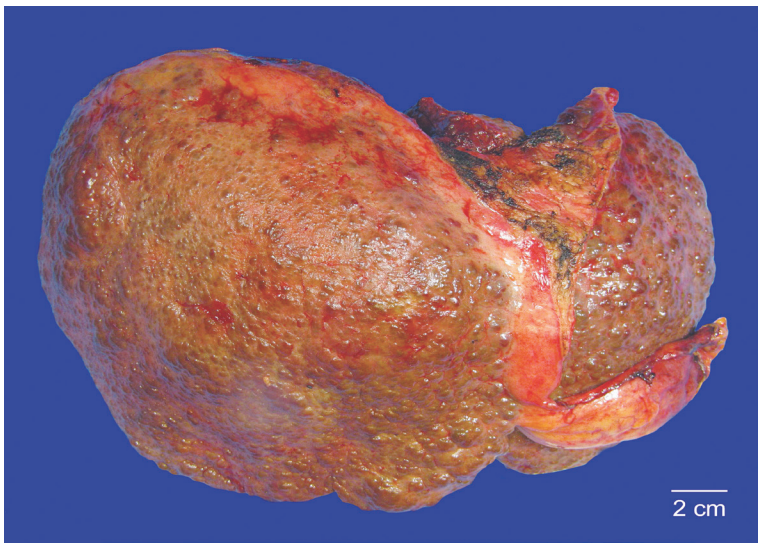

Fig. 3-2 Alcoholic cirrhosis. Micronodules are present at the surface of the liver.

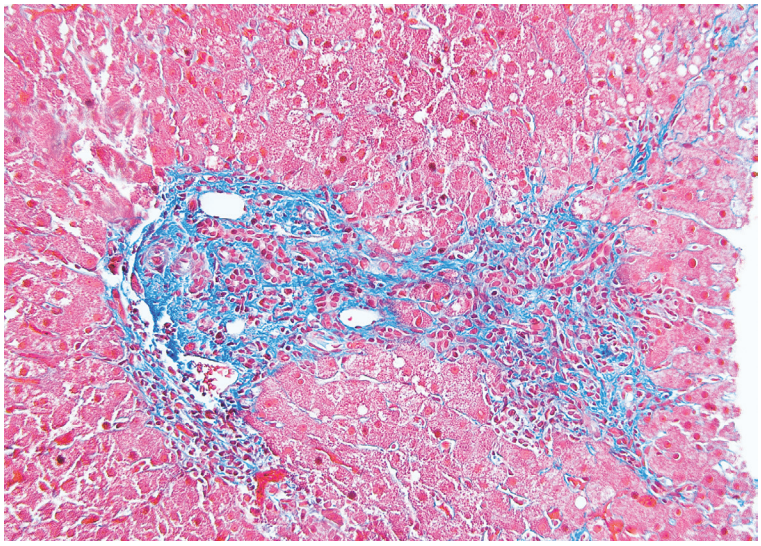

Fig. 3-3. Periportal fibrosis. The portal tracts have thin irregular fibrous extensions

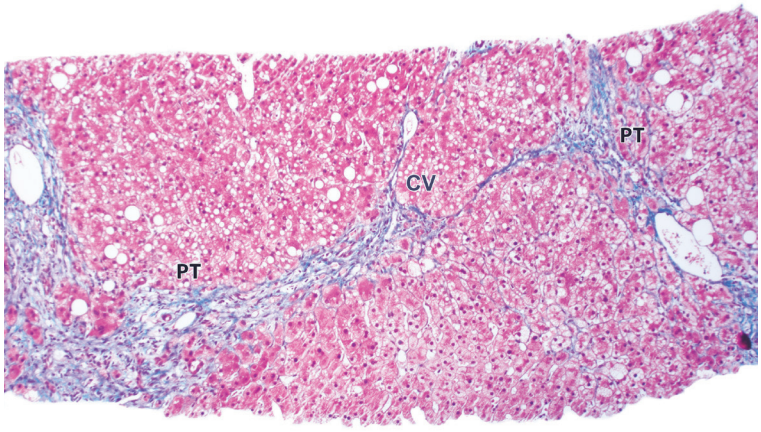

Fig. 3-4. Bridging fibrosis. This patient has steatohepatitis. Fibrous bands connect the portal tract (PT) to the central vein (CV).