The Pathology of Alcoholic Liver Disease

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KEYWORDS

• Steatosis • Alcoholic steatohepatitis • Ballooning degeneration • Cholestasis
• Sinusoidal fibrosis • Cirrhosis

KEY POINTS

- Macrovesicular steatosis is a common pathologic feature present in a wide variety of inflammatory, toxic, congenital, metabolic, and neoplastic diseases that affect the liver, including alcoholic liver disease.
- There is a continuum between macrovesicular steatosis and steatohepatitis, but when evidence of parenchymal inflammation and hepatocyte injury is present, a diagnosis of steatohepatitis is appropriate.
- Histologic distinction between alcoholic and nonalcoholic fatty liver disease is often impossible, but certain morphologic features are highly suggestive of alcohol as the source of liver injury.
- Accurate staging of fibrosis in cases of alcoholic liver disease is important for clinical management and prognostic purposes.
- Many patients with alcoholic liver disease have additional sources of liver injury, and detection of coexisting conditions has important therapeutic implications.

INTRODUCTION

In his seminal treatise *On Diseases of the Liver* from 1857, British physician George Budd vividly describes[1]

> *…a liver…taken from a drunkard…in a state of cirrhosis, as well as of fatty degeneration, [that] in consequence presented [with] a very remarkable "hob-nailed" appearance, from the nodules of cirrhosis being enlarged by the accumulation of oil. A portion of it blazed when thrown into the fire, and a particle from the lobular substance had under the microscope almost the appearance of ordinary fat tissue, from the number and size of the oil-globules it contained.*

Although evaluation of liver flammability is no longer a routine element of the diagnostic work-up for alcoholic liver disease, the gross and microscopic features of this

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condition remain striking to this day. Alcoholic liver disease is still one of the leading causes of liver failure in the United States and worldwide, and given the potentially reversible nature of this condition, the pathology of alcoholic liver disease remains a topic worthy of review.

The term "alcoholic liver disease" encompasses a spectrum of pathologic conditions ranging from isolated steatosis to established cirrhosis. Within this spectrum, varying degrees of inflammation, hepatocyte ballooning and necrosis, cholestasis, and fibrosis may be encountered. This article reviews the characteristic histologic features of the many forms of alcoholic liver disease.

STEATOSIS (FATTY LIVER)

Macrovesicular steatosis (Fig. 1) is a common pathologic feature present in a wide variety of inflammatory, toxic, congenital, metabolic, and neoplastic diseases that affect the liver. Although other causes of clear cytoplasmic vacuolization of hepatocytes must always be kept in mind, most do not cause displacement of the nucleus to the cell membrane, which is the characteristic feature of macrovesicular steatosis. A component of microvesicular steatosis, or small droplets of fat that do not cause nuclear displacement, may also be present (Fig. 2), particularly in the setting of binge drinking with acute decompensation (see later discussion of alcoholic foamy degeneration). The pathogenesis of lipid deposition in hepatocytes is beyond the scope of this discussion.

Steatosis in alcoholic liver disease is usually present in a centrilobular distribution (Fig. 3), although it may also be diffuse. Abstinence from ethanol is said to lead to disappearance of steatosis, although the duration of abstinence required for complete resolution of steatosis is hard to pinpoint. Certainly most patients with alcoholic cirrhosis who abstain to be listed for liver transplantation have minimal or no steatosis evident at 6 to 12 months after cessation of alcohol use, when the native liver is removed. In patients with only alcoholic steatosis, disappearance of lipid usually occurs within 1 to 3 months. However, small lipogranulomas, or aggregates of histiocytes and inflammatory cells surrounding extracellular lipid droplets, may be seen in the lobules or portal tracts long after the steatosis resolves. These

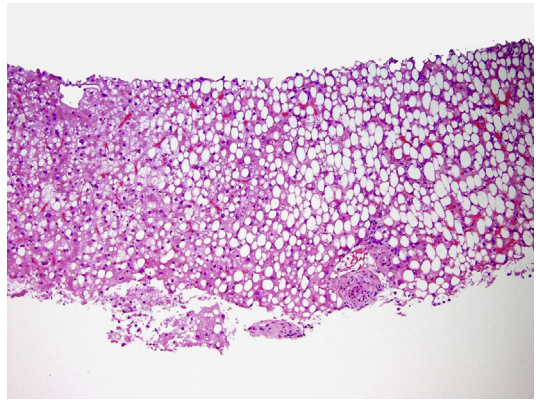

Fig. 1. Macrovesicular steatosis. The hepatocytes contain single clear vacuoles that occupy almost all the cytoplasm. There is no lobular inflammation, hepatocyte ballooning degeneration or necrosis, or Mallory-Denk bodies, ruling out steatohepatitis (hematoxylin-eosin, original magnification ×40).