Liver Biopsy in Primary Biliary Cholangitis

Indications and Interpretation

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KEYWORDS

• Liver biopsy • Histopathology • Primary biliary cholangitis
• Antimitochondrial antibody

KEY POINTS

- Primary biliary cholangitis is a disease characterized by immune-mediated bile duct destruction, followed by inflammation, scarring, and the development of chronic cholestasis and a slow progression to cirrhosis over the course of years.
- Liver biopsy is used in conjunction with clinical evaluation and serologic autoantibody testing to establish the diagnosis, but it is not required in typical cases.
- Liver biopsy is required to establish the diagnosis of PBC or alternative diagnoses in AMA-negative patients with unexplained chronic cholestasis.
- Liver biopsy is useful in assessing stage of disease and degree of progression, and it is the gold standard by which noninvasive tests are evaluated.

INTRODUCTION

Liver biopsy has traditionally been the gold standard in diagnosis of many diffuse or localized liver diseases and in the assessment of their severity.[1] Despite advances in laboratory tests, molecular diagnosis, and imaging, examination of liver biopsy specimens remains a source of otherwise unobtainable qualitative information about the structural integrity of the liver and changes that occur in liver diseases. Although a needle liver biopsy remains a primary tool for the diagnosis of liver diseases and for the staging of liver fibrosis, in the case of primary biliary cholangitis (PBC), liver biopsy is no longer recommended for diagnosis. Instead, careful clinical evaluation to exclude other causes of chronic cholestasis, followed by serologic screening for antimitochondrial antibody (AMA) and PBC-specific antinuclear antibodies, ultrasound, and magnetic resonance cholangiopancreatography imaging are recommended before

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considering a liver biopsy for diagnosis, whereas response to initial therapy and evaluation of liver stiffness are often sufficient for assessment of short-term prognosis.[2] Liver biopsy is most often indicated when atypical clinical or laboratory features are present or when there is doubt about the diagnosis or stage of disease.

PATHOLOGY AND PATHOGENESIS OF PRIMARY BILIARY CHOLANGITIS

Although early descriptions of patients with this disease date to the mid-nineteenth century, the first series with detailed description and the name "primary biliary cirrhosis," popularly called PBC, was published by Ahrens and colleagues[3] in 1950. Because the initial patients were at the end-stage of the disease, it was named a form of cirrhosis, but subsequent reports of earlier stage disease and elucidation of its natural history made the term a misnomer. Nevertheless, attempts to rename the disease were unsuccessful until the recent change to PBC with retention of the acronym PBC.[4]

Early Stage Primary Biliary Cholangitis

Rubin and coworkers[5] provided the first description of the key early lesion, chronic nonsuppurative destructive cholangitis, also frequently called the florid duct lesion (**Figs. 1–3**).[6] With careful observation, they and subsequent authors deduced the sequence of events and corresponding histologic lesions leading to end-stage cirrhosis.[5–8] The early stage is characterized by immune-mediated destruction of small interlobular bile ducts caused by aberrant expression of the E2 subunit of pyruvate dehydrogenase complex, the same antigen that is the target of AMA. Bile duct epithelial cell damage is mediated primarily by $CD8^+$ cytotoxic T cells along with a variable number of other inflammatory cells. B cells with occasional lymphoid follicles may be present, whereas eosinophils and plasma cells are sometimes numerous. Damaged ducts show epithelial cell irregularity, swelling, or apoptosis, usually with infiltration by lymphocytes and often with disruption of the basement membrane (see **Figs. 1–3**). The ducts may rupture, and there may be neutrophils or granulomatous inflammation in response to bile leaking from the damaged ducts. Affected bile

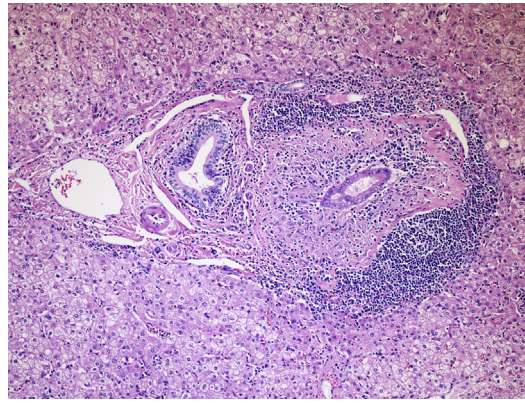

Fig. 1. Early stage PBC. A medium-size portal area with chronic lymphoplasmacytic inflammation and two damaged bile ducts. The duct on the left shows epithelial cell damage with irregular nuclear pseudostratification and infiltration by inflammatory cells, predominant lymphocytes. The duct on the right is more severely damaged with cytoplasmic eosinophilia surrounding granulomatous inflammation (hematoxylin-eosin ×40).