Autoimmune Hepatitis Overlap Syndromes and Liver Pathology

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KEYWORDS

• Autoimmune hepatitis • Overlap • Variants • Cholestatic • Histologic findings

KEY POINTS

- Autoimmune hepatitis may have cholestatic laboratory and histologic features that resemble primary biliary cholangitis, primary sclerosing cholangitis, or a cholestatic syndrome.
- Histologic findings may include destructive and nondestructive cholangitis, portal edema, portal fibrosis, periductal fibrosis, and ductopenia.
- Serum alkaline phosphatase levels greater than 2-fold the upper limit of normal range, concurrent inflammatory bowel disease, antimitochondrial antibodies, and recalcitrance to corticosteroid therapy are key clinical manifestations.
- Evaluation should include histologic assessment and endoscopic retrograde or MR cholangiography.
- Treatment recommendations emphasize mainly combination therapy with prednisone or prednisolone, azathioprine, and ursodeoxycholic acid, and outcomes vary depending on the predominant disease component.

INTRODUCTION

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease that is characterized by the presence of autoantibodies, hypergammaglobulinemia (especially increased serum levels of immunoglobulin G), and histologic findings of interface hepatitis (Fig. 1).[1–3] Lymphocytic aggregates in the portal tracts typically accompany interface hepatitis and, in 66% of patients, portal plasma cells are prominent (Fig. 2).[4] None of the serologic, laboratory, or histologic features of AIH is disease specific, and the diagnosis requires the presence of a constellation of compatible findings

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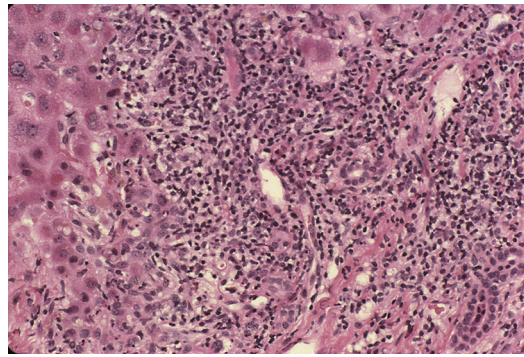

Fig. 1. Interface hepatitis associated with classical autoimmune hepatitis. Lymphoplasmacytic infiltrates extend from the portal tract into the acinar tissue with disruption of the limiting plate. Original magnification ×200. Hematoxylin and eosin stain.

and the exclusion of virus-related, drug-induced, alcoholic, metabolic, and hereditary liver diseases.[3,5]

The diagnostic criteria for AIH have been codified by the International Autoimmune Hepatitis Group,[6] and a revised comprehensive scoring system and a simplified diagnostic scoring system have been promulgated to aid in the diagnosis of difficult cases.[6–8] All diagnostic algorithms have emphasized the inflammatory components of AIH and the absence of prominent cholestatic manifestations.[9,10] The presence of cholestatic features in a patient with otherwise classical AIH constitutes a phenotype that must be categorized separately and managed individually.[11–14] The variable response of such patients to conventional immunosuppressive therapy is the most compelling reason for their early recognition.[11,13,14]

Three major cholestatic phenotypes of AIH have been described, and they constitute the overlap syndromes (**Table 1**).[13,14]

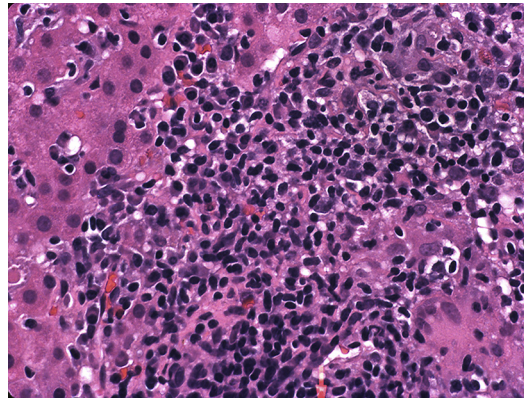

Fig. 2. Portal plasma cells associated with classical autoimmune hepatitis. Plasma cells characterized by cytoplasmic halo around the nucleus infiltrate the hepatic parenchyma. Original magnification ×400. Hematoxylin and eosin stain. (*From* Czaja AJ, Carpenter HA. Optimizing diagnosis from the medical liver biopsy. Clin Gastroenterol Hepatol 2007;5(8):899; with permission.)