Autoimmune Hepatitis

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KEYWORDS

• Autoimmune hepatitis • Chronic hepatitis • Overlap syndrome • Interface hepatitis • Autoantibodies • Diagnostic criteria • Histology • Differential diagnosis

ABSTRACT

Autoimmune hepatitis is a chronic necroinflammatory disease of unknown cause that is characterized by increased aminotransferases, autoantibodies, increased immunoglobulin G levels, and histologic interface hepatitis. Diagnostic criteria have been developed to aid in the differentiation from other liver disorders. Liver biopsy is an essential part of the diagnostic criteria and is also crucial to the management of the disease. This article presents an updated review of the diagnosis of autoimmune hepatitis, focusing on the microscopic features of the disease and their differential diagnosis. An overview of the variant phenotypes of autoimmune hepatitis, including overlap syndromes, is also presented.

Pathologic Key Features OF AUTOIMMUNE HEPATITIS

1. The hallmark of autoimmune hepatitis is interface hepatitis with lymphoplasmacytic infiltrates and varying degrees of lobular inflammation and damage.
2. Additional helpful features include hepatocyte rosette formation, emperipolesis, giant syncytial hepatocytes, and a lack of changes suggesting a different cause.
3. Acute-onset autoimmune hepatitis is characterized by panacinar hepatitis and/or centrilobular perivenulitis with or without interface activity.
4. Approximately 36% of patients with autoimmune hepatitis are cirrhotic at the time of presentation.

OVERVIEW

Autoimmune hepatitis (AIH) is a chronic necroinflammatory disease of unknown cause that is characterized by increased aminotransferases, autoantibodies, increased immunoglobulin G (IgG) levels, and histologic interface hepatitis. AIH has an incidence of 1 to 2/100,000 per year and a prevalence of 10 to 20/100,000.[1] It affects children and adults of all ethnicities and races, but is predominantly a female disorder with peak incidences in adolescence and again at ages 35 to 40 years.[1] A recent population-based survey found that 72% of cases are diagnosed in patients after age 40 years.[2] The presentation of AIH is highly variable and ranges from an asymptomatic increase of aminotransferases, to acute fulminant liver failure, to cirrhosis. Associations with other autoimmune diseases such as autoimmune thyroiditis, inflammatory bowel disease, rheumatoid arthritis, Graves disease, and celiac disease are common.[1] The clinical, laboratory, and histologic manifestations of AIH are found in a diverse group of acute and chronic liver diseases, and consequently the diagnosis of AIH requires the definitive exclusion of other causative factors. The examination of liver tissue is an essential component in this discriminative process.

DIAGNOSIS OF AIH

It is well recognized that timely and appropriate treatment of AIH leads to favorable short-term and long-term outcomes in most patients, although untreated disease confers a poor prognosis.[3] Because undiagnosed AIH means untreated AIH, it is critical for the disease to be identified in a timely

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fashion. However, this can be challenging, in part because AIH does not have a pathognomonic clinical, laboratory, or histologic feature. It is in conditions that lack such a specific and reliable diagnostic test that diagnostic criteria become particularly useful.[4] In 1992, a panel of physicians and pathologists, who became known as the International Autoimmune Hepatitis Group (IAIHG), convened to establish diagnostic criteria for AIH, and in 1998 met again to revise the initial criteria. Their consensus report included a descriptive set of criteria that could be used in routine clinical practice to diagnose patients as having either definite or probable AIH (**Table 1**).[5] Definite AIH requires both the exclusion of other conditions that may resemble the disease, as well as the presence of a constellation of histologic and laboratory findings that support its diagnosis. The descriptive criteria are sufficient to diagnose or exclude definite or probable AIH in most patients.[6]

Table 1
Revised diagnostic criteria of the IAIHG

Features	Definite AIH	Probable AIH
Liver histology	Interface hepatitis of moderate or severe activity with or without lobular hepatitis or central-portal bridging necrosis, but without biliary lesions or well-defined granulomas or other prominent changes suggesting a different cause	Same as for definite AIH
Serum biochemistry	Any abnormality in serum aminotransferases, especially if the serum alkaline phosphatase is not markedly increased. Normal serum concentrations of alpha-antitrypsin, copper, and ceruloplasmin	Same as for definite AIH, but patients with abnormal serum concentrations of copper or ceruloplasmin may be included, provided that Wilson disease has been excluded by appropriate investigations
Serum immunoglobulins	Total serum globulin or gamma globulin or IgG concentrations greater than 1.5 times the upper normal limit	Any increase of serum globulin or gamma globulin or IgG concentrations more than the upper normal limit
Serum autoantibodies	Seropositivity for ANA, SMA, or LKM-1 antibodies at titers greater than 1:80. Lower titers (particularly of anti-LKM-1) may be significant in children. Seronegativity for AMA	Same as for definite AIH but at titers of 1:40 or greater. Patients who are seronegative for these antibodies but who are seropositive for other antibodies specified in the text may be included
Viral markers	Seronegativity for markers of current infection with hepatitis A, B, and C viruses	Same as for definite AIH
Other causal factors	Average alcohol consumption less than 25 g/d. No history of recent use of known hepatotoxic drugs	Alcohol consumption less than 50 g/d and no recent use of known hepatotoxic drugs. Patients who have consumed larger amounts of alcohol or who have recently taken potentially hepatotoxic drugs may be included if there is clear evidence of continuing liver damage after abstinence from alcohol or withdrawal of the drug

Abbreviations: AMA, antimitochondrial antibody; ANA, antinuclear antibody; LKM-1, liver kidney microsome-1 antibody; SMA, smooth muscle antibody.

Adapted from Alvarez F, Berg PA, Bianchi FB, et al. International Autoimmune Hepatitis Group Report: review of criteria for diagnosis of autoimmune hepatitis. J Hepatol 1999;31:929–38.