

Autoantibodies Associated with Autoimmune Hepatitis *Serological Characterization of Two Types of AIH*

Summary:

The presence of specific autoantibodies can help diagnose and categorize patients with autoimmune hepatitis (AIH).

Autoimmune hepatitis (AIH) is a syndrome of unknown origin characterized histologically by periportal hepatocellular inflammation (piecemeal necrosis). Several autoantibodies, as well as liver specific cytotoxic T cells, have been detected in AIH, and are presumably responsible for the tissue damage observed. Based on the binding specificities of the autoantibodies detected, AIH can be grouped into two types.

Type 1 AIH

Formerly known as lupoid hepatitis or autoimmune chronic active hepatitis, type 1 AIH is characterized by the presence of antinuclear antibodies (ANA) and/or actin (smooth muscle) antibodies. The ANA binding specificity varies; ANA recognizing centromere, SS-A, histone, and ribonucleoprotein (RNP) have been observed. Recent studies have demonstrated that smooth muscle antibodies found in association with AIH are primarily directed toward actin.

Assays measuring actin-specific antibodies thus exhibit higher specificity for AIH than assays measuring smooth muscle antibodies. Most (70%) type 1 AIH patients are women, and about 50% are under 30 years of age. The onset of illness is often acute, and may be mistaken for viral hepatitis. Nearly all type 1 AIH patients exhibit hypergammaglobulinemia, particularly elevated IgG levels. Type 1 AIH is by far the most common form of AIH in the United States, accounting for 80-95% of cases.

An additional marker of type 1 AIH, antibodies to soluble liver antigen (SLA), was recently described. Although SLA antibodies were once considered to be synonymous with cytokeratin antibodies, elegant studies using molecular techniques have shown this concept to be incorrect. Rather, SLA antibodies are identical to antibodies recognizing liver-pancreas (LP) antigen, and bind to a transfer-RNA (tRNA)-associated protein. Before the target antigen of SLA antibodies was known, SLA antibody-positive AIH patients were categorized as having type 3 AIH, also called cryptogenic hepatitis. Based on this new information, in conjunction with demographic and

clinical presentation data, it now appears that type 3 AIH should be considered a variant of type 1 AIH.

Recent studies have shown that antibodies recognizing chromatin (DNA complexed with histone proteins) are associated with disease activity in patients with type 1 AIH. Chromatin antibodies are present in approximately 40% of type 1 AIH patients, and identify patients with active disease who commonly relapse after drug withdrawal.

Type 2 AIH

The presence of liver kidney microsomal type 1 (LKM-1) autoantibodies is the hallmark of type 2 AIH. LKM-1 antibodies recognize a linear epitope of cytochrome P450 2D6, a membrane surface protein expressed by human hepatocytes. Actin antibodies and ANA are not found in type 2 AIH patients. Two subgroups of type 2 AIH patients have been identified. Type 2a AIH patients are predominantly children (usually females) under 15 years of age; they typically experience clinically aggressive disease with an unfavorable prognosis.

Extrahepatic syndromes, such as arthritis and thyroiditis, are common in type 2a patients. Type 2b AIH patients are adults (usually older than 40 years of age) with hepatitis C virus infection, but no extrahepatic syndromes. There is no female predominance in type 2b, and the clinical course is usually milder than that observed for type 2a patients. Type 2 AIH is rare, constituting only 4% of AIH cases in the United States. Actin antibodies, LKM-1 antibodies, and SLA antibodies are measured using enzyme-linked immunosorbent assays (ELISA). ANA are measured by IFA using HEp-2 cells as substrate.

Summary

Two types of autoimmune hepatitis can be defined on the basis of clinical presentation and the types of autoantibodies present in patients' sera. Type 1 is associated with actin antibodies, SLA antibodies, and /or antinuclear antibodies; type 2 is associated with LKM-1 antibodies (see Table 1). Focus Diagnostics' Reference Laboratory offers assays to detect all these autoantibodies, thus providing a comprehensive resource for the serologic characterization of patients with suspected AIH.

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Autoantibodies Associated with Autoimmune Hepatitis

Table 1: Serologic Characterization of Autoimmune Hepatitis (AIH)

Syndrome (US)	Autoantibodies	Reported Prevalence
Type 1 AIH	Actin (Smooth Muscle) Antibodies, Antinuclear Antibodies (ANA), and/or Soluble Liver Antigen Antibodies (SLA)	~80 to 95 percent of cases
Type 2 AIH	Liver Kidney Microsomal type 1 (LKM-1) Antibodies Serum or Urine	~ 4 percent of cases

For complete specimen information and CPT codes view our Reference Laboratory test listing on our Web site at www.focusdx.com

Code #	Test Description
4966	Autoimmune Hepatitis Antibody Panel
40665	Actin (Smooth Muscle) Antibody, ELISA
20180	Antinuclear Antibody (ANA), IFA
20199	Liver-Kidney Microsomal Type 1 Antibody, ELISA
41740	Soluble Liver Antigen (SLA) IgG Antibody, ELISA
20505	Chromatin Antibodies, ELISA

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For technical assistance, contact Focus Diagnostics' Scientific Director of Immunology.



800-445-0185 • 714-220-1900 • Fax: 714-220-9213
 Cypress, California 90630 USA
www.focusdx.com