Autoimmune Hepatitis Diagnostic Panel

Test Code: 19873(X)

Specimen Requirements: 2.5 mL refrigerated serum; 0.6 mL minimum

CPT Codes*: 83516, 86038, 86255, 86376

CLINICAL USE

- Diagnose autoimmune hepatitis (AIH)

- Differentiate AIH from primary biliary cirrhosis (PBC)

- Monitor disease activity in children with AIH

CLINICAL BACKGROUND

AIH is a chronic disorder characterized by progressive hepatocellular loss and cell-mediated immunologic attack. Histologic inflammation is present and is usually accompanied by fibrosis, which can progress to cirrhosis and liver failure. AIH accounts for 11% to 23% of chronic liver disease in North America and about 4% to 6% of adult liver transplants in the United States and Europe.[1,2] Early diagnosis and initiation of immunosuppressive therapy are essential to prevent severe liver damage.

Although patients may present with acute symptoms (eg, arthralgia), about 34% to 45% are asymptomatic and are identified subsequent to abnormal liver function tests such as increased alanine and/or aspartate aminotransferase (generally <500 U/L but occasionally 500 U/L to 1000 U/L).[2,3] Elevated levels of globulin, gamma globulin, or immunoglobulin G (≥1.5 times the upper limit of the reference ranges) are typically present.[2] Because the clinical features of AIH overlap with other forms of hepatitis, ruling out hereditary, infectious, and toxicity-related causes of liver disease is an important component of diagnosis.[2] Interface hepatitis (piecemeal necrosis) in liver biopsy tissue is considered essential for diagnosis; portal plasma cell infiltration is typically present but not specific for AIH.[2]

Once other causes of hepatitis have been excluded, several autoantibody markers are useful to support AIH diagnosis.[2] The AIH Diagnostic Panel includes tests for actin (smooth muscle) antibody, antinuclear antibodies (ANAs), and liver/kidney microsome antibody (LKM-1). ANAs and actin antibody are associated with type 1 AIH, the most common form in adults in the United States, while LKM-1 antibody is associated with type 2 AIH, which is more commonly found in children.[2] The panel also includes mitochondrial antibody, which can help differentiate AIH from PBC (see Interpretive Information below). Remission after initiation of immunosuppressive therapy confirms the diagnosis of AIH.[4]

Antibody titers have been found to correlate with disease activity in pediatric AIH patients, whereas the correlation in adults is less clear.[2]

INDIVIDUALS SUITABLE FOR TESTING

- Individuals with chronic or acute hepatitis of unknown cause

- Individuals with allograft dysfunction after liver transplantation

METHOD

- Actin (smooth muscle) antibody (IgG): enzyme-linked immunosorbent assay (ELISA)

- ANA screen: IFA with reflex to titer and pattern when screen is positive (at additional charge [CPT code 86039])

- Liver kidney microsomal (LKM-1) antibody (IgG): ELISA

- Mitochondrial antibody screen: immunofluorescence assay (IFA) with reflex to titer when screen is positive (at additional charge [CPT code 86256])

Table. Antibody Frequencies (%) Observed in AIH and PBC

	Actin Antibody[6,7]	ANA[4,8]	LKM-1 Antibody[4]	Mitochondrial Antibody[5]
AIH type 1	72	67	--[a]	--[a]
AIH type 2	27[b]	--[a]	100	--[a]
PBC	30	50	--[a]	85

AIH, autoimmune hepatitis; PBC, primary biliary cirrhosis; ANA, antinuclear antibody; LKM, liver kidney microsome.

[a] Typically absent.

[b] Data are from one study, n = 22.[7]

Panel components can be ordered separately: actin (smooth muscle) antibody IgG (15043), ANA screen (249), LKM-1 antibody (15038), mitochondrial antibody screen (259).

REFERENCE RANGE

Actin (smooth muscle) antibody (IgG)	Negative: <20 U
	Positive: ≥20 U
ANA screen (IFA)	Negative: <1:40
	Positive: ≥1:40 U
Liver kidney microsome (LKM-1) antibody (IgG)	Negative: <20 U
	Equivocal: 20.1-24.9 U
	Positive: ≥25.0 U
Mitochondrial antibody screen	Negative: <1:20
	Positive: ≥1:20 U

INTERPRETIVE INFORMATION

Antibody patterns associated with AIH types 1 and 2 and PBC are shown in the **Table**. During the course of AIH type 1, actin antibody and ANAs frequently disappear and reappear; thus, negative or weak positive antibody results do not rule out the presence of the disease.[2] Furthermore, patients with negative results in whom other AIH diagnostic criteria are satisfied (13% of patients with AIH) may have soluble liver antigen and/or antineutrophil cytoplasmic antibodies.[1]

The presence of LKM-1 antibody is consistent with AIH type 2. However, LKM-1 antibody has been detected in up to 10% of patients with chronic hepatitis C virus (HCV) infection; if not previously performed, testing for HCV infection should be considered for patients in whom LKM-1 is positive.[1]

Detection of mitochondrial antibody, typically absent in AIH, has a sensitivity of 85% and specificity of 98% for PBC.[5]

Since autoantibody levels in AIH types 1 and 2 are lower in children than in adults, a weak positive or equivocal antibody result in conjunction with other diagnostic criteria may be sufficient for diagnosis in children.[2] Actin (smooth muscle) antibody, but not ANA, titers correlate with disease activity in children with type 1 AIH.[9] For children with type 2 AIH, disease activity correlates with LKM-1 antibody titers.[9]

The presence of immune complexes or other immunoglobulin aggregates in the specimen may lead to false-positive ELISA results. Antibody results should be interpreted in conjunction with other laboratory and clinical findings in patients with suspected AIH.

References

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