自體免疫肝炎 Autoimmune Hepatitis

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Autoimmune hepatitis (AIH) is an unresolving inflammation of the liver of unknown etiology. The pathogenic mechanisms of AIH are unknown. The most popular hypotheses include a triggering agent, genetic predisposition, and displaying autoantigen, and so on. The diagnostic criteria for AIH and a diagnostic scoring system were established by an international panel in 1993 and revised in 1999. The clinical criteria for the diagnosis are sufficient to make definite or probable AIH in the majority of patients. The serologic assays essential for diagnosis are antinuclear antibodies (ANA), smooth muscle antibodies (SMA), and antibodies to liver-kidney microsome type 1 (anti-LKM1). The definite diagnosis of AIH requires exclusion of other diseases with similar manifestation; laboratory findings that indicate certain immunoreactivity; and histologic features of interface hepatitis. A probable diagnosis is considered when findings are compatible with AIH but insufficient for a definite diagnosis. A pretreatment score of 15 points indicates of definite AIH. A pretreatment score of 10 points or higher, or a posttreatment score of 12 points or higher, indicate probable AIH at presentation.

Two types of AIH have distinctive serologic profiles. Type 1 AIH is characterized by SMA, ANA, or both. Type 1 AIH can occur at any age and in either gender. Over third quarters of patients are women, and 38% have concurrent extrahepatic immunologic diseases. Human leukocyte antigen (HLA)-DR3 and HLA-DR4 are independent risk factors for the disease in Western. Type 2 AIH is characterized by the expression of anti-LKM1. Most affected persons are children. The target antigen of type 2 AIH is the cytochrome P450 CYP2D6. The amino acid sequence spanning 193-212 of the CYP2D6 molecule is the target of anti-LKM1. There are homologies between CYP2D6 and the genomes of the hepatitis C virus, cytomegalovirus, and herpes simplex type 1 virus. Several variant forms of AIH (variant with PBC, PSC, cholestatic type and ANA-negative type) are classified as the findings that are incompatible with AIH by current diagnostic criteria.

The clinical features of AIH reflect the inflammatory activity of the liver or the complications of cirrhosis. Most patients with AIH are treated regardless of disease activity at presentation. Prednisone, alone or at a lower dose in combination with azathioprine, is effective therapy. Treatment should be instituted with prednisone (starting with 30 mg daily and tapering down to 10 mg daily within 4 weeks) in combination with azathioprine (50 mg daily or 1-2 mg/kg body weight) or a higher dose of prednisone alone (starting with 40-60 mg daily and tapering down to 20 mg daily within 4 weeks) in adults with AIH. Glucocorticoid therapy is continued until remission, treatment failure, incomplete response, or drug toxicity occurs. The average treatment interval until remission is 22 months. Treatment with glucocorticoids also may reduce hepatic fibrosis. Relapse occurs in 50% of patients within six months of discontinuing therapy. After the initial relapse, therapy with prednisone and azathioprine is re-started and continued until clinical and laboratory resolution is achieved again. Treatment after relapse does not need to be indefinite.