Revised Criteria for Diagnosis of Autoimmune Hepatitis

Key words: primary biliary cirrhosis, primary sclerosing cholangitis

Autoimmune hepatitis (AIH) is one of the autoimmune liver diseases, in which the autoimmune attack against hepatocytes plays an important role in its development and perpetuation. It forms a contrast with primary biliary cirrhosis, the other autoimmune liver disease, in which the primary injured site is in the interlobular and septal bile ducts. The concept of AIH was proposed by Mackay in Australia (1, 2). At the time of his proposal, no hepatitis viruses had been isolated or identified. However the concept of AIH survived the progress of diagnostic modalities for hepatitis virus B, A and C, and other chronic liver diseases.

In Japan where viral hepatitis is more prevalent than in Western countries, we have confronted various difficulties in the diagnosis of AIH. This disease has no specific marker for diagnosis. The positivity for autoantibodies and hypergamma-globulinemia that characterize AIH is also noticed in some patients with viral hepatitis. There are no histological findings specific for AIH. Response to immunosuppressive therapy is characteristic of AIH. However it is hazardous to start the therapy without the firm diagnosis. Another reason for the difficulty confronted is the difference in some clinical features between the patients with AIH in Japan and in Western countries. AIH used to be considered a disease of young females (1, 2). Although the female sex is also predominant in the patients with AIH in our country, young female patients are very rare and almost all female patients were middle-aged (3). Subsequent studies have revealed that the age distribution of Caucasian patients was bimodal, one peak in young females and the other around menopause (4). Another discrepancy is genetic background of the patients. In our country, no patients had a HLA haplotype A1-B8-DR3, which was significantly frequent in the Caucasian patients (5, 6), but 80 to 90% of the patients had HLA-DR4 (7). This discrepancy was solved by a report that the frequency of HLA-DR4 was significantly higher in HLA-DR3-negative Caucasian patients than in the healthy individuals (8). Interestingly HLA-DR4-positive patients were older than HLA-DR3-positive ones (8, 9). Furthermore the clinical presentation and course are more mild in the former patients than in the latter ones. Another difficulty in the diagnosis of AIH was differentiation from virus-induced chronic hepatitis. This was partly solved by the identification of hepatitis C virus in 1989 (10).

Under these circumstances, a diagnostic criteria for AIH was proposed by the International AIH group in 1993 (11). This enabled us to study this disease on the worldwide common basis. This criteria were composed of the descriptive system and scoring one. The international AIH group recommended the former system to be used in routine clinical paractice and the latter to be used for selection of homogeneous groups of patients for research purpose. In the scoring system, positive scores were given to the clinical, laboratory and histological findings compatible with AIH, and negative scores to those which were not compatible with AIH, suggesting an etiology different from AIH. Diagnoses of definite and probable AIH were made in the patients before treatment, when the aggregate scores were 15 or more and 14 to 10, respectively. The aggregate scores under 10 indicated exclusion of AIH. The scoring system was applied to 496 Japanese patients before treatment, who were enrolled in the nationwide survey for AIH in 1995 (12). Diagnosis of AIH in the patients enrolled in this survey was made according to the diagnostic criteria proposed by the Study Group for Intractable Hepatitis supported by the Japanese Ministry of Public Health and Welfare (13). Forty eight % and 45.6% of them were diagnosed as having definite and probable AIH, respectively. The sensitivity was 93.6% and the scoring system does work well in our country. The specificity of the system was tested in patients with primary sclerosing cholangitis (PSC) in Norway and those with primary biliary cirrhosis (PBC), PSC or autoimmune cholangitis in United States, however, 33.3% and 51.7% of them, respectively, gave scores indicative of probable AIH. These findings necessitated revision of the diagnostic criteria, and thus a revised criteria was proposed in 1999 (14). In this new criteria, only minor modifications were made in the descriptive criteria, whereas the negative scores for the biochemical, immunological and histological findings suggestive of biliary diseases, PBC and PSC, were increased in the scoring system. The increased negative score were also conferred on the absence of histological findings suggestive of chronic hepatitis with a high activity and the history suggestive of drug-induced liver injury. Antineutrophilic cytoplasmic antibodies (pANCA) were added to other defined autoantibodies. A negative score for the absence of response to immunosuppressive therapy was omitted in the posttreatment diagnostic criteria. When the scoring system of new criteria was applied to 496 patients before pretreatment, who were enrolled in the nationwide survey in 1995, 50.4% and 40.1% of them were diagnosed as having definite and probable AIH, respectively, giving a sensitivity of 90.5%. In this issue, Omagari et al reported a similar figure for sensitivity on application of the revised scoring system of the pretreatment diagnostic criteria to 89 patients. Taken together, the
revised diagnostic criteria does work well, though the sensitivity was decreased as compared with that obtained in the previous diagnostic criteria (15).

See also p 1008.

As discussed by Omagari et al, the patients with an overlap of AIH with PBC or PSC, in whom immunosuppressive therapy is supposed to be effective to suppress hepatitis, may be classified as others. Although the scoring system is useful for clinical practice, its real value is in making it possible to study AIH on a common scientific basis all over the world. It will make a great contribution to the progress of research on AIH.

Gotaro Toda, MD
The Division of Gastroenterology and Hepatology, Department of Internal Medicine, Jikei University School of Medicine, 25-8 Nishishinbashi, Minato-ku, Tokyo 105-8461

References