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CLINICAL STUDIES

Diagnostic value and utility of the simplified International Autoimmune Hepatitis Group criteria in acute-onset autoimmune hepatitis

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Keywords
autoimmune hepatitis – fulminant hepatitis – liver histology – scoring system – severe hepatitis

Abbreviations
AIH, autoimmune hepatitis.

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Abstract

Background: The diagnosis of autoimmune hepatitis (AIH) is already difficult, and that of acute-onset AIH with atypical features is even more challenging, even though the revised original diagnostic criteria created by an international AIH group were widely accepted and incorporated into clinical practice. *Aims:* Recently, simplified diagnostic criteria were proposed. We compared the performance parameters of the simplified scoring system in patients with acute-onset AIH and examined its usefulness and limitations. *Methods:* Fifty-five patients with acute-onset AIH (29 non-severe, 14 severe and 12 fulminant) were assessed according to the simplified scoring system and compared with the revised original one. *Results:* Of the 55 patients, 22 (40%) were diagnosed as 'definite' AIH, 28 (51%) as 'probable' and five (9%) as 'non-diagnostic' based on the revised original scoring system. By the simplified scoring system, six (11%) were diagnosed as 'definite' AIH, 16 (29%) as 'probable' and 33 (60%) as 'non-diagnostic'. Anti-nuclear antibody titres did not differ among the three groups. The immunoglobulin G level was higher in fulminant than in non-severe patients ($P = 0.01$). Sixty-five per cent showed acute hepatitis (massive necrosis, submassive necrosis and severe acute hepatitis) and 35% showed chronic hepatitis. *Conclusions:* The revised original scoring system performed better in patients with acute-onset AIH than the simplified scoring system.

Autoimmune hepatitis (AIH) is generally regarded as a clinically and histologically 'chronic' hepatitis, characterized by the presence of autoantibodies, hypergammaglobulinaemia and interface hepatitis and plasma cell infiltration on histological examination (1, 2). As AIH patients with clinical features of acute, severe and fulminant hepatitis (acute-onset AIH) do not show such typical features of AIH, they are at a risk of losing the timing for the initiation of immunosuppressive therapy and are sometimes resistant to the therapy in liver regeneration and have a poor prognosis. The survival rate of fulminant AIH has been $< 20\%$ without liver transplantation, and this is recognized everywhere around the world as well as in our unit (3–6).

Diagnostic criteria for AIH based on the clinicopathological features were created by an international AIH group in 1993 (7) and revised in 1999 (8), and were widely accepted and incorporated into clinical practice. Nevertheless, the diagnosis of AIH is still a challenging task, and especially in patients with atypical features. There is no gold standard for making the diagnosis, and the diagnosis of acute-onset AIH is the most challenging.

The revised original criteria from 1999 provided clinical guidelines for the diagnosis of AIH, but they were complex and intended purely for scientific purposes. To resolve these difficulties, a simplified scoring system for routine clinical practice was proposed in 2008 (9). This new scoring system can be easily put to use in daily clinical practice for chronic AIH with a high sensitivity and specificity, but this does not apply to the evaluation of acute-onset AIH.

Recently, we examined the clinical and histological features of acute-onset AIH and reported that centrilobular necrosis/collapse was characteristic and that the disease severity was associated with advanced histology (6, 10–12).

In the present study, we compared the performance parameters of the revised original scoring system and the simplified one in patients with acute-onset AIH (non-severe, severe and fulminant) and examined the usefulness and limitations of each system.

Patients and methods

Selection criteria of patients

Patients with acute-onset AIH were enrolled between 2000 and 2009. A diagnosis of AIH was made based on the criteria of the International AIH Group defining the score for probable or definite AIH (8) and/or on liver histological

findings compatible with AIH, consisting of interface hepatitis, centrilobular necrosis and plasma cell infiltration.

The eligibility criteria of clinically 'acute-onset' AIH were as follows in addition to the AIH criteria described above: (i) acute-onset liver injury, (ii) no histories of chronic liver injury, (iii) negativity of active viral markers such as hepatitis A, B, C and E viruses, Epstein–Barr virus (EBV), cytomegalovirus (CMV) and herpes simplex virus (HSV), drug-induced liver injury, toxic and metabolic disorders and (iv) no signs of chronicity on the basis of physical examination, laboratory data and abdominal ultrasound findings.

The eligibility criteria of severe and fulminant AIH, in addition to the criteria described above, were as follows: patients with prothrombin time (PT) activity $< 50\%$ of the control or the total bilirubin (T-Bil) level > 20 mg/dl during the disease course were defined as severe AIH, and patients with PT activity $< 40\%$ of control and hepatic encephalopathy were defined as fulminant AIH. Informed consent was obtained from all patients or appropriate family members. The work described in this manuscript has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Clinical, biochemical and immunoserological analysis

Data obtained from patients were as follows: sex; age at diagnosis; time of onset; non-severe, severe and fulminant disease; serum levels of alanine aminotransferase (ALT), T-Bil, alkaline phosphatase, PT activity, immunoglobulin G (IgG), anti-nuclear antibody (ANA), anti-smooth muscle antibody (ASMA), liver kidney microsomal antibody-1 (LKM-1) and anti-mitochondrial antibody (AMA); and human leucocyte antigen. They were also examined for any histories of recent exposure to drugs and chemical agents as well as heavy alcohol consumption (> 50 g/day). ANA and ASMA were examined by a fluorescent antibody method, and AMA was examined by a fluorescent antibody method or an enzyme-linked immunosorbent assay (ELISA), and LKM-1 was examined by ELISA.

The ANA assay should be performed using rodent frozen tissues or HEp2 cells according to the original articles of revised original criteria (8) and simplified criteria (9). In almost all Japanese hospitals including university hospitals, it has been performed using HEp2 cells. Therefore, we halved the values according to the original article in the application of the simplified scoring system.

In acute-onset AIH, early symptoms including fever, general malaise, fatigue, nausea, vomiting and right upper quadrant discomfort are frequently observed; hence, we defined the beginning of these symptoms as clinical onset.

Virological analysis

Patients were examined for viral markers such as IgM anti-hepatitis A virus antibody (IgM-HA), IgM anti-HBc antibody (IgM-HBc), HBsAg, anti-HCV antibody, HCV RNA, HEV RNA (for severe and fulminant patients), IgM anti-EBV antibody (IgM-EBV), IgM anti-HSV antibody (IgM-HSV) and IgM anti-CMV antibody (IgM-CMV). None of the patients had clinical or laboratory evidence of acquired immune deficiency syndrome.

Histological analysis

Histological examination was performed in 49 patients by the percutaneous approach, transjugular approach, explanted liver or post-mortem. Thirty-nine were percutaneous needle biopsy, two transjugular needle biopsy, two explanted liver and six post-mortem. Three specialists (M. N., K. F. and O. Y.) independently reviewed the histopathological changes by evaluating the degrees of portal and lobular changes and plasma cell infiltrations on haematoxylin–eosin-stained sections. Staging and grading were evaluated based on the classification of Desmet *et al.* (13).

Scoring systems

The revised original scoring system of the international AIH group (8) and the simplified system of the same group (9) were applied to all patients before treatment.

Model of end-stage liver disease scores

Scores by the model of end-stage liver disease (MELD) (14) at admission were calculated for severe and fulminant patients.

Statistical analysis

Differences in proportions among the groups were compared by Fisher's exact probability test, Student's *t*-test and Welch's *t*-test ($P < 0.05$ was considered significant).

Results

Clinical and biochemical features

Fifty-five patients, 12 men and 43 women, were enrolled in the study. Twenty-nine has non-severe hepatitis, 14 had severe hepatitis and 12 had fulminant hepatitis. The clinical and biochemical features of all patients at admission are provided in Table 1. The mean age at the time of diagnosis was 51.6 ± 14.3 years. The mean ALT was 612 ± 478 IU/l, the mean T-Bil was 9.5 ± 9.4 mg/dl and the mean PT activity was $65 \pm 31\%$.

The mean IgG was 2192 ± 960 mg/dl. The IgG level was normal [$< 1.0 \times$ upper normal value (UNV)] in 17 of 55 (31%), 1.0–1.5 $\times$ UNV in 24 (44%), 1.5–2.0 $\times$ UNV in nine (16%) and $> 2.0 \times$ UNV in five (9%). It was 1.0–1.1 $\times$ UNV in six (11%) and $> 1.10 \times$ UNV in 32 (58%).

Anti-nuclear antibody was positive ($\geq$1:40) in 49 of 55 (89%) patients, $<$ 1:40 in six (11%), 1:40 in eight (15%), 1:80 in 16 (29%) and $>$ 1:80 in 25 (46%). ASMA was positive ($\geq$1:40) in 15 of 50 (30%). One patient was positive for LKM-1.

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Table 1. Clinical features of patients

	Non-severe type	Severe type	Fulminant type
n	29	14	12
Sex (male/female)[(1)]	4/25	4/10	4/8
Age (years)[(2)]	51.7 ± 14.0	48.7 ± 14.4	54.8 ± 15.8
PT (%)[(3)]	90 ± 17	46 ± 8	25 ± 8
ALT (IU/l)[(4)]	626 ± 392	600 ± 534	597 ± 625
T-Bil (mg/dl)[(5)]	3.3 ± 3.6	12.9 ± 8.3	20.8 ± 8.1
ANA ≥40 (fold)[(6)]	20	10	11
IgG (mg/dl)[(7)]	1874 ± 571	2448 ± 1400	2662 ± 885
Revised original score before treatment[(8)]	13.6 ± 3.4	14.8 ± 3.1	16.5 ± 3.1
Simplified score before treatment[(9)]	4.6 ± 1.6	4.6 ± 1.6	5.5 ± 1.1

Values are mean ± SD or number.

(1), (2), (4), (6), (9)No statistical significance among the three groups.

(3)Significant difference ($P < 0.001$) between non-severe and severe by Welch's *t*-test, between non-severe and fulminant by Welch's *t*-test, between non-severe and fulminant by Student's *t*-test.

(5)Significant difference between non-severe and severe by Welch's *t*-test ($P < 0.001$), between non-severe and fulminant by Welch's *t*-test ($P = 0.02$), between non-severe and fulminant by Student's *t*-test ($P < 0.001$).

(7)Significant difference between non-severe and fulminant by Welch's *t*-test ($P = 0.01$).

(8)Significant difference between non-severe and fulminant by Student's *t*-test ($P = 0.02$).

ALT, alanine aminotransferase; ANA, anti-nuclear antibody; PT, prothrombin time; SD, standard deviation; T-Bil, total bilirubin.

No patients were positive for HBs Ag. Two patients were positive for HCV Ab. One is a non-severe patient with HCV RNA, and the other is a patient who developed fulminant disease during peg-interferon plus ribavirin treatment without HCV RNA. In two patients with non-severe and severe disease, AIH was triggered by hepatitis A.

The duration from the onset to admission to our unit was 43.2 ± 33.8 days for all patients, consisting of 42.6 ± 33.1 days for non-severe, 49.1 ± 34.9 for severe and 37.7 ± 35.9 for fulminant. The differences were not significant among the three groups.

Histological features

The pathological characteristics of the patients are shown in Tables 2–4 and are summarized in Figure 1. Histological examination was performed in 49 of 55 patients, with 32 (65%) showing acute hepatitis, exhibiting zonal, submassive and massive necrosis with or without plasma cell accumulation in portal and centrilobular areas. Seventeen (35%) showed chronic hepatitis.

Forty-six of the 49 (94%) patients showed severe activity, nine with massive necrosis, three with submassive necrosis, 20 with severe acute hepatitis and three with moderate activity with fibrosis stage 1–3.

The proportion of acute hepatitis increased with disease severity, and the difference was significant between non-severe and fulminant patients ($P = 0.04$).

In eight severe and fulminant patients, histological examinations were performed in explanted livers and post-mortem. We could not perform a histological examination before the start of the treatment because of the complicated coagulopathy and ascites in these patients. It is possible that this might influence histological appearance and therefore influence the results of the scoring, and that the histological findings in these patients might be misleading as a result of changes because of critical illness during ICU treatment.

We could find emperipolesis (15, 16) frequently in periportal and lobular areas in patients with high activity, although there was a limitation in terms of its evaluation by light microscopic examination.

Comparison of scoring systems for autoimmune hepatitis

The revised original diagnostic criteria (revised original criteria) proposed by the International AIH Group in 1999 (8) and the simplified diagnostic criteria (simplified criteria) by the same group in 2008 (9) were used to score all patients (Tables 2–4, Figs 2 and 3).

In the revised original criteria, the AIH score ranged from 7 to 22 (14.5 ± 3.4) before treatment. Twenty-two of 55 patients (40%) were diagnosed as 'definite' AIH (score > 15), 28 (51%) as 'probable' (score 10–15) and five (9%) as 'non-diagnostic' (score < 10). Five non-diagnostic patients were all non-severe (Fig. 2).

In the simplified criteria, the AIH score ranged from 2 to 7 (4.8 ± 1.5) before treatment. Six of 55 patients (11%) were diagnosed as 'definite' AIH (score ≥7), 16 (29%) as 'probable' (score ≥6) and 33 (60%) as 'non-diagnostic' (score < 6). Only nine (31%) were diagnostic in non-severe, five (36%) in severe and eight (67%) in fulminant patients (Fig. 3). Regarding the points of each variable, the titre of autoantibodies was slightly higher in fulminant than in non-severe and severe patients, although there was no statistical significance ($P = 0.10$ and $P = 0.18$ respectively). The IgG level was higher in fulminant patients than that in non-severe ones ($P = 0.002$). The point of liver histology was higher in non-severe than that in severe and fulminant patients ($P = 0.04$ and $P = 0.003$ respectively).

Table 2. Histological features and scores of non-severe patients

Patient	Liver histology	Revised original score	Simplified score	Variables of simplified criteria			Absence of viral hepatitis
				Autoantibody	IgG	Liver histology	
1	CH (F1A3)	16	7	2	2	1	2
2	sAH	15	2	0	0	0	2
3	sAH	16	3	1	0	0	2
4	sAH	9	4	2	2	0	0
5	ND	14	6	2	2	0	2
6	CH (F2A2)	19	7	2	2	1	2
7	sAH	11	4	2	0	0	2
8	sAH	14	6	2	2	0	2
9	SMN	15	3	1	0	0	2
10	ND	13	5	1	2	0	2
11	sAH	16	3	1	0	0	2
12	CH (F3A3)	15	4	0	1	1	2
13	CH (F3A3)	9	6	1	2	1	2
14	sAH	9	4	1	1	0	2
15	CH (F1A3)	18	7	2	2	1	2
16	CH (F2A3)	16	7	2	2	1	2
17	sAH	7	2	0	2	0	2
18	CH (F3A3)	10	5	2	0	1	0
19	CH (F2A3)	15	4	0	0	2	2
20	CH (F2A3)	14	5	2	2	1	2
21	CH (F1A1)	18	5	1	0	2	0
22	sAH	13	4	1	1	0	2
23	CH (F3A3)	15	3	0	0	1	2
24	CH (F2A3)	18	6	2	1	1	2
25	CH (F2A3)	11	5	1	0	2	2
26	sAH	14	6	2	2	0	2
27	sAH	7	2	0	0	0	2
28	sAH	18	5	2	1	0	2
29	sAH	10	2	0	0	0	2

CH, chronic hepatitis; ND, not done; sAH, severe acute hepatitis; SMN, submassive necrosis.

Table 3. Histological features and scores of severe and fulminant patients

Patient	Liver histology	Revised original score	Simplified score	Variables of simplified criteria			Absence of viral hepatitis
				Autoantibody	IgG	Liver histology	
S1	CH (F1A3)	15	7	2	2	1	2
S2	sAH	17	2	0	0	0	2
S3	CH (F4A3)	12	6	1	2	1	2
S4	ND	12	5	1	2	0	2
S5	CH (F3A3)	10	5	0	2	1	2
S6	sAH	16	3	1	2	0	0
S7	sAH	16	6	2	2	0	2
S8	ND	13	6	2	2	0	2
S9	MN	15	2	0	0	0	2
S10	sAH	16	5	1	2	0	2
S11	MN	15	3	1	0	0	2
S12	sAH	22	6	2	2	0	2
S13	SMN	11	4	0	2	0	2
S14	sAH	17	4	2	0	0	2
F1	MN	14	6	2	2	0	2
F2	ND	11	6	2	2	0	2
F3	CH (F2A2)	14	7	2	2	1	2
F4	MN	17	5	1	2	0	2
F5	SMN	15	5	1	2	0	2
F6	MN	13	3	1	0	0	2
F7	MN	20	6	2	2	0	2
F8	MN	19	4	0	2	0	2
F9	ND	16	6	2	2	0	2
F10	MN	20	6	2	2	0	2
F11	sAH	20	6	2	2	0	2
F12	MN	19	6	2	2	0	2

CH, chronic hepatitis; F, fulminant; MN, massive necrosis; ND, not done; S, severe; sAH, severe acute hepatitis; SMN, submassive necrosis.

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Table 4. Variables and points for simplified diagnostic criteria

Variable	Points non-severe ($n = 29$)	Severe ($n = 14$)	Fulminant ($n = 12$)
Autoantibodies[(1)]	1.2 ± 0.8	1.1 ± 0.8	1.6 ± 0.7
IgG[(2)]	1.0 ± 0.9	1.4 ± 0.9	1.8 ± 0.6
Liver histology[(3)]	0.6 ± 0.7	0.2 ± 0.4	0.1 ± 0.3
Absence of viral hepatitis[(4)]	1.8 ± 0.6	1.9 ± 0.5	2.0 ± 0.0

Values are mean ± SD or number.
[(1)]No statistical significance among the three groups.
[(2)]Significant difference ($P = 0.002$) between non-severe and fulminant by Welch's *t*-test.
[(3)]Significant difference between non-severe and severe by Welch's *t*-test ($P = 0.04$), and between non-severe and fulminant by Welch's *t*-test ($l = 0.003$).
[(4)]No statistical significance among the three groups.

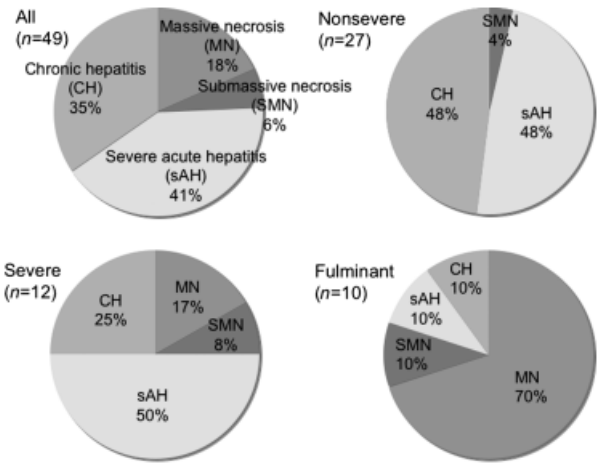

Fig. 1. Pathological characteristics of acute-onset autoimmune hepatitis patients.

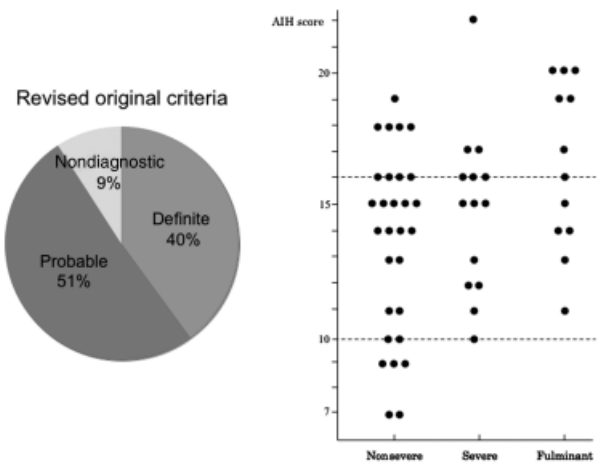

Fig. 2. Discrimination of acute-onset autoimmune hepatitis patients using the revised original scoring system.

The absence of viral hepatitis did not differ among non-severe, severe and fulminant patients (Table 4).

As described above, 32 patients showed acute hepatitis (14 of 27 non-severe patients, 9 of 12 severe ones and 9 of 10 fulminant ones). In these real acute-onset patients, the simplified score before treatment was 4.1 ± 1.5 and 3.6 ± 1.4 in non-severe ones, 3.8 ± 1.5 in severe ones and 5.2 ± 1.1 in fulminant ones respectively. None of the patients was diagnosed as 'definite' AIH, nine (28%) as 'probable' and 23 (72%) as 'non-diagnostic' (Tables 2 and 3).

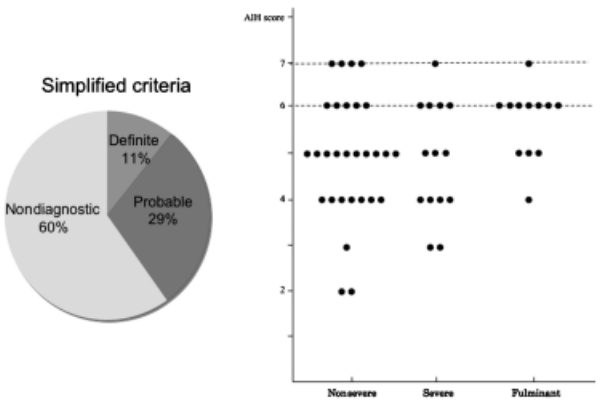

Fig. 3. Discrimination of acute-onset autoimmune hepatitis patients using the simplified scoring system.

We analysed 21 high-score patients whose scores were > 15 and diagnosed as 'definite' in revised original criteria. Six patients showed chronic hepatitis (acute on chronic) and 15 showed acute hepatitis (real acute onset: severe acute hepatitis, massive necrosis or submassive necrosis). In the simplified criteria, four (19%) were diagnosed as 'definite', seven (33%) as 'probable' and 10 (48%) as 'non-diagnostic'. In six acute on chronic patients, four (67%) were diagnosed as 'definite, one (17%) as 'probable and one (17%) as 'non-diagnostic'. In 15 real acute-onset patients, none was diagnosed as 'definite', six (40%) 'probable' and six (60%) 'non-diagnostic' (Fig. 4).

Regarding the specificity of the criteria, we cannot show it because we analysed only AIH patients and did not include non-AIH patients in this study.

Model of end-stage liver disease scores

The MELD scores at admission were 18.5 ± 7.9 (10–42) in severe and 26.3 ± 6.6 (18–37) in fulminant patients. The difference was significant ($P = 0.01$).

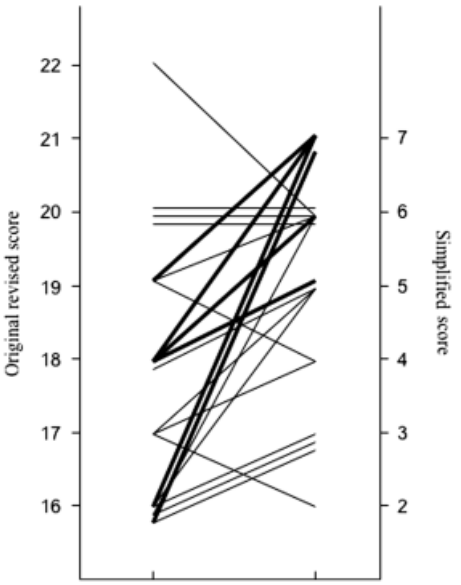

Fig. 4. Comparison of the scores by revised original criteria and simplified criteria in 21 patients whose scores were > 15 and diagnosed as 'definite' in revised original criteria. Thin solid and thick solid lines denote patients with histologically acute hepatitis and chronic hepatitits respectively.

Discussion

After the establishment of the criteria of the International AIH Group (8) and the recognition of acute-onset AIH (17), the diagnosis of acute-onset AIH was made. However, the diagnosis of AIH is challenging, and the diagnosis of acute-onset AIH is even more of a challenge. In the present study, we could diagnose > 90% of acute-onset AIH using the original scoring system, but only 40% by the simplified scoring system.

Acute-onset AIH patients often lack the typical features of AIH, and some patients have no autoantibodies and/or no hypergammaglobulinaemia. At present, they are being diagnosed as cryptogenic hepatitis. It was reported that severe acute and chronic cryptogenic hepatitis was similar to AIH in clinical, biochemical and histological features as well as responsiveness to immunosuppressive therapy, and that severe cryptogenic hepatitis patients might have an autoimmune liver disease with no identified immunoserological marker (18, 19). On the other hand, it was reported that autoantibodies were present in 30% of patients with acute liver failure, and that significantly higher international AIH scores were found in patients with cryptogenic disease as compared with those with other aetiologies, suggesting that it is difficult to evaluate whether primary autoimmune processes are responsible for the condition, although cryptogenic cases have features of autoimmune pathogenesis (20).

Thus, acute-onset AIH patients are at a risk of not being diagnosed and losing the timing for the initiation of immunosuppressive therapy. We have had 14 severe and 12 fulminant AIH patients between 2000 and 2009. Severe AIH patients were often resistant to immunosuppressive therapy in liver regeneration, and fulminant AIH patients were usually resistant to the therapy and showed a poor prognosis, with < 20% survival without liver transplantation (6, 11).

It was reported that severe and fulminant patients had higher titres of ANA and higher levels of IgG than non-severe patients (21, 22). In our present study, ANA negativity (< 1:40) was 11% in all patients, 31% in non-severe, 29% in severe and 8% in fulminant. The IgG level was normal in 31% of all patients, 41% of non-severe, 29% of severe and 8% of fulminant. Thus, our fulminant patients also had relatively higher titres of ANA ($P = 0.13$) and higher levels of IgG ($P = 0.01$) than non-severe patients, as described in previous reports. These findings suggested that the period of initial symptoms to the diagnosis of severe and fulminant hepatitis was occasionally longer than that of non-severe hepatitis (21, 22), but we observed that the duration from onset to admission to our unit was 43 days in all patients, with no statistically significant difference among non-severe, severe and fulminant patients. Patients with acute-onset AIH did not have severe disease at onset, progressing to severe and fulminant during the subacute clinical course without precise diagnosis and treatment. We speculate that this shows the heterogeneous nature of the progression of AIH, and that ANA titre and IgG level do not depend on the time duration but rather on the disease severity, based on our histological observation.

Our recent study of 28 severe and fulminant AIH showed that AIH with low PT activity had very severe and advanced histology (submassive to massive necrosis) and presented impaired hepatocellular regeneration that might be associated with resistance to immunosuppressive therapy, and that the difference in histological findings (massive necrosis, submassive necrosis, severe acute hepatitis and chronic hepatitis) did not depend on the timing of the histological examination (11).

In our previous study of 18 non-severe acute-onset AIH, liver histology showed severe activity with centrilobular necrosis in 95% of the patients, despite PT activity being maintained (10). The duration from onset to admission to our unit of these 18 patients was 32 days, while it was 43 days in the present study of 29 non-severe patients, with the differences not being significant among non-severe, severe and fulminant patients.

Regarding the scoring systems, Czaja (23) reported that the revised original system is useful for diagnosing patients with atypical features of AIH and that the simplified scoring system has superior specificity and predictability and can exclude diagnosis in diseases with concurrent immune manifestations, concluding that each system can support but not supercede the clinical diagnosis. Yeoman *et al.* (24) reported that the simplified criteria retain high specificity but exhibit lower sensitivity and that only 24% of fulminant AIH patients were

diagnostic based on the simplified criteria, but 40% on the revised original criteria. Miyake *et al.* (25) reported that 77% of patients with acute presentation and 50% of those with histologically acute hepatitis were diagnostic based on the simplified criteria.

In our present study, 91% of acute-onset patients were diagnostic based on the revised original criteria, all of severe and fulminant, and 83% of non-severe patients. In contrast, only 40% of patients were diagnostic based on the simplified criteria, 67% fulminant, 36% severe and 31% non-severe. The simplified criteria include the titre of autoantibodies, level of IgG, liver histology and absence of viral hepatitis as variables. In acute-onset AIH patients, especially non-severe, the titre of autoantibodies and level of IgG were lower than those in chronic AIH, and liver histology often showed acute hepatitis, with the total points becoming lower as a result. Only 28% of patients with histologically acute hepatitis were diagnostic, 56% fulminant, 22% severe and 14% non-severe respectively. The revised original scoring system was found to perform better than the simplified scoring system in our patients with acute-onset AIH, as described in other reports.

In conclusion, it is very difficult to diagnose acute-onset AIH because of the lack of a gold standard. When we diagnose patients with acute-onset AIH, we should use the scoring system properly, the revised original scoring system rather than the simplified scoring system, after excluding other causes systematically. Multicentre studies are also needed to clarify the features of acute onset, especially severe and fulminant AIH, and to clearly define the standard for diagnosis.

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