A Comparative Light Microscopic Study and Clinical Evaluation on Acute Viral Hepatitis Type A, B, and Non-A, Non-B

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Abstract: We studied a total of 55 patients with acute hepatitis type A (7 patients), B (20 patients) and non-A, non-B (28 patients) on light microscopic differences of their liver biopsies and their clinical evaluations. We found that the frequency and degree of some histological features seem to be characteristic to each type of hepatitis. In the liver parenchyma, the degree of necrosis was observed to be more severe in type A and B, extending necrosis was observed in type B and non-A, non-B, and reticuloendothelial reaction was more prominent in type B and non-A, non-B. In the portal area, bile duct lesions were frequently seen in type B and non-A, non-B. Although some predominant findings in each type hepatitis were observed, we could not find any specific differences which separate the three types of hepatitis histologically. Clinically and biochemically acute hepatitis type A showed the high degree of liver dysfunction and more rapid resolution than other types of B and non-A, non-B. On the other hand, acute hepatitis type non-A, non-B showed relatively mild liver dysfunction than other types of A and B but slowly resolved during the convalescent stage and some of them showed progression to chronicity.

Key words: Microscopic study, Acute hepatitis type A, B and non-A, non-B, Clinical evaluation

INTRODUCTION

The clinical features and final outcome of the acute viral hepatitis caused by hepatitis A, B and non-A, non-B viruses can be different in their complete resolution or development of the various forms of chronic liver diseases, such as, chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. For these reasons, there should be some different

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morphological pictures among each type of viral hepatitis during their acute phases. Vanstapel *et al.* (1983) observed that polymorphonuclear neutrophil (PMN) infiltration in acute hepatitis appears to be a useful prognostic feature of chronicity in hepatitis B and non-A, non-B. Some authors reported that they could not find any definite specific morphological pictures of each type of hepatitis (Kryger *et al.*, 1983; Schmid *et al.*, 1982). At the present time, the RIA, ELISA and PCR techniques are the most useful methods to detect and identify the causative viruses and get the diagnosis of each type of acute viral hepatitis. However, the histological study of the liver biopsies is very important to get the definite diagnosis and determine the prognosis and progression of the diseases. The purpose of this paper is to describe the histopathological changes and some specific pictures of liver biopsies from the patients with acute hepatitis type A, B and non-A, non-B and evaluate the histological value for the prognosis of the diseases, considering with clinical and laboratory data.

Materials and Methods

Biopsy materials from 55 patients with acute viral hepatitis who admitted to the Nagasaki University Hospital were used for this study. Seven were type A, 20 were B and 28 were non-A, non-B. The relevant clinical and laboratory data from each case were collected. The patients who showed positive for anti-HAV antibody of IgM class (anti-HAVIgM) and negative for hepatitis B surface antigen (HBsAg) were defined as acute hepatitis type A. The patients who showed positive for HBsAb or had seroconversion during convalescence were defined as acute hepatitis type B. The patients defined as acute hepatitis type non-A, non-B were negative for serological markers of hepatitis A and B viruses, Epstein-Bar virus and cytomegalovirus, and showed of typical, clinical and biochemical signs of acute hepatitis. All patients with clinical suspicions of hepatotoxicity due to alcohol or drug-induced liver diseases were excluded. The liver biopsy was performed percutaneously according to routine procedure and liver tissue was fixed in 10% formalin solution, embedded in paraffin, cut into 5μm sections and stained with hematoxylin and eosin (HE), Mallory's for collagen fibers and silver impregnation for reticulin fibers. The slides were blindly evaluated for quantitative and qualitative light microscopic differences. For statistical analysis, we used the chi-square test.

Results

Sex, age and laboratory data are shown in table 1. The high frequency of acute hepaitis type A was seen in the male. There were no differences on sex ratio in type B and non-A, non-B. The mean age of patients with type non-A, non-B was slightly younger than that of type A and B (35.2, 38.6 and 38.4 years old, respectively). The liver function data showed broad variation in all types of acute hepatitis. However, when all types of hepatitis were compared non-A, non-B hepatitis was less severe with lower peak value for

Table 1. Sex, age and laboratory data in patients with acute hepatitis type A, B and non-A, non-B

	A (n=7)	B (n=20)	non−A, non−B (n=28)
Sex ratio (Male/Female)	5 : 2	11 : 9	15 : 13
Mean age (years and range)	38.6 (22−59)	38.4 (22−71)	35.2 (15−66)
Mean total bilirubin (mg/dl and range)	10.4 (2−21.4)	6.7 (0.7−30.8)	3.6 (0.6−16.1)
Mean alkaline phosphatase (IU and range)	414 (21.7−638)	320 (10.2−693)	257 (11.7−387)
Mean SGOT (IU and range)	1,938 (234−5,275)	1,417 (192−6,600)	381 (97−1,091)
Mean SGPT (IU and range)	2,456 (511−5,200)	1,651 (352−7,100)	686 (153−2,509)
Mean interval between peak level of serum transaminase and biopsy (days and range)	21 (11−41)	32 (10−87)	47 (14−126)

total bilirubin, alkaline phosphatase and transaminases (SGOT, SGPT) than hepatitis A and B. The mean duration (interval between peak serum transaminase levels and initial liver biopsy) was the longest in type non-A, non-B, compared with type B and A (47, 32 and 21 days, respectively). This showed slow subsidence of acute hepatitis type non-A, non-B and rapid resolution of acute hepatitis type A.

Table 2 and 3 show the frequency of histological changes in liver parenchyma and portal area of liver biopsies. The common classical pictures of acute viral hepatitis in liver parenchyma are characterized by Kupffer cell mobilization (Photo. 1), ceroid body, spotty necrosis (Photo. 2) and degeneration of central veins (Photo. 3). Kupffer cell mobilizations were commonly seen in all types of hepatitis in our cases. Sinusoidal lymphocytic infiltrations (Photo. 1) were frequently seen in type B and non-A, non-B and Councilman's bodies (Photo. 4) were frequenly seen in type A hepatitis. Central vein thickening (Photo. 3) were more predominant in type B and non-A, non-B hepatitis than type A ($P<0.05$). Ceroid bodies were frequently found in all types. Cholestasis (Photo. 5), mitotic figure and variation of nuclear size were infrequently seen in all types. Microvesicular fatty change (Photo. 6) were frequently found in type A. Bridging necrosis and centrilobular fibrosis were observed in several cases of type B and non-A, non-B hepatitis but never seen in type A ($P<0.05$).

In the portal area, bile duct lesions, especially, degeneration of epithelial cells (Photo. 7) occured frequently in type B and non-A, non-B. Bile ductular proliferation occured in all types similarly. The portal plasma cell and neutrophil infiltration were found more frequently in type A than in type B and non-A, non-B ($P<0.05$). Eosinophilic infiltration was found only one case of hepatitis type A and lymphoid follicle was found only one case of hepatitis type B. Ceroid bodies in portal area were frequently observed in type A but the degree was more severe in type B. Piecemeal necrosis (Photo. 8) was found only in type B and non-A, non-B. However periportal immature fibrosis occured in all types in almost same degree.

Table 2. Histological changes in liver parenchyma

	A (n=7) (%)	B (n=20) (%)	Non-A, non-B (n=28) (%)
Kupffer cell mobilization	86	75	82
Sinusoidal infiltration	57	80	82
Councilman's body	71	45	46
Ceroid body	100	100	89
Central vein degeneration	86	85	93
Central vein thickening	29	75	75
Cholestasis	29	15	4
Bridging necrosis	0	25	11
Spotty necrosis	100	100	96
Centrilobular fibrosis	0	75	57
Mitotic figure	14	10	7
Variation of nuclear size	43	30	21
Fatty change	86	50	36

Table 3. Histological changes in portal area

	A (n=7) (%)	B (n=20) (%)	non-A, non-B (n=28) (%)
Bile duct lesion			
Bile duct proliferation	43	50	39
Multilayered epithelium	0	5	7
Cholangitis	43	60	54
Degenerative bile duct	29	70	57
Periportal immature fibrosis	57	70	46
Piecemeal necrosis	0	25	7
Portal inflammation			
Lymphocyte	100	100	68
Neutrophil	57	20	7
Plasma cell	86	60	36
Eosinophil	14	0	0
Lymphoid follicle	0	5	0
Ceroid body	86	60	57

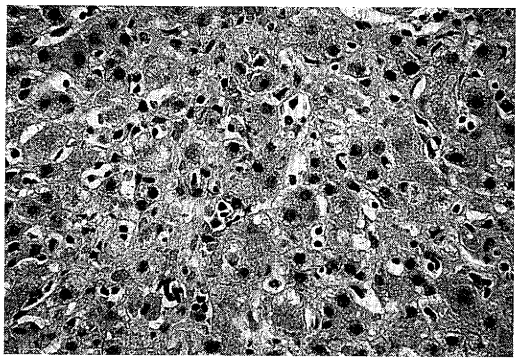

Photo. 1. Kupffer cell mobilization and sinusoidal lymphocytic infiltration. (HE, ×200)

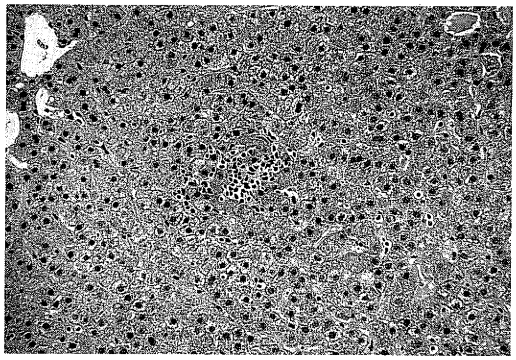

Photo. 2. Spotty necrosis. (HE, ×100)

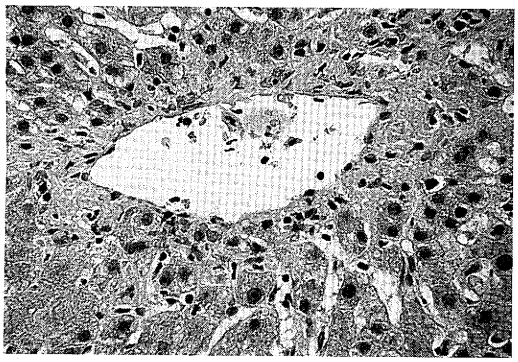

Photo. 3. Perivenular necrosis, degeneration and thickening of central vein. (HE, ×200)

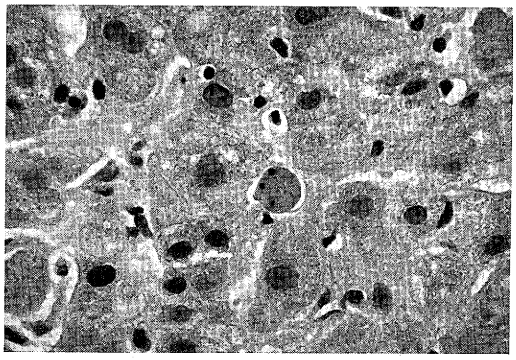

Photo. 4. Councilman's body. (HE, ×400)

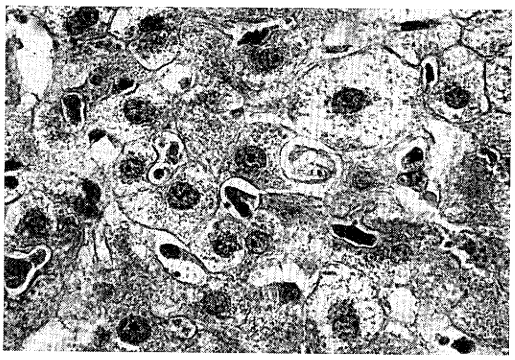

Photo. 5. Bile plugs in dilated bile canaliculi. (HE, ×400)

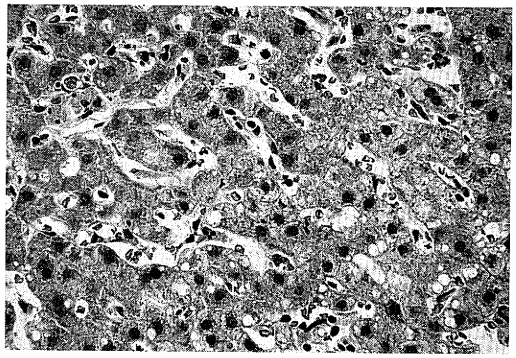

Photo. 6. Microvesicular fatty change of hepatocytes. (HE, ×200)

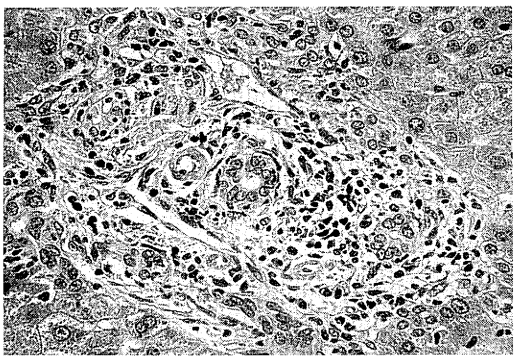

Photo. 7. Slight lymphocyte and plasma cell infiltration, bile duct proliferation and degeneration in portal area. (HE, ×200)

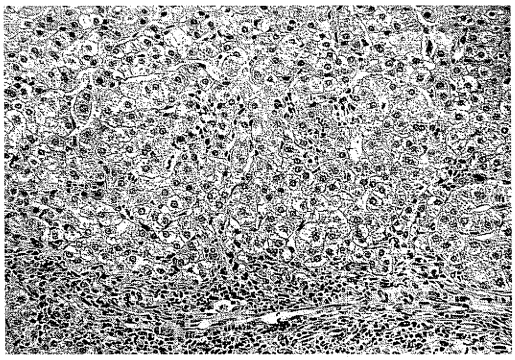

Photo. 8. Piecemeal necrosis of periportal area and spotty necrosis in liver parenchyma. (HE, ×100)

DISCUSSION

The high peak of the value for total bilirubin, transaminase and alkaline phosphatase in acute hepatitis type A and B and longer interval between the peak of transaminase level and biopsy in acute non-A, non-B hepatitis suggested that acute type non-A, non-B hepatitis has a less severity but slowly resolves during convalescent stage. These findings are compatible with prolonged low grade histological activity in acute hepatitis type non-A, non-B (Kryger, 1983) and a high percentage of acute non-A, non-B hepatitis progressed to chronicity (Barcena *et al.*, 1985; Laskus *et al.*, 1990).

There are common findings in acute hepatitis type A, B and non-A, non-B characterized by Kupffer cell mobilization, ceroid body in liver parenchyma and portal area, spotty necrosis, Councilman's body, central vein degeneration and bile ductular proliferation. Sinusoidal lymphocytic infiltration was more frequently observed in type B and non-A, non-B than type A, but portal inflammation, especially neutrophil infiltration was more frequently seen in type A. Acccording to these findings, we could not confirm the previous report that portal inflammation with neutrophils is the picture of progression to chronicity (Kryger *et al.*, in press). Bile duct lesions as described by Christoffersen *et al.* (1970) had been reported to be the specific value for histological recognition of hepatitis non-A, non-B (Schmid *et al.*, 1982), but some authors had observed abnormal bile duct in all types of hepatitis (Kryger, 1982). We also could not find any difference of bile duct lesion in all types of acute viral hepatitis. Bamber, M. *et al.* (1981) reported a high frequency of steatosis in non-A, non-B hepatitis, but in our findings microvesicular fatty change was frequently seen in type A hepatitis. Since, steatosis is influenced by many factors such as drugs, alcohol intake, malnutrition and obesity (Bianchi *et al.*, 1974), this finding is not specific for any acute viral hepatitis. Multi-nucleated hepatocytic giant cells were reported in non-A, non-B hepatitis (Spichtin *et al.*, 1982; Tabor *et al.*, 1979), and we also found

variation of nuclear size including multi-nucleated hepatocytes in all types of acute viral hepatitis.

Piecemeal necrosis, bridging necrosis and centrilobular fibrosis which are the significant features of chronicity (Schmid *et al.*, 1981; Sciot *et al.*, 1986; Vanstapel *et al.*, 1983) were observed only in acute viral hepatitis type B and non-A, non-B of our cases.

We were not able to find any definite difference between the three types of acute hapatitis histologically, but the frequency and degree of several histological features seemed to be important to know characteristics of each type of acute viral hepatitis.

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