

AGGRESSIVE ACUTE VIRAL HEPATITIS

T Mathew
Chan-So Ha

SYNOPSIS

Acute viral hepatitis in some patients may progress directly to a state of chronic hepatitis. In such patients, there are often certain morphological markers in liver biopsies which may predict such an outcome. Density of chronic inflammatory cell infiltrate in portal tracts, presence of "piece-meal" necrosis, portal fibrosis and bridging hepatic necrosis are indicators of an aggressive illness. On the basis of the absence or presence of these changes, 64 patients with acute viral hepatitis were divided into two types — Type I, (without aggressive changes) and Type II, (with aggressive changes). Type II was found to be associated with a significantly higher proportion of female patients. A significant reduction of blood group O patients was also present in this Type and it is proposed such patients are more resistant to the possibly dangerous sequelae of acute viral hepatitis. No significant difference in HBs antigenaemia was observed between Type I and Type II cases.

INTRODUCTION

Acute viral hepatitis in the majority of patients is a self-limiting disease which undergoes spontaneous clinical remission with reversion of the histological changes in the liver back to normal. However, in some patients, liver biopsies show morphological changes that may indicate possible transition to a state of chronic liver disease. Several patterns of liver cell injury have been described to predict possible transition to chronic hepatitis. Two histological patterns of acute hepatitis have been associated with greater than usual likelihood of chronicity. Both patterns have major similarities with Chronic Aggressive Hepatitis (C.A.H.) and in each situation, a report of acute viral hepatitis with "possible transition to C.A.H." is appropriate (Bianchi et al, 1971). The first of these two patterns shows a severe degree of portal and periportal inflammation by chronic inflammatory cells with "piece-meal" necrosis (Bianchi et al, 1971). The second pattern is Bridging Hepatic Necrosis (B.H.N.) (Boyer and Klatskin, 1970; Ware et al, 1975). Here septa of confluent necrosis link portal tracts to central veins and/or portal tracts to portal tracts. The simple linking of portal tract to portal tract without involvement of central veins represents in the opinion of some authors a severe example of "piece-meal" necrosis due to

University Pathology Department
Singapore General Hospital

T Mathew, MBBS, FRCPA.
Senior Lecturer

W.H.O. Immunology Research & Training Centre
Faculty of Medicine
University of Singapore
Chan Soh Ha, MD, Ph. D.
Senior Lecturer

periportal inflammation and necrosis and not a true example of confluent necrosis. (Review of an International Group, 1972). The rationale for this more restrictive definition is that when there is linking between central veins or between portal tracts and central veins, the septa so formed dissect the lobules creating portal-systemic shunts resulting in ischaemia of the affected lobules causing unevenly distributed regeneration and hastening the development of cirrhosis. However, B. H. N. may not be the sole factor in the evolution of C.A.H. and though it undoubtedly plays an important role in chronicity many authors believe "piece-meal" necrosis and cellular infiltration are the more important prognostic features (Dietrichson et al, quoted from Scheur, 1977). But, not all patients showing either of the two patterns will necessarily progress to chronic liver disease. Many cases in fact recover without serious morphological sequelae.

The present study was done to assess the frequency of aggressive changes in acute viral hepatitis among patients admitted to the Singapore General Hospital, and to consider possible factors that may have a bearing in such cases.

MATERIALS AND METHOD

During the period between January 1975 and October 1976, all liver biopsies done on patients with acute viral hepatitis were submitted for pathological examination. As the purpose of this study was to consider morphological changes during the acute phase of the disease, only liver biopsies taken during the first one week of onset of symptoms were reviewed. A total of 64 liver biopsies met this requirement.

Each liver biopsy was fixed in 10% formol-saline and paraffin sections were cut and stained with H & E, Gomori's reticulin, Masson's trichrome and Shikata's orcein stain.

The histological criteria used in this study for making a diagnosis of acute viral hepatitis with possible transition to C.A.H. were:— (1) density of chronic inflammatory infiltrate in portal tracts, (2) "piece-meal" necrosis, (3) portal fibrosis, and (4) presence of B.H.N. Any liver biopsy satisfying two or more of these criteria was classified as showing aggressive features (Figures 1 — 3).

Sera from all patients were examined for HBs antigen by the counterimmunoelectrophoresis (C.I.E.) technique. Whenever heparinised blood was available blood groups within the ABO system was typed.

RESULTS

Among the 64 patients, there were 45 males and 19 females. The ages of these patients were 36.73 years ± 10.76 (S.D.), range 13-67 years. All patients were Chinese with the exception of 6 Malays and 4 Indians. As the predominant Singapore population is Chinese and as there were only 10 non-Chinese in this study, the material to be discussed pertains to the Chinese component.

A total of 16 patients showed in their liver biopsies aggressive changes on the basis of the criteria listed above. Among these 8 were males and 8 females.

Of the total number of 64 cases, HBs antigenaemia was found in 32 cases (50%). In the group which showed no aggressive features (Type I), there were 27/48 (56.3%) who were antigenaemic. In the other group showing

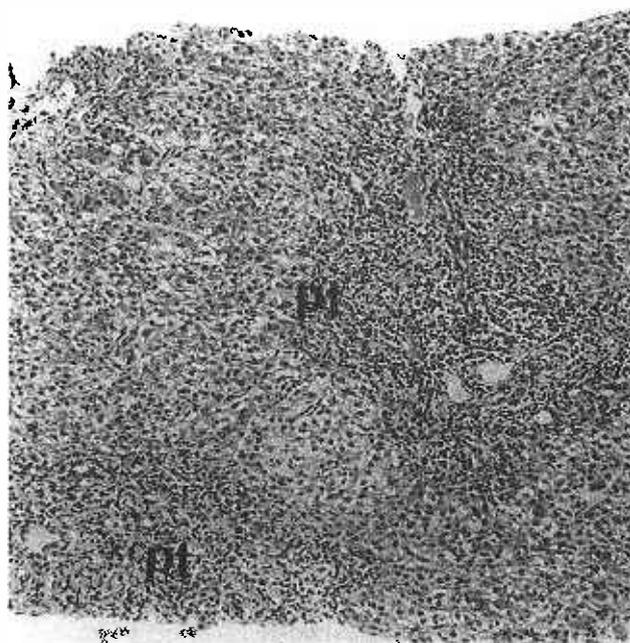


Fig. 1 Heavy chronic inflammatory cells in two portal tracts. (PT—portal tracts) H & E x 100

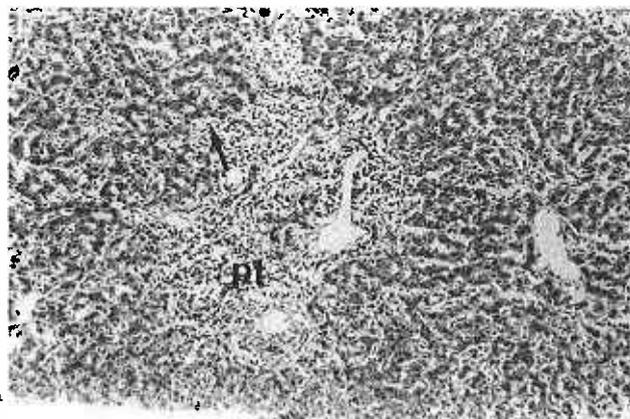


Fig. 2 "Piece-meal" necrosis. (PT—portal tract. Arrow points to an eroded area in the limiting plate) H & E x 100

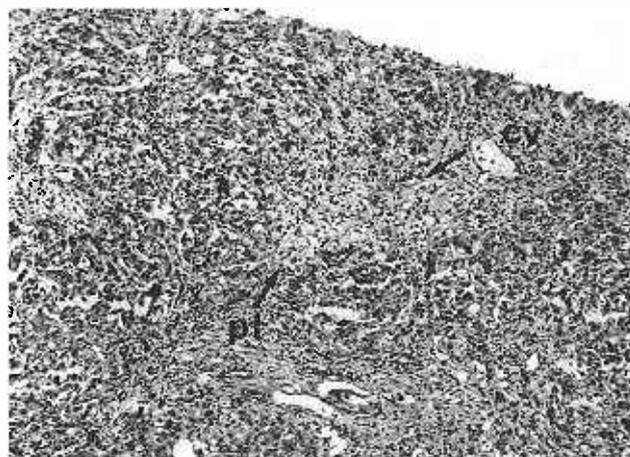


Fig. 3 Bridging Hepatic Necrosis linking portal tract and central vein. (PT — portal tract, CV — central vein. Arrows point towards the band of necrotic liver cells) H & E x 100.

histologically aggressive changes (Type II), there were 5/16 (31.3%) who were antigen positive.

Shikata's orcein stain was negative in all cases including those 32 who were HBs antigenaemic.

Distribution of ABO blood groups showed the following pattern. Of the 48 patients in Type I, 38 cases typed showed Group A in 14, Group B in 9 and Group O in 15. In Type II, 11 cases typed showed 5 Group A, 5 Group B and 1 Group AB. No Group O was identified.

DISCUSSION

The orcein stain (Shikata et al, 1974) has been reported by several authors (Kostich et al, 1977; Gerber et al, 1974) to be positive in as high as 50-60% of HBs positive cases of chronic hepatitis and among asymptomatic carriers. However, it has been claimed that in acute viral hepatitis, the orcein reaction is nearly always negative (Deodhar et al, 1975; Popper, 1975; Galbraith et al, 1976). To ascertain if this stain may show different patterns of reactivity in Type I and Type II cases, all liver biopsies in this study were stained with this histochemical method. However, in none of them was a positive reaction demonstrated. This finding, however, was not wholly unexpected as in acute viral hepatitis, HBsAg is found on the surface membranes of liver cells (Alberti et al, 1975). And this would prompt an immediate immunological response with almost complete destruction of infected hepatocytes leading to release of the antigen and negative results with orcein.

HBs antigenaemia which was 27/48 (56.3%) in Type I and 5/16 (31.3%) in Type II, showed no statistically significant difference ($p \geq 0.05$). As HBs antigenaemia does not appear to show any particular bias against either of the two types, then there must exist other incriminating factors responsible for the morphological variations seen.

In Type I there were 37 males and 11 females, while in Type II there were 8 males and 8 females. Comparing Types I and II a statistically significant excess of female patients was found in the latter group ($p < 0.05$). Why females should predominate in this type is uncertain. It has been reported by several authors (Mistilis and Blackburn, 1970; Soloway et al, 1972) that females also tend to be more prone to C.A.H. It would therefore seem to appear that Type II female patients have as some yet undetermined predisposing factors which might aid the progression of aggressive changes during the acute phase of the disease to C.A.H.

Several authors have commented on the excess of Group A patients in acute viral hepatitis (Aronoff et al, 1973; Hadziyannis et al, 1972; Zuckerman and McDonald, 1963). The incidence of ABO blood groups among the Singapore Chinese population is Group O (43.3%), Group A (26.4%), Group B (24.5%) and Group AB (5.8%) (Low et al, 1976). The distribution of the ABO blood groups in Type I patients showed no statistically significant excess or decrease of any particular group. However, in Type II patients, while no statistically significant increase in Group A or Group B patients could be demonstrated ($p =$

>0.1), there was a conspicuous and significant absence of Group O patients ($p < 0.01$). We feel therefore that Group O patients are probably more resistant to the more dangerous sequelae of acute viral hepatitis and the apparent increase in patients with other blood groups is not real but reflects the reduction of Group O patients.

ACKNOWLEDGEMENTS

I am grateful to M. Low, T.C. Tan, E. Chan, L. Ng and V. Mok for valuable technical and secretarial assistance.

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