A STUDY ON THE RELATIONSHIP BETWEEN THE PROGNOSIS OF CHRONIC ACTIVE HEPATITIS AND THE HBV ASSOCIATED ANTIGEN/ANTIBODY SYSTEMS

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Summary

The relationship between the prognosis of the disease based on liver histology and HB virus (HBV) associated antigen/antibody systems was investigated in twenty seven patients with chronic active hepatitis (CAH). These patients were followed up over extended periods with mean duration of 44.3 months. On initial liver biopsy five of twelve patients with CAH with spotty or focal necrosis were HBs antigen (HBsAg) positive, as were also five of six patients with sublobular necrosis and six of nine patients with lobular disorganization. Most of the HBsAg negative patients were anti-HBs or anti-HBc positive: HBV associated antigen or antibody was completely undetectable in only three of the twenty seven patients. There was no difference in the frequency of progression to liver cirrhosis (LC) between the sixteen HBsAg positive and the eleven HBsAg negative patients with CAH. On the other hand, progression to LC occurred in only one of seven HBe antigen (HBeAg) negative patients, compared to four of nine HBeAg positive patients, who were HBsAg positive. There were four patients who were HBeAg positive initially but then became HBeAg negative in the course of observation. LC developed in two of these four patients.

These results suggest that in HBsAg positive patients with CAH the presence or absence of HBeAg and the variation in its level can provide useful indicators of the prognosis of the disease.

Key Words: HB virus associated antigen/antibody system, chronic active hepatitis, liver biopsy, HBs antigen, HBe antigen.

Introduction

A number of factors have been implicated in the pathogenesis of chronic hepatitis, including viruses, alcohol, drugs, autoimmunity etc. Particularly chronic hepatitis caused by hepatitis virus has drawn the attention of clinicians.

For last ten years hepatitis B virus (HBV) and hepatitis A virus (HAV) have been extensively studied and more recently the existence of non A non B virus has been suggested. Acute hepatitis due to HAV, which may occasionally lead to fulminant hepatic failure, nevertheless virtually never becomes chronic, no healthy carrier state being reported to exist for this type of hepatitis virus. In contrast, such a carrier
state exists for HBV and non A non B virus\(^3\), both of which are intimately involved in the progression of chronic hepatitis.

HBV infection in normal adults may either remain subclinical, resulting in the development of antibody to HBV, or it may lead to the onset of acute hepatitis, in which the patients are usually recovered without further transition to chronic hepatitis. The majority of HBV positive patients with chronic hepatitis are believed to have been asymptomatic carrier of HBV. At present many investigators are concerned about the fact that there are nearly ten times as many HBV carriers in our country as in European or American countries and that LC and carcinoma of the liver are of high incidence among patients with chronic hepatitis\(^4\).

HBV associated antigen/antibody systems consist of HBsAg/anti-HBs, HbcAg/anti-HBc and HBeAg/anti-HBe systems. These systems can be detected by using radioimmunoassay (RIA). Of these, the HBsAg/anti-HBs system has been a subject of intensive study with regard to its relation to the progress of chronic hepatitis\(^5\-7\). In contrast, much remains to be studied as to the clinical significance of the relationship between the HBeAg/anti-HBe system and the progress of the disease.

This led us to undertake the study presented here with the intention of clarifying the relationship between the progress of chronic active hepatitis based on repeated liver biopsy and HBV-associated antigen/antibody systems particularly the HBeAg/anti-HBe system as determined by the RIA method.

**Subjects and Methods**

Our series consisted of twenty-seven patients admitted to our clinic with diagnosis of chronic active hepatitis over the period of eleven years from Jan. 1, 1969 until Dec. 31, 1979. The diagnosis was based on liver histology in all these patients followed up with liver biopsy performed subsequently at an interval of more than a year.

Initial liver biopsy revealed spotty of focal hepatic cell necrosis (CAH) in twelve, sublobular hepatic cell necrosis (CAH with SN) in six and lobular disorganization (CAH with LD)\(^6\) in nine of twenty-seven patients. The mean age of patients and mean duration of study in each of these subgroups are shown in Table 1.

Determination were made by the RIA method of HBsAg, anti-HBs, HBeAg, anti-HBe and anti-HBc in blood serum taken from each patient on initial and final liver biopsy. The serum specimens were kept frozen at \(-20^\circ\text{C}\) until used. An attempt was made to examine the relationship between the HBV associated antigen/antibody systems so determined and progress of chronic hepatitis based on follow-up liver biopsy.

**Results**

The clinical course and liver histology as judged by follow-up liver biopsy in these

<table>
<thead>
<tr>
<th>Table 1. Subjects</th>
<th>No. of cases</th>
<th>Age (mean ± SD)</th>
<th>Observation period (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic active hepatitis CAH</td>
<td>12</td>
<td>40.3 ±12.4 y.o.</td>
<td>52.5 ±30.8 months</td>
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<tr>
<td>Chronic active hepatitis CAH with SN</td>
<td>6</td>
<td>37.2 ±12.7</td>
<td>37.6 ±35.4</td>
</tr>
<tr>
<td>Chronic active hepatitis CAH with LD</td>
<td>9</td>
<td>41.1 ±10.4</td>
<td>37.9 ±31.9</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>39.9 ±11.5</td>
<td>44.3 ±31.8</td>
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