CASE REPORT

Chronic HCV Histology is Predictable From HCV RNA and IgM Anti HCV Results

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Summary

The aim of this study was to determine if knowledge of both the serum *HCV RNA* and serum anti core IgM antibody status enabled one to predict the histological severity in chronic hepatitis C. We studied 45 female patients with chronic hepatitis C infection. The presence or absence of IgM antibodies to HCV and HCV RNA by PCR in each patient's serum was determined. Liver biopsies performed were scored according to a modified Desmet's histological activity index. Negative *HCV RNA* patients had least histological change. *HCV RNA* positive patients who were also IgM antibody positive had lower scores than their IgM negative counterparts. The grade of histological severity is more accurately predictable from knowledge of both the *HCV RNA* and *IgM anti HCV* status of the patient.

Key Words: Hepatitis C, IgM antibody, HCV RNA, Histology

Introduction

The hepatitis C virus was identified in 1989 by Kuo and colleagues[1]. Infection by the hepatitis C virus (HCV) is frequently subclinical and may be diagnosed serologically by detecting antibodies to HCV using ELISA and immunoblot tests, or branched-chain cDNA assays. HCV RNA may be detected by polymerase chain reaction (PCR)[2]. Liver histology in hepatitis C may vary from normal to acute or chronic hepatitis, cirrhosis and hepatocellular carcinoma[3]. Liver biopsy which provides histology remains the current gold standard investigation, but is invasive and potentially hazardous.

Detection of serum *HCV* or total anti-HCV antibodies does not help distinguish patients with on going liver disease caused by HCV from carriers of HCV who are either healthy or have a liver disease unrelated to HCV[4]. The search for new markers of HCV induced liver damage is now focusing on anti HCV core IgM antibody in the hope that this antibody could fulfil the role of a prognostic indicator.

This study was undertaken to determine if knowledge of both the serum HCV RNA and serum anti core IgM antibody status enables one to more accurately predict histological severity in chronic hepatitis C.

Patients and Methods

45 female patients with chronic HCV infection as a result of contaminated anti-D immunoglobulin in 1977 (38), 1979 (1), 1987 (1), 1991 (4), 1994 (1) were studied. Each patient had a detailed history and thorough examination.

IgG antibody to HCV was tested by enzyme linked immunoassay (ELISA; Ortho & Murex, Abbott Laboratories) and confirmed by radioimmunoblot assay (RIBA-3). The presence of HCV RNA was determined using polymerase chain reaction (PCR, Roche Diagnostic Systems).

The presence or absence of IgM antibody to HCV in each patient's serum was determined using enzyme

linked immunoassay (ELISA) kits from Abbott Diagnostics, Weisbaden, Germany. The IgM antibody used in this study was directed against c-22.

All patients had serum alanine transaminase (ALT) levels measured and liver biopsy performed using the Menghini technique[5]. Liver histology was then scored and graded as minimal (0-3), mild (4-8), moderate (9-12) or severe (13+) according to a modified Desmet's (6) histological activity index.

The histological scores for *HCV RNA* and *IgM anti HCV* negative patients were compared both with those who were *HCV RNA* and *IgM anti HCV* antibody positive and with those who were HCV RNA positive and IgM antibody negative. The differences between the actual scores were tested for significance by the Wilcoxon rank sum test and the differences between the grades of histological change by the χ^2 test with a correlation factor of Yeat's included for values of five or less.

Results

Of the 45 patients seven were *HCV RNA* and *anti HCV IgM* negative (Group 1); 29 were *HCV RNA* and IgM positive (Group 2) and nine were *HCV RNA* positive and IgM negative (Group 3). The histology scores for the three groups are shown in Table I and the histology grades in Table II.

The histology scores for Group 1 were significantly lower than both those in Group 2 ($p<0.01$) and those in Group 3 ($p<0.01$). The scores for Group 2 were significantly lower than those in Group 3 ($p<0.05$).

There was significantly more minimal grades in Group 1 compared with Group 2 ($\chi^2=10.29$ $p<0.01$). There was significantly more moderate or severe grades in Group 3 in comparison to Group 2 ($\chi^2=6.41, p<0.02$).

Table I
Histological Scores

Group 1 HCV RNA- IgM anti HCV-	Group 2 HCV RNA+ IgM anti HCV+	Group 3 HCV RNA + IgM anti HCV-
0	5 6 2 3	9
3	3 2 2 1	6
0	4 3 6 6	4
1	3 5 6 6	13
1	2 8 6 2	4
3	5 6 6	4
1	3 6 3	8
	2 3 8	4
		6

Table II
Grade of histological abnormality

Histology Grade	Group 1 RNA-IgM (n=7)	Group 2 RNA+IgM+ (n+29)	Group 3 RNA+IgM-(n=9)
Minimal (0.3)	7	13	0
Mild (4-8)	0	16	7
Moderate (9-12)	0	0	1
Severe (13+)	0	0	1

Discussion

Anti HCV IgM antibodies have been found in patients both in acute and chronic hepatitis C[7]. This study has shown that least histological abnormality is noted in HCV RNA negative patients: all of these patients were IgM antibody negative as well. It has shown that in *HCV RNA* positive patients, the ability to mount an immune response (IgM antibody positive) results in less severe liver disease. *HCV RNA* positive IgM antibody negative patients had higher histological scores. IgM anti HCV may therefore be involved in the complement mediated *cell* lysis of HCV infected hepatocytes and may neutralise circulating HCV in the serum [8,9].

In keeping with the suggestion of other authors that cirrhotics are less likely to have IgM anti HCV production, our only cirrhotic patient was also IgM negative[10,11].

These findings suggest that the grade of histological severity is predictable from knowledge of both the *HCV RNA* and IgM antibody status of the patient. *HCV RNA* negative patients have minimal changes; *HCV RNA* positive IgM antibody positive patients have minimal or mild changes whilst *HCV RNA* positive IgM antibody negative patients have mild, moderate or severe changes.

In chronic HCV infection IgM antibody status used in conjunction with *HCV RNA* status allows one to more accurately predict the grade or grades of histological abnormality.

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