Monoclonal Gammopathy among Patients with Chronic Hepatitis C Infection

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Key Words

Monoclonal gammopathy · Hepatitis C virus · Interferon

Abstract

Objective: To determine the prevalence of monoclonal gammopathies in Kuwait and its association with chronic hepatitis C virus (HCV) infection. **Methodology:** Serum protein electrophoresis and measurement of immunoglobulin levels were carried out prospectively in 100 consecutive patients with chronic HCV infection. **Results:** Among the 100 patients tested (82 males, 18 females; median age 45 years), 59 had polyclonal band in serum protein electrophoresis while the other 41 had a normal pattern. None of the patients had monoclonal gammopathy. The mean serum immunoglobulin levels were: IgG 18.4 g/l (range 4–39), IgA 2.9 g/l (range 0.09–8) and IgM 1.6 g/l (range 0.14–6.08). **Conclusion:** There was no evidence of monoclonal gammopathies in patients with chronic HCV infection in Kuwait.

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Introduction

The clinical course of chronic hepatitis C virus (HCV) infection is often associated with extrahepatic manifestations. Hematological consequences of HCV infection include essential mixed cryoglobulinemia (EMC) and lymphoma [1, 2]. EMC is the most common extrahepatic manifestation of HCV infection and often occurs in patients with long-standing infection [3]. However, there is no obvious association between EMC and specific HCV genotype [4, 5]. There are several studies that link lymphoma with HCV infection in both HCV-related type II EMC subjects and also in patients without EMC [6–10]. The issue of monoclonal gammopathies among patients with chronic HCV is controversial and there seems to be some regional variation [11–13]. Therefore, the present study examined patients with a long-standing HCV infection and studied the effect of interferon- α on the prevalence of monoclonal gammopathies.

Patients and Methods

From November 2000 to January 2001, all known confirmed cases of chronic HCV in Kuwait at the time were recruited for the study. These patients came from Thunayan Al Ghanim Center and Mubarak Al Kabir Hospital, the main gastrohepatology centers in

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Table 1. Patient characteristics and laboratory investigations

Characteristics	All patients (n = 100)	Interferon therapy (n = 44)	No interferon therapy (n = 56)
Median age, years (range)	45 (11–70)	45 (16–63)	45 (11–70) (p = 0.6)
Gender			
Males (%)	82	36 (81.8%)	46 (82.2%)
Females (%)	18	8 (18.2%)	10 (17.8%)
Nationality			
Kuwaiti (%)	20	10 (22.7%)	10 (17.8%)
Non-Kuwaiti Arabs (%)	77	33 (75%)	44 (78.6%)
Others (%)	3	1 (2.3%)	2 (3.6%)
Median duration since diagnosis, months (range)	48 (3–168)	48 (5–132)	48 (3–168)
SPE			
Normal	59	30	29
Polyclonal	41	14	27 (p = 0.07)
Monoclonal	0	0	0
Mean serum immunoglobulin, g/l			
IgG	18.4	17.8	18.7 (p = 0.4)
IgA	2.9	3.2	2.8 (p = 0.2)
IgM	1.6	1.5	1.8 (p = 0.2)

p values refer to differences between groups receiving interferon therapy and those that did not receive this treatment.

Kuwait. Chronic HCV infection was diagnosed on the basis of serum positivity for anti-HCV antibodies using a second-generation enzyme-linked immunosorbent assay (ELISA), the presence of HCV RNA in blood and elevated serum alanine aminotransferase level in the absence of other causes of liver disease.

Laboratory Testing for Immunoglobulins

Serum protein electrophoresis (SPE) was performed on agarose gels (Beckman Paragon SPE) and serum immunoglobulin levels were measured by using rate nephelometry (Beckman Array). A sample from a known case of monoclonal gammopathy was run as a positive control in SPE.

Statistical Analysis

Data analysis was performed using SPSS statistical software version 11 (SPSS Inc., Chicago, Ill., USA). A p value of ≤ 0.05 was considered statistically significant. Student's nonpaired t test was used to compare the different patient groups.

Results

The study comprised 100 patients with chronic HCV infection. Patients' characteristics are shown in table 1. There were 82 males and 18 females with a median age of 45 years. The median duration from the time of HCV diagnosis was 48 months (range 3–168). The majority of patients were non-Kuwaiti Arabs (75%). A

total of 44 patients had previously received combination anti-HCV treatment with interferon and ribavirin without sustained response. Interferon was given for a minimum of 3 months, and responding patients were given an extra 3 months of interferon therapy. Liver biopsies were performed in all the patients who received interferon and in 30 of the 54 patients who did not get interferon. SPE showed polyclonal bands in a total of 41 patients [14/44 (31.8%) in the interferon group and 27/56 (48.2%) in the no-interferon group]. The difference between the two groups was not statistically significant (p = 0.07). A total of 59 patients [30/44 (68.2%) in the interferon group and 29/56 (51.7%) in the no-interferon group] had a normal SPE. No patient was found to have a monoclonal band on SPE pattern. The mean serum IgG level was 18.4 g/l (range 4–39), IgA 2.9 g/l (range 0.09–8) and IgM 1.6 g/l (range 0.14–6.08). Immunoglobulin levels were not significantly different between the two groups.

Discussion

The prevalence of monoclonal gammopathies among patients with chronic HCV infection is controversial. In the study by Andreone et al. [12], a monoclonal band was

detected in 11% of HCV-positive patients, while Mangia et al. [11] showed that the prevalence of monoclonal gammopathies in patients with chronic HCV infection without cryoglobulinemia did not seem to differ from that in the general population. However, the latter study did not report the characteristics of the study sample or the methods used to screen for monoclonal gammopathy. Further, an in vitro study has shown that interferon- α may interfere with the production of monoclonal bands [14]. The present study clearly defines the patient population. Results were analyzed separately for patients who received interferon- α and those who did not. None of these cases had monoclonal gammopathy. These findings are in agreement with Mangia et al. [11] in terms of a low prevalence of monoclonal gammopathies associated with hepatitis C. These data also showed that interferon suppressed the polyclonal proliferation of B lymphocytes. It was not possible for us to obtain viral genotypes in our patients to assess the role of this factor in paraproteinemia. However, it is known that the majority of HCV patients in our region are infected with genotype 4 [15, 16]. A common

source of infection might have been the use of unsterilized needles to treat Bilharzia.

The absence of monoclonal gammopathies reported in this study could be due to the fact that monoclonal gammopathies are diseases of the elderly. The prevalence of this condition in individuals between 25 and 65 years of age is about 1% in the general population and most of our patients are young. It has been reported previously that the detection rate of monoclonal protein in Kuwait is very low [17].

Although this study showed no statistical differences between the two groups of patients (with and without interferon), the interferon treatment group had a lower incidence of polyclonal immunoglobulin production compared to the no-interferon group.

In conclusion, our results show that the prevalence of monoclonal gammopathies in patients with chronic HCV liver disease is extremely low and hence routine screening of these patients for monoclonal bands may not be necessary in Kuwait.

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