Serum Antibodies against Hepatitis C Virus in Iranian Patients with Graves’ Disease

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ABSTRACT

Hepatitis C virus (HCV) infection has been associated with a plethora of immune and autoimmune perturbations. A variety of conditions ranging from endocrinopathies to different skin diseases has been described in HCV infection. The aim of this study was to investigate the prevalence and clinical significance of HCV infection in patients with graves’ disease (GD).

A total of 55 patients with GD (30 women, 25 men, mean age: 35.24 ± 12.27 years) and 50 control subjects (28 women, 22 men, mean age: 33.34 ± 11.99 years) were examined. Third generation ELISA test was used for detection of antibodies to HCV in human sera, and anti-HCV seropositivity was confirmed by recombinant immunoblot assay (RIBA).

All normal controls were anti-HCV negative whereas anti-HCV antibody was present in 1 patient with GD and confirmed by Western blotting. These results indicate that there was no significant difference of anti-HCV antibodies between patients and controls.

In this study no relationship was found between GD and HCV infection, which imply that hepatitis C virus has not a direct causal role in the pathogenesis of GD, however, this does not rule out a “hit and run” virus induced disease.

Keywords: Autoimmunity; Graves’ Disease; Hepatitis C Virus

INTRODUCTION

GD is an organ-specific autoimmune disorder, characterized by diffuse goiter, thyrotoxicosis, infiltrative orbitopathy, and occasionally dermatopathy.1-3 The etiology of GD is obscure and numerous potential causal factors including infection, emotional stressors and diet have been studied.4,5 Thus far, no single environmental exposure has been consistently recognized as a causal factor in GD. Several observations suggest that certain viral infection may lead to autoimmune thyroid disorders in genetically susceptible persons.5 HCV is one of the viruses that has been gaining interest as a potential trigger of thyroid autoimmunity in individuals having genetic predisposing factors.6

It seems hepatitis C virus may initiate programmed cell death of thyroid follicular cells, resulting in development of autoimmune thyroid diseases.7 In addition GD and HCV infection share common features and a potential relationship between autoimmune thyroiditis and HCV infection was proposed by several investigators.8-12 However, a clear role for HCV in the pathogenesis of GD is not yet elucidated.

The purpose of this study was to investigate the prevalence and significance of HCV infection in patients with GD in Iran.
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MATERIALS AND METHODS

Sera of 55 patients with GD (30 women, 25 men, mean age 35.24 ± 12.27 years) were collected in endocrinology clinics. The clinical diagnosis of patients was accomplished by consultant endocrinologist. The diagnosis of GD was confirmed by suppressed or an undetectable serum TSH levels (<0.36 mIU/L), and an increased T₃ (>3.14 nmol/L) and T₄ (>142 nmol/L) concentrations. Sera from 50 healthy individuals (28 women, 22 men, mean age 33.34 ± 11.99 years), with no history of either GD or autoimmune disorders, such as Hashimoto’s thyroiditis, Insuline-dependent diabetes mellitus, Vitiligo and Alopecia areata were used as controls. Third generation enzyme-linked immunosorbent assay (ELISA) was used for the detection of antibodies to HCV in human sera (Bioelisa HCV, Spain). Anti-HCV immunoreactivity by enzyme immunoassay was confirmed by RIBA test (HCV Blot 3.0 kit, Genelabs diagnostics S.A., Switzerland). T₃ (reference values, 1.08 to 3.14 nmol/L), T₄ (reference values, 59 to 142 nmol/L) and thyroid stimulating hormone (reference values, 0.36 to 3.98 mIU/L) levels were measured with commercial radioimmunoassay kits (Kavoshyar Kit, Iran). Hepatic function was estimated with serum levels of total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase using conventional methods (Ziestchem, Iran).

Statistical Analysis

Student’s t-test was used to evaluate the statistical differences of the means between the two groups, and relative frequencies were compared using Fisher’s exact test \( \chi^2 \). All data are presented as mean ± SD. P-values lower than 0.05 were considered statistically significant.

RESULTS

Fifty five patients with GD and fifty normal controls were included in the study. Patients were characterized with respect to the presence of associated autoimmune disorders: 42 had no family history of autoimmune disease and no other disorder, 10 had a family history of autoimmune disease but had no other disease, 3 had other autoimmune disorders. Autoimmune diseases were: vitiligo (2 cases) and alopecia areata (1 case). The mean age of the patients in this study was 35.24±12.27 years (female patients, 33.90±12.95 years, male patients, 36.84±11.44 years). The mean duration of GD was 4.27±3.95 years (female patients, 4.68±4.37 years, male patients, 3.78±3.39 years). Only one out of 55 patients (2%) and none of the 50 controls was anti-HCV positive. Anti-HCV immunoreactivity by enzyme immunoassay was confirmed by RIBA test. This patient had higher levels of aminotransferase, alkaline phosphatase and total bilirubin than normal controls, although, there was no statistically significant difference in liver function tests among patients and controls.

Circulating TSH levels were significantly lower, and T₃ and T₄ levels were significantly higher, in patients with GD than in the control group. Altogether, in our study, there was no difference in HCV infection prevalence between the patients with GD and control group. The features and laboratory results of patients with GD and controls are shown in Table 1.

| Table 1. The features and laboratory results of patients with Graves’ disease and controls |
|----------------------------------|----------------|----------------|----------------|
| **Patients (N= 55)**             | **Controls (N= 50)** | **Statistical significance** |
| Age (years)                      | 35.24±12.27     | 33.34±11.99     | NS              |
| Sex (female/male)                | 30/25           | 28/22           | S               |
| T₃ (nmol/L)                      | 3.21±0.93       | 1.18±0.35       | S               |
| T₄ (nmol/L)                      | 145.55±41.17    | 85.66±13.75     | S               |
| TSH (mIU/L)                      | 0.28±0.52       | 2.11±0.85       | NS              |
| AST (U/L)                        | 22.15±10.03     | 20.36±2.84      | NS              |
| ALT (U/L)                        | 20.56±11.19     | 19.30±2.29      | NS              |
| ALP (U/L)                        | 74.91±16.79     | 72.36±10.24     | NS              |
| Total bilirubin (mg%)            | 0.56±0.19       | 0.49±0.19       | NS              |
| Anti-HCV ( positive patients)    | 1               | 0               | NS              |

NS: not significant  S: significant
DISCUSSION

Autoimmune diseases are diverse groups of acquired disorders. The mechanisms for the autoimmunity are multiple and complex. It is unlikely that a single explanation is adequate to account for the different phenomena that are observed in autoimmune disorders. The description of the agents that may participate to induce or perpetuate the autoimmunity is difficult, but there are several evidences that viruses have been implicated in the pathogenesis of autoimmune diseases,\(^{13-16}\) including autoimmune thyroiditis.\(^{5,17-19}\) The mechanisms by which the viruses could trigger autoimmunity in thyroid is not completely known. It is possible that viruses, by virtue of their ability to induce cell damage with release of autoantigens, expression of new antigens, and molecular mimicry may participate in the induction of autoimmune diseases in thyroid.\(^{20,21}\) In the present study the relationship between GD and HCV infection was investigated because many clinical and laboratory manifestations related to autoimmunity are shared between GD and HCV infected patients. There are a number of reports indicating the association of HCV infection and GD with other autoimmune diseases including vitiligo, systemic lupus erythematosus and sjogren’s syndrome.\(^{22-26}\)

Another relevant issue is an increased prevalence of anti-HCV antibodies in thyroid autoimmune diseases and high levels of anti-thyroid antibodies in HCV-infected patients.\(^{9,12,27}\)

In the present study, we analysed a series of sera from GD patients and normal controls for anti-HCV antibodies. These antibodies were detected in one out of 55 patients and confirmed by RIBA test. There were no statistical difference in HCV seropositivity between patients and normal controls. To our knowledge, this survey was the first study to investigate the relationship between GD and hepatitis C virus in Iran. There are limited reports of the prevalence and significance of anti-HCV antibodies in GD. Leri and colleagues\(^{28}\) found anti-HCV antibodies (by second generation ELISA) in 4 of 39 patients with autoimmune thyroid diseases, although hepatitis C virus RNA was detected in the sera of three of these four subjects, all of whom had GD. In another study Hung et al.\(^ {28}\) found out of the 23 hepatitis C virus infected patients who were seropositive for thyroid autoantibodies, two had GD. Lai et al introduced a patient with a chronic hepatitis C infection and GD.\(^ {26}\) The pathogenic role of HCV in the onset or exacerbation of GD is still unclear. As for the association between HCV and thyroid autoimmunity, hypothesized in the literature, in the present investigation, we analysed the prevalence of HCV infection among GD patients. The present data indicated that HCV seropositivity was not related to GD. However the relationship between GD and HCV remains unknown and additional investigations should be conducted to clarify the direct or indirect role of HCV in the pathogenesis of GD.

REFERENCES

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