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ORIGINAL ARTICLE

Hashimoto's Thyroiditis and Its Association with Hepatitis C Virus Infection

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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 have been described in HCV infection. The association of Hashimoto's thyroiditis (HT) with HCV infection has been reported in literature. Some data so far accessible are controversial. The aim of this study was to investigate the prevalence and clinical significance of HCV infection in patients with HT.

Materials and Methods: A total of 50p atients with HT (35 women, 15men , mean age: 33.82 ± 13.68 years) and 50co ntrol subjects (33 women, 17 men, mean age: 32.90 ± 13.07 years) were examined. Third generation ELISA test was used for detection of antibodies for HCV in human sera, and anti-HCV positive patients were tested for HCV RNA by polymerase chain reaction (PCR).

Results: All normal controls were anti-HCV negative whereas anti-HCV antibody was present in 2 patients with HT, cn firmed by RT-PCR. Fisher's exact test was used to compare relative frequencies. Results indicated that there wa no significant difference of anti -HCV antibodies between patients and controls.

Conclusion: In this study no relationship was found between HCV infection and HT, implying that hepatitis C virus has no a direct causal role in the pathogenesis of HT, this however does not rule out a "hit and run" virus induced disease.

Key Words: Hashimoto's thyroiditis/ Hepatitis C Virus/ autoimmunity

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Introduction

Hashimoto's thyroiditis is a chronic autoimmune thyroid disease, characterized by gradual destruction of thyroid follicles, infiltration of the thyroid with mononuclear cells and production of various autoantibodies.[1,2] The cause of HT is not definitely known and several hypotheses have been proposed.[3-5] It is likely that both genetic and environmental factors such as infection have been implicated in the pathogenesis of the disease.[6] It seems HT and HCV infection share common features and a potential relationship between autoimmune thyroiditis and HCV infection was proposed by several investigators.[7-10] However, a clear role for HCV in the pathogenesis of HT has not yet been elucidated. The purpose of this study was to investigate

the prevalence and significance of HCV infection in patients with HT in Iran.

Materials and Methods

Sera of 50 patients with HT (35 women, 15 men, mean age 33.82±13.68 years) were collected in endocrinology clinics. The clinical diagnosis of patients was made by a consultant endocrinologist. Patients were divided into two groups; 20 newly diagnosed HT, who had not received any treatment for this disease previously, and a group of 30 patients who had been treated with levothyroxine. Sera from 50 healthy individuals (33 women, 17 men, mean age 32.90 ± 13.07 years), with no history of either HT or autoimmune disorders, such as Graves' disease, Hashimoto's thyroiditis, Insulin-dependent diabetes mellitus, Vitiligo, or Alopecia areata, were used as controls. Patients were characterized with respect to the presence of associated autoimmune disorders: 41 had no family history of autoimmune disease or any other disorder, 7 had a family history of autoimmune disease but had no other disease, 2 had an autoimmune disorder. Autoimmune diseases were: alopecia areata, 1; and IDDM, 1. 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 reverse transcriptase (RT) polymerase chain reaction (RT-PCR, Amplicor, Roche-Diagnostic System, Basel, Switzerland). All serum samples of patients and controls were tested for thyroglobulin and thyroid peroxidase autoantibodies by ELISA (Labodia, Switzerland). T_4 (reference 59 to 142 nmol/L) and thyroid stimulatng hormone (reference, 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 standard laboratory 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 [χ^2]. All data are presented as mean ± SD. P values lower than 0.05 were considered statistically significant.

Results

Table 1 reports the features and laboratory results of patients with HT and controls. The diagnosis of HT was confirmed by the elevated thyroid stimulating hormone concentrations (>3.98 mIU/L), normal or subnormal serum T_4 value (≤ 59-142 nmol/L), high concentrations of antibody to thyroid peroxidase (> 40 IU/ml), with or without increase in anti- thyroglobuline antibodies.

Table 1. The features and laboratory results of patients with Hashimoto's thyroiditis and controls

	Patients (n=50)	Controls (n=50)	Statistical significance
Age (years)	33.82±13.68	32.90±13.07	NS
Sex (female/male)	35/15	33/17	
Anti-thyroid peroxidase antibody (IU/mL)	909.78±673.61	11.52±4.69	P<0.05
Anti-thyroglobulin antibody (IU/mL)	701.14±598.43	31.70±17.99	P<0.05
AST (U/L)	21.82±14.24	19.18±2.56	NS
ALT (U/L)	23.40±16.23	18.92±2.30	NS
ALP (U/L)	77.58±24.18	74.60±12.60	NS
Total bilirubin (mg%)	0.47±.24	0.73±0.16	NS
Anti-HCV	2	0	NS

NS= not significant

Thirty five patients (70%) were female and fifteen (30%) were male. The mean age of the patients in this study was 33.82±13.68 years (female patients, 34.11±13.60 years, male patients, 33.13±14.31 years). The mean duration of HT was 6.27±7.69 years (male patients, 6.10±4.53 years, female patients, 6.34±8.76 years). Only two out of 50 patients (4%) and none of the 50 controls was anti-HCV positive.

Anti-HCV immunoreactivity by enzyme immunoassay was confirmed by RT-PCR test. These two patients had higher aminotransferase levels, alkaline phosphatase and total bilirubin than did normal controls, although, there was no statistically significant difference in liver function tests among patients and controls. Serum anti-tyroglobulin and anti-thyroid peroxidase antibody titers were also significantly higher in patients than in the controls.

Discussion

Autoimmune diseases are a diverse group 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 observed in autoimmune disorders. The description of the agents that may participate in the induction or perpetuation of autoimmunity is difficult, but there is much evidence that viruses have been implicated in the pathogenesis of autoimmune diseases,[11-14] such as autoimmune thyroiditis.[15-19]

The mechanisms by which the viruses could trigger autoimmunity in thyroid are not completely known. It is possible that viruses, by virtue of their ability to cause cell damage with release of autoantigens, expression of new antigens, and molecular mimicry may play a role in the induction of autoimmune diseases in thyroid.[20,21] Since many clinical and laboratory manifestations related to autoimmunity are shared between HT and HCV infected patients, in the present study the relationship between HCV infection and HT was investigated. There are a number of reports indicating the association of HCV infection and HT with 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.[7-9,27] In addition the presence of circulating autoantibodies such as anti-smooth muscle antibodies and anti-nuclear antibodies have been described in both diseases.[28 -31]

In the present study, we evaluated a series of sera from HT patients and normal controls for anti-HCV antibodies. These antibodies were detected in two out of 50 patients and confirmed by RT-PCR test. According to our study, HCV antibody prevalence in Iranian patients and normal controls were 4% and 0%, respectively. There was no statistical difference in HCV seropositivity between patients and normal controls. In addition when we used the prevalence of anti-HCV antibody (0.1%) among 319375 healthy blood donors[32] for comparison as the control group, there was again no significant difference between the two groups.

To our knowledge, this survey was the first study to investigate the relationship between HT and hepatitis C virus in Iran. There are limited reports of the prevalence and significance of anti-HCV antibodies in HT. Duclas-Vallee et al[9] found anti-HCV antibodies (by ELISA) in 12 of 50 patients, although RIBA showed antibody positivity in only 5 patients. In another study Wagner et al[33] found anti-HCV antibodies in 3 of 118 patients with HT confirmed by polymerase chain reaction. Conversely, other investigators including Wong et al[34] could not demonstrate a statistically significant association between HCV and HT. The pathogenic role of HCV in the onset or exacerbation of HT is still unclear. The relation of HT and seropositivity for HCV is not a conclusive reason to evaluate

the role of HCV infection in the pathogenesis of HT.

In conclusion the results of this study indicated that HCV seropositivity was not related to HT and, does not support a key or predisposing role of HCV in the initiation of HT. However the possibility of a role for viruses or other pathogens does exist.

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