Mintage Journal of Pharmaceutical & Medical Sciences
RESEARCH ARTICLE

DO HERPES SIMPLEX VIRUSES (TYPE 1 AND 2) PLAY A ROLE IN THE PATHOGENESIS OF HASHIMOTO'S THYROIDITIS?

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Received -15-06-13; Reviewed and accepted -24-06-13

ABSTRACT

Objective: Autoimmune thyroid disease is a complex disease with genetic, endogenous and environmental etiologies. This review examines the data related to the role of viruses in the development of Hashimoto's thyroiditis.

Materials and methods: This study was conducted on Hashimoto's thyroiditis patients, whom diagnosis was confirmed by testing their post-thyroidectomy specimens histopathologically, along with hormonal assays for their T3, T4 and TSH. The study samples were collected randomly from different hospitals in Al-Hilla City, Babylon-Iraq; during the period from August 2011 to December 2012. The study included 28 patients; 27 of them were females with only one male. Patients' ages ranged from 22 to 51 years, with a mean age of 36.82±7.703 years. A blood samples were drawn from all the above mentioned patients to detect a herpes simplex virus (Type 1 and 2) (HSV 1 and 2) infections and the diagnosis was established by testing the patients' sera with a virus-specific IgM and IgG antibodies using ELISA technique.

Results: This study demonstrated an abundant negative result (92.8%) for HSV 1-specific IgG among the patients; with equal negative and positive antibody titres for HSV 1-specific IgM. On the other hand; the data concerning HSV 2 showed a complete negativity in IgG specific for the virus among the study patients with plentiful negativity (96.4%) regarding the titre of HSV 2-specific IgM.

Conclusion: The possible role of human herpes viruses in the pathogenesis of Hashimoto's thyroiditis is not supported by our study; hence our raised question stays open for more investigation on more patients and in different regions of the country, in order to develop new strategies for prevention and/or treatment.

Key words: Herpes simplex virus, Hashimoto's thyroiditis, IgM, IgG, ELISA.

INTRODUCTION

Hashimoto's thyroiditis or chronic lymphocytic thyroiditis is an autoimmune disease in which the thyroid gland is attacked by a variety of cell -and antibody-mediated immune processes. It was the first disease to be recognized as an autoimmune disease. It was first described by the Japanese specialist Hakaru Hashimoto in Germany in 1912 [1]. The symptoms are generally the same as for other forms of hypothyroidism, but if left untreated the gland may ultimately be destroyed. It is marked by the presence of autoantibodies and is often associated with other autoimmune conditions [2].

A significant number of those diagnosed with Hashimoto's are completely asymptomatic, while a small proportion of both men and women are subclinical. The disease can eventually cause a depletion of circulating thyroid hormones, creating symptoms of low thyroid function; though not everyone with the autoantibodies goes on to develop hypothyroidism [3]. It is most prevalent in women, generally developing between the ages of 30 and 50. By age 60, it is estimated that 20% of women are hypothyroid [4].

Herpes simplex virus infections are common and range from mild to severe disease. Those who are infected with HSV types 1 and 2 (HSV-1 and HSV-2) often have few or no symptoms [5]. Several members of this family cause lifelong infections that are characterized by periods of quiescence followed by reactivation due to psychological stress, sun exposure, and onset of menses [6].

Viral infections are frequently cited as a major environmental factor implicated in subacute thyroiditis and autoimmune thyroid diseases (AITD) [7]. Herpes viruses have been suggested as potential cofactors, and have occasionally been detected in AITD [8].

The aim of this study was the investigation of the possible association between Hashimoto's thyroiditis and herpes simplex virus infection.

MATERIALS AND METHODS

This study was conducted on Hashimoto's thyroiditis patients, whom diagnosis was confirmed by testing their post-thyroidectomy specimens histopathologically, along with hormonal assays for their T3, T4 and TSH. The study samples were collected randomly from different hospitals in Al-Hilla City, Babylon-Iraq; during the period from August 2011 to December 2012.

The study included 28 patients; 27 of them were females with only one male. Patients' ages ranged from 22 to 51 years, with a mean age of 36.82±7.703 years.

A blood samples were drawn from all the above mentioned patients to detect a herpes simplex virus (Type 1 and 2) (HSV 1 and 2) infections and the diagnosis was established by testing the patients' sera with a virus-specific IgM and IgG using ELISA technique.

The HSV 1 IgM and IgG antibodies; HSV 2 IgM and IgG antibodies were analyzed according to the procedures recommended by the following kits: ab108738 Herpes Simplex Virus 1 (HSV 1) IgM Human ELISA Kit, ab108737 Herpes Simplex Virus 1 (HSV 1) IgG Human ELISA Kit, ab108740 Herpes Simplex Virus 2 (HSV 2) IgM Human ELISA Kit and ab108739 Herpes Simplex Virus 2 (HSV 2) IgG Human ELISA Kit, respectively. All those kits were manufactured by Immunology Consultants Laboratory, Inc., USA [9].

RESULTS

The frequency distribution of HSV 1 infection among patients with Hashimoto's thyroiditis is shown in Figure (1); which demonstrates that for HSV 1-specific IgM, 50% of patients were found to have a positive antibody titre whereas the other 50% of them were negative. On the other hand; the majority of patients (92.8%) were having a negative titre for HSV 1-specific IgG with only 7.2% of them having a positive titre for the same antibody

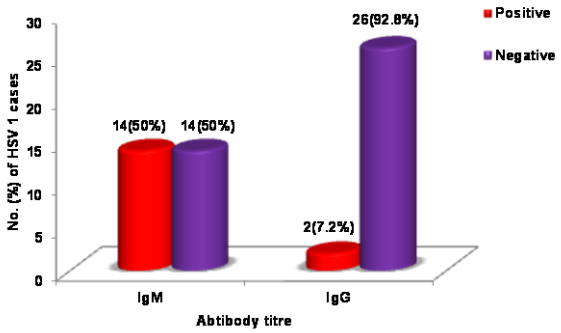

Figure 1: Frequency distribution of herpes simplex virus type 1 (HSV 1) infection among patients with Hashimoto's thyroiditis.

For HSV 2 infection, its frequency distribution among patients with Hashimoto's thyroiditis is shown in Figure (2), demonstrating that for HSV 2-specific IgM, 96.4% of patients were negative and the remaining 3.6% were positive for the antibody titre; while for HSV 2-specific IgG, no cases (0%) were found to have a positive antibody titre with a 100% negativity for it.

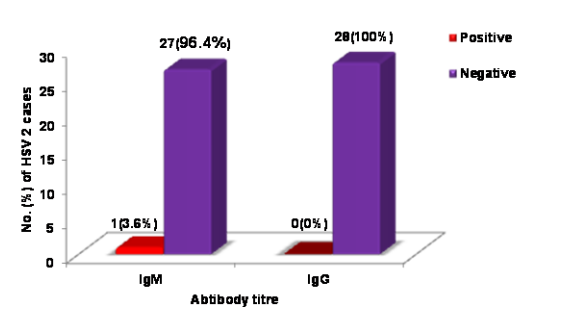

Figure 2: Frequency distribution of herpes simplex virus type 2 (HSV 2) infection among patients with Hashimoto's thyroiditis.

DISCUSSION

The mechanisms by which infection may induce an autoimmune response are many, and this makes infections an attractive hypothesis for disease initiation [10]. Paradoxically, infections may enhance AITD but may also be protective. Indeed, the hygiene hypothesis implies that the immune system is educated by multiple exposures to different infections allowing it to control autoimmune responses better. Thus, improved living standards associated with decreased exposure to infections are associated with an increased risk of autoimmune disease and the lower socio-economic groups have a reduced prevalence of thyroid auto antibodies [11, 12].

In this review, the findings of the antibody titres specific to HSV 1 and 2 were showing an abundant negativity, with an equal negative and positive results regarding HSV 1-specific IgM titre. These findings may be consistent with what was stated by Prummel *et al*. [7] and Desailloud and Hober [13] that viral infections have been frequently cited as important environmental factors implicated in AITD, but no specific virus has yet been conclusively associated to the disease. In particular, herpes viruses have been implicated, with conflicting evidence.

Thomas *et al*. [8] declared that it is not known if HSV 1 and HSV 2 have the tropism to the thyroid gland, and if they are capable of persisting in the thyroid gland after primary infection. Thyroid tissue specimens were obtained postoperatively from patients with Hashimoto's thyroiditis. Virus DNA was detected using PCR-based assays. No statistically significant differences were observed concerning the specific strains HSV1 and HSV2. Thus; their findings (despite the use of a different technique in detecting the virus) may show an agreement with our results and can explain the inadequately detectable herpes virus antibodies in our samples.

For HSV 1-specific IgM results, it's probable that those patients were having a previous attack of the virus and possibly that they got a latent infection which was reactivated then by their surgical trauma. Agreement to this explanation is in what was stated by Levinson [14] that HSV virus replicates in the skin or mucous membrane at the initial site of infection, then migrates up the neuron and becomes latent in the sensory ganglion cells. The virus can be reactivated from the latent state by a variety of inducers, e.g., sunlight, hormonal changes, trauma, stress, and fever, at which time it migrates down the neuron and replicates in the skin, causing lesions. In our work, the reason that the rise was only in IgM titre and not in IgG could perhaps be due to the fact that the post-thyroidectomy specimens were tested immediately after the operation for the presence of those antibodies and according to the statement of Brooks *et al*. [15] that "IgM is the main immunoglobulin produced early in the primary immune response and IgG is the predominant antibody in secondary responses and constitutes an important defense against bacteria and viruses. When an individual encounters an antigen for the first time, antibody to that antigen is detectable in the serum within days or weeks depending on the nature and dose of the antigen and the route of administration (eg, oral, parenteral). The first antibodies formed are IgM, followed by IgG, IgA, or both. IgM levels tend to decline sooner than IgG levels". So this statement might explain the slight rise in HSV 1-specific IgM only.

Identifying etiological infections in human disease is difficult. Besides the fact that organ tissue is not always available for direct study, the interpretation of virological data must be cautious. The presence of antibodies directed towards a virus does not prove that this pathogen is responsible for the disease, especially when the agent is common in the general population. On the other hand, the absence of viral markers at the onset of the disease does not refute the viral hypothesis [13].

In our study, a direct evidence of the presence of the virus components is present but not sufficient enough to determine whether they are responsible for thyroid diseases or whether they are just innocent bystanders.

CONCLUSION

The possible role of human herpes viruses in the pathogenesis of Hashimoto's thyroiditis is not supported by our study; hence our raised question stays open for more investigation on more patients and in different regions of the country, in order to develop new strategies for prevention and/or treatment.

ACKNOWLEDGEMENTS

Special thanks and gratefulness to all the patients who participated in this study and to everyone helps and facilitates our work.

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