

Incidence of Seropositivity for HTLV-I in Patients with Graves' Disease in Mashhad, North East of Iran

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Abstract. Graves' disease is an autoimmune thyroid disease and is the most common cause of thyrotoxicosis. Viral infections are frequently cited as a major environmental factor contributing to autoimmune thyroid diseases. Some reports indicate that the incidence of human T-cell leukemia virus type I (HTLV-I) antibody is higher in patients with Graves' disease. The objective of this study was to determine whether HTLV-I infection and Graves' disease are related. Our method was to determine the seropositivity rate of HTLV-I in patients with Graves' disease in Mashhad, an endemic city in north east Iran. We recruited all patients with Graves' disease who consecutively attended our endocrinology clinic at the University Hospital of Mashhad. Blood samples were collected from 105 Graves' patients. We screened the patients' serum for HTLV-I using an enzyme-linked immunosorbent assay. We then compared the seroprevalence of HTLV-I in the patient group with the viral infection rate calculated for the entire population of blood donors in Mashhad. No cases in our patient group were positive for HTLV-1 ($0/105 = 0\%$). By comparison, the control group had a seropositivity of 0.664% ($404/60,892$). In this study, we found no association between HTLV-I and Graves' disease in Mashhad. Further studies are needed to determine whether there is a relationship between the two conditions.

Keywords. Graves' disease • HTLV-I • Human T-cell leukemia virus type I • Iran • Mashhad

Introduction

Human T-cell leukemia virus type I (HTLV-I) is a human retrovirus endemic to southern Japan, inter-tropical Africa, Melanesia, Latin America, and the Caribbean basin.^[1] The virus is a causative agent in adult T-cell leukemia^[2] and HTLV-I-associated myelopathy/tropical spastic paraparesis.^[3,4] HTLV-I may also be the cause of some other inflammatory disorders, such as uveitis,^[5] chronic arthropathy,^[6] pulmonary alveolitis,^[7] Sjögren's syndrome,^[8] and autoimmune thyroiditis.^[9-13]

The autoimmune thyroid diseases, which are common, include Hashimoto's thyroiditis and Graves' disease. Both disease are characterized by lymphocytic infiltration and the presence of serum antithyroid antibodies. The association of autoimmune thyroiditis and HTLV-I has been extensively investigated, and there are reports of a correlation between Graves' disease and uveitis in HTLV-I car-

riers (14,15). The virus is endemic in Mashhad in northeastern Iran.^[16] We recently reported an association between Hashimoto's thyroiditis and HTLV-I in Mashhad.^[17] The objective of this study was to determine whether there is an association in Mashhad between Graves' disease, another common autoimmune thyroid disease, with HTLV-I.

Materials and Methods

We recruited all patients with Graves' disease who consecutively attended our endocrinology clinic in the University Hospital of Mashhad between February 1, 2008 and March 30, 2009. After the aim of the study was explained to the patients, those who gave informed consent were asked to participate.

Blood samples were collected from 105 patients with Graves' disease. Serum samples were screened for HTLV-I using an enzyme-linked immunosorbent assay (ELISA; Dia. Pro diagnostic Bioprobes, Italy).

Data were descriptively expressed as mean \pm SD or number.

To compare the seroprevalence rate of HTLV-I found in Graves' disease with that of the society at large, we used the viral infection rate calculated for the entire population of blood donors in Mashhad (n = 60,892) referred to the Blood Transfusion Organization between March 2001 and March 2002.^[16]

Results

A total of 105 patients with Graves' disease were tested for HTLV-I. The patients included 36 males and 69 females who ranged in age from 17-68 years. The mean age of the group was 34.31 ± 11.52 years. All patients were Iranian and living in Mashhad (an HTLV-I endemic area), north east of Iran.

No Graves' patients were positive for HTLV-I. Therefore, the seropositivity rate for the patient group was 0% (0/105) compared to 0.664% (404/60,892) for the control group.

Discussion

Graves' disease is a common autoimmune disease and is considered the most common cause of thyrotoxicosis. Specific infections may trigger Graves' disease. They may do so by initiating the liberation of antigens (via cell destruction or apoptosis), by forming altered antigens or causing molecular mimicry, by cytokine and chemokine secretion, and by inducing aberrant HLA-DR expression and Toll-like receptor activation.^[18] Viral infections are often cited as a major environmental factor that initiates autoimmune thyroid diseases.^[9-13]

HTLV-I is a human retrovirus endemic to some areas of the world.^[1] The virus may cause a systemic immune-mediated inflammatory disease that involves many tissues, including the thyroid gland. The role of HTLV-I in the pathogenesis of autoimmune thyroid diseases has been demonstrated in animals and human.^[19-23] Most of these studies have involved patients with Hashimoto's thyroiditis. However, researchers have reported that in Fukuoka Prefecture, Japan, the incidence of HTLV-I antibody in Graves' patients is higher (6.6%) than expected in the general population (2.2%).^[11]

Anti-HTLV-I antibodies and proviral DNA has been detected in the peripheral lymphocytes of Graves' patients.^[24,25] In addition, proviral load in HTLV-I-infected patients with Graves' disease was

significantly higher than in asymptomatic HTLV-I carriers.^[26] It appears that Graves' disease and HTLV-I infection interact and result in the onset of uveitis.^[24,25] The provirus load was significantly higher in uveitis patients with Graves' disease than in those without Graves' disease.^[28] As in Hashimoto's thyroiditis, HTLV-I infectivity in the thyroid was proven: HTLV-I DNA was detected by polymerase chain reaction in the thyroid tissue of an HTLV-I-infected male who was afflicted with Graves' disease followed by uveitis. Also, HTLV-I was isolated from thyroid tissue by coculture with peripheral blood lymphocytes.^[29]

There is some evidence of HTLV-I or its components in the organs of patients with Graves' disease. However, it remains to be determined whether the virus is responsible for the thyroid disease or whether it is just innocent bystanders. There are only limited epidemiologic studies of the role of HTLV-I in Graves' disease.^[11]

In this study we evaluated the incidence of serum positivity for HTLV-I among Graves' patients in Mashhad, an endemic city in Iran. Contrary to the results reported by Mizokami et al.,^[10] we found no association between HTLV-I and Graves' disease. None of our patients with Graves' disease were infected with HTLV-I.

Conclusion

We found no correlation between HTLV-I and Graves' disease. Further studies are needed to clarify the relationship between viruses and autoimmune thyroid diseases, including HTLV-I and Graves' disease.

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