

Spontaneous conversion from Graves' disease to Hashimoto's thyroiditis: a case report

Graves hastalığından Hashimoto tiroiditine spontan dönüşüm: olgu sunumu

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Abstract

Graves' disease and autoimmune thyroiditis are part of the spectrum of thyroid diseases known to develop with an autoimmune etiology. The presence of anti-thyroid autoantibodies is known, and the thyroid is the organ where autoimmune diseases are most commonly seen in the all body. A 29-year-old woman who admitted our clinic with tremor in the hands, sweating and palpitation was diagnosed with Graves' disease with accompanying laboratory findings and was started on anti-thyroid therapy. The patient entered into remission at the end of two years. She was then regarded as euthyroid and followed-up for another 18 months without using anti-thyroid drugs. At the end of 18 months, Hashimoto's thyroiditis was determined to have developed at routine polyclinic follow-up.

Keywords: Graves disease, Hashimoto's disease, autoantibodies

Öz

Graves hastalığı ve otoimmün tiroiditler, otoimmün etiyoloji ile oluştuğu gösterilmiş tiroid hastalıkları spektrumunun içinde yer alır. Tiroide karşı otoantikörlerin varlığı bilinmektedir ve tiroid tüm vücutta otoimmün hastalıkların en sık görüldüğü organdır. Elllerinde titreme, terleme ve çarpıntı şikayetleri ile başvuran 29 yaşında bayan hastaya laboratuvar bulgular eşliğinde Graves hastalığı tanısı konularak anti-tiroid tedavi başlandı. Hasta iki yılın sonunda remisyona girdi. Remisyona giren hasta 18 ay anti-tiroid ilaç kullanımı olmadan ötiroid olarak takip edildi. 18. ayın sonunda rutin poliklinik kontrolünde Hashimoto tiroiditi geliştiği tespit edildi.

Anahtar Kelimeler: Graves hastalığı, Hashimoto hastalığı, otoantikörler

Introduction

Graves' disease has an autoimmune etiology and is the most common cause of clinical hyperthyroidism. The disease is caused by stimulating autoantibodies binding to the TSH receptor. Although the great majority of antibodies forming against the TSH receptor have a stimulant effect and are capable of establishing hyperthyroidism, some have a blocking nature, as with autoimmune hypothyroidism, and

give rise to clinical hypothyroidism. In the literature, cases of conversion from hypothyroidism to hyperthyroidism have been reported but conversion from hyperthyroidism to hypothyroidism is very rare although reported

We report a case diagnosed with and treated for Graves' disease that spontaneously converted into autoimmune hypothyroidism after being follow-up for 18 months without medication after the end of treatment.

Case Presentation

A 29-year-old female patient admitted with tremor in the hands, sweating and palpitation for about a month. About 5 kg weight loss was present in her history same period. On physical examination the thyroid gland was symmetrically enlarged and stage 2 was assessed. Thin tremor was observed in the hands, with a heart rate of 110/min regularly. No ocular findings were present. At thyroid function tests were: fT3: 3.85 ng/ml (1.71-3.70), fT4: 12.48 ng/dl (0.7-1.48) and TSH: 0.000 μ U/L (0.35 -4.95), anti-TPO: 127 IU/ml (<5.6), anti-TG: 57.4 IU/ml (<4.1) and TSH receptor antibody (TRAb):13 IU/L (nl<1). Thyroid ultrasonography showed right lobe 55x23x30 mm, left lobe 53x27x28 mm and isthmus 6 mm. Gland sizes and blood flow increased at the ultrasonography. Tc-99m-pertechnetate thyroid scan was activity increased and the distribution was homogeneous, reported as compatible with Graves' disease. The patient was diagnosed with Graves' disease and received methimazole therapy for 2 years. The patient entered remission and was followed up as euthyroid for 18 months without anti-thyroid therapy. At routine polyclinic follow-up at the end of 18 months, TSH was 22 μ U/L, fT4: 0.49 ng/dl, fT3: 0.5 ng/ml, anti-TPO: 358 IU/ml, and anti-TG: 22 IU/ml. And also TSH receptor antibody was negative and TSH receptor-blocking antibody was 0.68 IU/L (<1.22 IU/L negative). Thyroid ultrasonography showed that the thyroid parenchyma is heterogeneous, innumerable small hypoechoic nodules measuring and thyroid blood flow normal. Hashimoto's thyroiditis was diagnosed on that basis. The case had spontaneously turned into one of autoimmune hypothyroidism.

Discussion

Autoimmune thyroid disease (AITD) is the most prevalent organ-specific autoimmune disease, affecting 2-5% of the general population in Western societies [1]. Autoimmune thyroid diseases including Graves' disease and Hashimoto's thyroiditis develop on a basis of both environmental and genetic triggers. Although the interaction between environmental factors and genetic triggers and the pathogenesis are not known for certain, Graves' disease and Hashimoto's thyroiditis are known to share similar immune-mediated mechanisms [2].

Autoimmune thyroid diseases develop as a result of an

immune attack against thyroid tissue due to dysregulation occurring in the immune system. Autoimmune thyroid diseases are T cell-mediated conditions. While the estimated prevalence of these diseases is 5%, that of anti-thyroid antibodies is higher [3]. This shows that the presence of autoantibodies is not by itself sufficient for these diseases to occur, and that interaction with environmental and other factors is required.

The genetic factors identified for autoimmune thyroid diseases include major histocompatibility genes (HLA), immunoregulatory genes (cytotoxic T lymphocyte-associated Factor 4 (CTLA4), the protein tyrosine phosphatase-22 gene (PTPN22), CD25, CD40, the Fc receptor-like 3 gene (FRCL3), and thyroid-specific genes (TSHR and Tg). Environmental factors include iodine intake, smoking, alcohol, selenium and Vitamin D levels, infections, stress, use of estrogen-containing drugs, female gender and age [4,5]. Regulatory T cells (Tregs) control immune responses, prevent excessive inflammation, and may be dysfunctional in AITD [6,7]. Regulatory T cells in particular play a key role in the maintenance of self tolerance, with their dysfunction leading to severe or even fatal immunopathology [8].

The immunomodulator effects of antithyroid drugs used in the treatment of autoimmune thyroid diseases, which are the result of loss of immune tolerance, are well known. Studies reporting immunomodulatory effects of antithyroid drugs are available in the literature.

Methimazole treatment reduced the proliferative activity of CD3+ T cells in pediatric Graves' disease patients and increased the proliferation rate of regulatory T cells [9]. The significant modifications of lymphocyte subsets, as well as the reduction of thyroid autoantibodies, support a direct or mediated effect of methimazole on the immune system [10].

Both diseases are characterized by infiltration of the thyroid gland by reactive B and T lymphocytes causing the production of thyroid-specific antibodies against thyroid antigens. Despite sharing common features they give rise to different clinical pictures. Graves' disease occurs as a result of lymphocytic infiltration and activation of TSH receptor (TSHR)- reactive B cells causing production of TSHR-stimulating antibodies, resulting in hyperthyroidism. In contrast, Hashimoto's thyroiditis is characterized by thyroid cell apoptosis and results in hypothyroidism [11].

Spontaneous conversion into chronic autoimmune hypothyroidism has been reported in approximately 15-20% of patients diagnosed with Graves' disease. The balance between a TSH receptor activating antibody (TSAb) responsible for hyperplasia and hyperfunction by stimulating the thyroid gland in Graves' disease and a TSH stimulation blocking antibody (TSBAb) responsible for the atrophy occurring in the gland and consequent hypothyroidism in Hashimoto's thyroiditis affects and changes the behavior of the thyroid gland [12].

Cases shown to have converted into Hashimoto's thyroiditis following diagnosis and treatment of Graves' disease take the form of case reports in the literature [13,14].

Umar et al. [13] reported four cases of conversion into Hashimoto's disease following diagnosis of Graves' disease. Conversion to autoimmune hypothyroidism was observed 7-25 years after treatment for Graves' disease in three cases, while in the fourth case autoimmune hypothyroidism was observed a few months after. Shigemasa et al. [14] reported conversion to Hashimoto's thyroiditis following anti-thyroid treatment in three patients diagnosed with Graves' disease.

Again there are in the literature cases reports which conversion to Graves' disease from Hashimoto's thyroiditis [15,16].

Ohye et al. [15] reported four cases of painful autoimmune hypothyroidism developing after Graves' disease. The patients were all middle-aged women. All these cases with autoimmune hypothyroidism were determined to have high initial anti-thyroid antibody titers.

Ouleghzal et al. [16] reported 18-year old patient who has followed autoimmune hypothyroidism. Two years later conversion to Graves' disease that diagnosis positivity of TSH-receptor antibody.

Definite diagnosis can be made with fine-needle aspiration biopsy. We can't used fine-needle aspiration biopsy for definite diagnosis of our patient because she didn't want thyroid biopsy. We used for diagnosis that laboratory and clinical findings. The case was thus shown to have converted to hypothyroid disease. The pathogenesis of the conversion from Graves' disease to autoimmune hypothyroidism is not known for certain.

Two different mechanisms are involved in the pathogenesis of autoimmune hypothyroidism, cell destruction caused by humoral and cellular mechanisms or the blocking of cell functions in forms of thyroiditis with goiter [16].

Tamai et al. [17] reported that development of autoimmune hypothyroidism after Graves' disease might be possible by three mechanisms – autoimmune destruction, presence of a high level of blocking antibodies and focal or diffuse thyroiditis.

TSBAb to TSAb switching occurs in patients treated with levothyroxine (LT4); the reverse switch (TSBAb to TSAb) occurs after anti-thyroid drug therapy. Furthermore, in Graves' disease, the spontaneous change from hyperthyroidism to hypothyroidism may occur in two ways: by the unexpected development of TSBAb or the process of thyroid damage reflected in chronic lymphocytic thyroiditis overcomes the stimulatory effects of TSAb [18].

In conclusion, Graves' disease and Hashimoto's thyroiditis are diseases that cause different clinical findings through different etiopathological processes. Graves' disease and Hashimoto's thyroiditis are clinical conditions well known to produce consecutive clinical findings in the same patient. It is therefore very important for cases of both Graves' disease and Hashimoto's thyroiditis to be followed-up closely in order for patients' existing treatments to be more effective and in terms of diagnosing potential complications.

Declaration of conflicting interests

The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

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