UDK: 616.441-008

CASE REPORT

RARE CASE OF CONVERSION OF AUTOIMMUNE HYPOTHYROIDISM TO HYPERTHYROIDISM

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Abstract

Up to date, the literature data have presented various case reports of conversion from hyperthyroidism to hypothyroidism, but conversion from hypothyroidism to hyperthyroidism is very rare. In this context we present a rare case of primary hyperthyroidism which converted spontaneously to hypothyroidism and 18 years later hyperthyroidism and thyrotoxicosis were once again confirmed. Hashimoto thyroiditis is an autoimmune disease. Thyrotoxicosis is a clinical state of inappropriately high levels of circulating thyroid hormones.This case report confirms that although it is very rare, after long condition of hypothyroidism, immunological shift is possible with development of consecutive hyperthyroidism with stimulating auto antibodies.

Key Words: *autoimmunehyperthyroidism, autoimmune hypothyroidism, thyrotoxicosis.*

Introduction

Autoimmune thyroid diseases are one of the most common autoimmune diseases in the world affecting 2-4% of women in the world and 1% of men (1,2,3).
Graves' disease and Hashimoto's thyroiditis are the most common autoimmune thyroid conditions. Hyperthyroidism following hypothyroidism is a rare phenomenon. Hypothyroidism was once thought to be a permanent state requiring lifelong replacement therapy,but there are increasing numbers of cases in the literature whichoppose this postulation.
Both have complex etiology with complex pathogenesisinfluenced by a variety of environmental factors, as well as hereditary components which play a major role in all autoimmune diseases (4).
Autoimmune thyroid disease can involve one or more types of thyroid antibodies. These include the thyroid stimulating hormone (TSH) receptor antibodies, which can be divided into

stimulating or blocking types. Additionally, thyroid peroxidase antibody and thyroglobulin antibody are thyroid-specific antibodies commonly found in thyroid autoimmunity.
It is already known that thyrotoxicosis may be followed by hypothyroidism. However, development of thyrotoxicosis after a long period of hypothyroidism is not a common phenomenon (5).

Case Report

We present a 48-years-old femalewith 3months history of fatigue, heat intolerance, sweating, weight loss, tremor and tachycardia. Ultrasound of the thyroid gland presented diffuse enlargement, twice the normal size. Clinical suspicion of primary hyperthyroidism was made and then confirmed by standard laboratory analysis. Treatment was initiated with propylthiouracil of 100mg three times a day. For the next twelve monthsthe patient was scheduled for regular followcheck-ups. Total T4 decreased and treatment with propylthiouracil was also reduced subsequently gradually. One year after, the laboratory results presented decreased total T4 values with increased TSH levels. Treatment was immediately stopped. The patient was left without therapy for observation. Spontaneous conversion of hyperthyroidism to hypothyroidism was confirmed. Increased levels of antithyroid antibodies were also detected, both anti-thyroglobulin and anti-peroxidase. Hypothyroidism due to Hashimoto thyroiditis was confirmed and adequate treatment with levothyroxine was initiated.The condition remained for 18 years after diagnosis.18 years after diagnosing this condition, the patientpresented with symptoms such as weight loss, tachycardia and tremor. Laboratory analyses were performed and they were in favor of hyperthyroid state. Treatment was stopped and the patient was left for observation. After one-month, standard biochemical analysis was performed and decreased levels of TSHand increased levels FT3 which were again confirmed. Additionally, increased thyroid stimulating immunoglobulins was also detected. Hyperthyroidism relapse and T3 thyrotoxicosis was confirmed afterwards and treatment with propylthiouracil was initiated. Up to date, the patient is stable and the thyrosupresive therapy is still ongoing.

Discussion

In the presented case report initial hyperthyroid state spontaneously converted into hypothyroidism. The patient had been on thyroxine replacement therapy for approximately 18 years. During this period thyroid antibodies, in favor of Hashimoto's thyroiditis, were positive and TSH levels were in normal range due to the effects of levothyroxine.
The conversion of Hashimoto's thyroiditis to Graves' disease is documented in the literature, but such cases are rare and are postulated to be due to a combination of atypical destructive thyroiditis, and the development of antibodies associated with hyperthyroidism. It is also stated that autoimmune destruction initially produces a hypothyroid state, but the stimulatory effect of thyrotropin receptor stimulating antibodies (TSAb/ TSI) and thyroid destruction may alter and

subsequently create a hyperthyroid state (6).
Other 2 studies regarding several similar cases propose that the damage to the thyroid tissue may act as the triggering factor for hyperthyroidism. This also involved the production of TSH receptor antibodies which changed effects from blocking to stimulating thusproducing a state of hyperthyroidism (7,8).
The pathogenesis of this conversion is not well explained in the literature due to its complex etiology, but there are different theories postulated behind this conversion.
The first similar case was described by Joplin and Fraser in 1959 and several others followed in the years to come (9,10,11,12). In 1990 Takasu *et al*. (13) described a case series converting to Graves' disease following previous Hashimoto's disease, and it was observed that those cases could be divided into three groups: a group of transient Graves' disease following hypothyroidism, a group of persistent Graves' thyrotoxicosis following hypothyroidism and a group of persistent hypothyroidism despite positive thyroid-stimulating immunoglobulins.
Our patient was diagnosed with hypothyroidism and achieved euthyroid state following treatment with levothyroxine. This hypothyroid state converted spontaneously after 18 years when hyperthyroidism was again confirmed. The precipitating factors are unclear. The percentage of conversion of hypothyroidism to hyperthyroidism isestimated to occur in 1.2% of patients according to the largest reported series in the literature (14).
One of the possible mechanisms for conversion is an environmental trigger in a genetically susceptible individual whichmay alter the thyroid gland by altering the balance in the activity of blocking and stimulating antibodies and the response of the thyroid gland to these antibodies (15).
Another theory is that thyroid damage from an autoimmune phenomenon initially causes thyroid hypofunction, but once thyroid tissue has recovered enough, it is stimulated by the stimulating autoantibodies and consecutive hyperthyroidism occurs (15). Some researchers are suggesting that this conversion between blocking and stimulating antibodies occurs in some patients after using treatment for Graves' disease and levothyroxine for hypothyroidism (16).
More recent studies show that patients can develop Graves' disease in the background of a hypothyroid state, and this conversion might be postulated secondary to a combination of atypical destructive thyroiditis and a switch of autoantibodies from blocking to stimulating ones (17). Also, it is noted that this phenomenon could occur at any time during the disease process even if patients have hypothyroid for decades (18).
Hashimoto thyroiditis(HT) preceding Graves' disease (GD) can be a subtype of autoimmune thyroiditis, as not all patients with HT convert to GD. According to some recent studies, HT preceding GD occurs more frequently than has previously been reported. The clinical characteristics do not necessarily match those reported in HT or GD, suggesting the need to be especially careful when determining treatment strategies (19).
Other findings suggest active surveillance of hypothyroid patients who require frequent reduction of levothyroxine during follow up and testing for TSH-R antibodies in these patients (20).

Occurrence of Graves' disease after primary hypothyroidism may not be as rare as previously thought. Diagnosis requires careful clinical and biochemical assessment. Otherwise, the case can be easily confused for over-replacement of levothyroxine. Different studies are suggesting measuring both anti-thyroid peroxidase (TPO) antibodies and TSH receptor antibodies (TRAB) in suspected cases.The underlying etiology for the conversion is not exactly known, but probably involves autoimmune switch by an external stimulus in genetically susceptible individuals (21). According to some studies, the phenomenon of the conversion of one autoimmune thyroid disease to another, in addition to the scientific interest, is important for the practitioners, since a timely change in the diagnostic paradigm can significantly change the treatment strategy and affect the prognosis of disease, thus preventing the development of complications (22).

Conclusion

In conclusion, conversion of hypothyroidism to thyrotoxicosis is still an underestimated clinical feature for most clinicians.

This case demonstrates that although it is very rare, after long condition of hypothyroidism, immunological shift is possible with development of recurrent hyperthyroidism with stimulating antibodies.

Further research, however, is needed to establish the exact pathogenesis of this phenomenon.

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