Autoimmune Switch of Hashimoto's thyroiditis to Graves' Disease: A Rare Case Report

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ABSTRACT

Hashimoto's thyroiditis and Graves' disease (GD) represent two ends of the autoimmune thyroid disease spectrum. While progression from GD to Hashimoto's thyroiditis is relatively common, the reverse transition is rare. We report a case of a 47-year-old woman with long-standing Hashimoto's thyroiditis and positive anti-thyroid peroxidase antibodies who remained euthyroid on levothyroxine for 10 years. Later, she developed symptoms of thyrotoxicosis, including palpitations, exertional dyspnea, and rapid, unintentional significant weight loss. The reported case demonstrated that the formation of thyroid-stimulating autoantibodies can cause an immunological transition from hypothyroidism to hyperthyroidism, however this is rare.

Keywords: Autoimmune switch, Hashimoto's thyroiditis, Graves' disease.

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INTRODUCTION

Autoimmune thyroid diseases are among the most prevalent autoimmune disorders worldwide, affecting approximately 2–4% of women and around 1% of men globally (1-3). The two most common entities within this spectrum are Graves' disease and Hashimoto's thyroiditis. Hashimoto's thyroiditis is primarily characterized by immune-mediated destruction of thyroid follicular cells through the action of autoantibodies, ultimately leading to hypothyroidism. In contrast, Graves' disease results from the production of stimulating autoantibodies directed against thyroid cells, particularly thyroid-stimulating immunoglobulins and thyroid-stimulating hormone (TSH) receptors, which cause excessive thyroid hormone production and clinical hyperthyroidism. The occurrence of hyperthyroidism following an established period of hypothyroidism is considered a rare and unusual clinical phenomenon. Traditionally, hypothyroidism was believed to represent a permanent and irreversible condition requiring lifelong thyroid hormone replacement therapy; however, an increasing number of reports in the medical literature challenge this long-held assumption. Both Graves' disease and Hashimoto's thyroiditis have a multifactorial etiology with complex pathogenic mechanisms that are influenced by a combination of environmental triggers and genetic susceptibility, the latter playing a significant role in the development of autoimmune disorders (4).

Autoimmune thyroid disease may involve the presence of one or more thyroid-specific autoantibodies. These include antibodies against the TSH receptor, which may exhibit either stimulating or blocking activity. In addition, thyroid peroxidase antibodies and thyroglobulin antibodies are commonly detected and serve as important markers of thyroid autoimmunity. While it is well established that thyrotoxicosis may eventually progress to hypothyroidism, the development of thyrotoxicosis after a prolonged period of hypothyroidism remains an uncommon and poorly understood clinical event (5).

CASE REPORT

A 47-year-old woman with a history of hypothyroidism came for a follow-up at INMAS, Kushtia. She had a highly positive thyroid peroxidase antibody (TPO) level with clinical evidence of hypothyroidism. She took levothyroxine (LT4) for 10 years with intermittent follow-up. On initial presentation she had symptoms of hypothyroidism, including cold intolerance, fatigue, and weight gain. However, thyroid function tests (TFTs)

revealed: Thyroid-stimulating hormone (TSH) 43 mIU/ml [Normal 0.5 mIU-4.78 mIU], free thyroxine (FT4) 4.0 pmol/L [Normal 11.5 pmol/L-22.7 pmol/L]. Autoantibody (AAb) workup revealed anti-TPOAb 870.0 IU/L [Normal <34 IU/ml] and anti-TGAb 241 IU/ml [Positive ≥4.5 IU/ml]. At those clinical circumstances, she was marked primarily as having hypothyroidism due to Hashimoto's thyroiditis and was treated with levothyroxine with a further recommendation for doing a high-resolution ultrasonography of the thyroid. Unfortunately, the patient skipped the initial follow-up appointment with the same doctor and refused more examination. His doctor did not recommend either fine needle aspiration or thyroid receptor antibody (TRAb).

During the time of presentation at the thyroid division of INMAS, Kushtia, patient had symptoms of hyperthyroidism in the form of panic attacks, palpitations, tremors, and proptosis. Biochemical findings revealed thyroid-stimulating hormone (TSH) 0.001 mIU/mL, free thyroxine (FT4) 33.0 pmol/L, and free tri-iodothyronine 7.1 pmol/L. Autoantibody (AAb) workup revealed anti-TPOAb 31.0 IU/L and thyroid receptor antibody (TRAb) 7.76 IU/L. High-resolution ultrasonography of the neck shows both thyroid lobes mildly enlarged with heterogeneous echotexture (Figures 1A & 1B), whereas a 99mTc-thyroid scan shows mild thyromegaly with uniformly increased radiotracer concentration in both lobes (Figure 2).

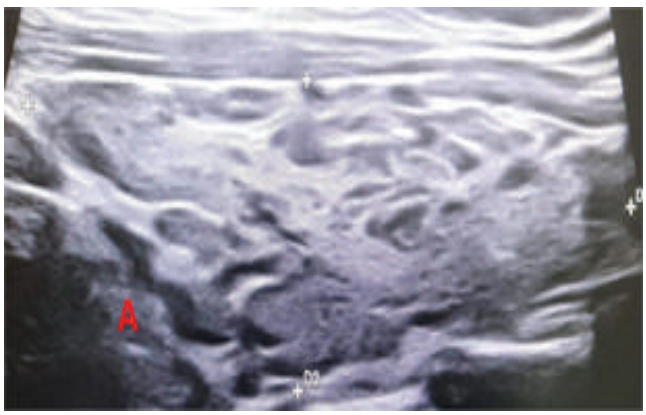

Figure (1A,1B) : Gray scale images of high-resolution ultrasonography of thyroid gland, showing mild thyromegaly with heterogeneous parenchymal echotexure.

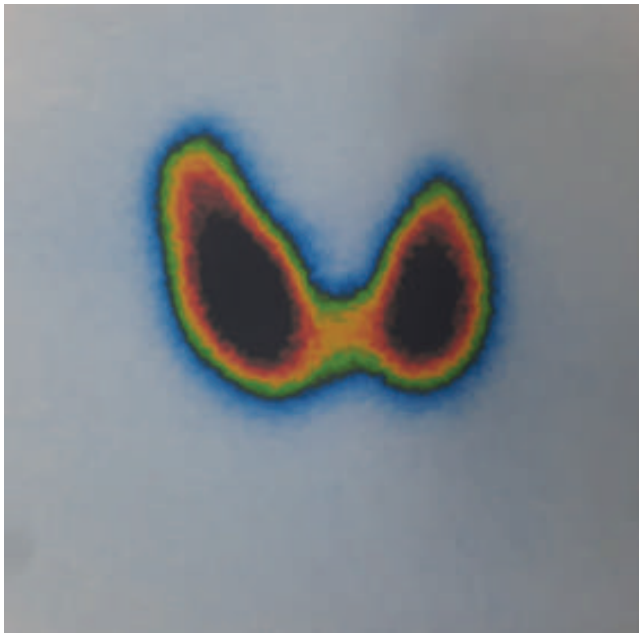

Figure :2 99m Tc thyroid scintigraphy image showing mildly enlarged both thyroid lobes with uniformly increased radio tracer concentration and negligible background uptake.

Patient had no history of lithium or amiodarone intake or recent CT scans. Clinically and biochemically a diagnosis of GD was done. Subsequently, Propranolol and methimazole (MMI) were started, but TFTs continued to oscillate between hypo- and hyperthyroid states. Within few months, patient became hypothyroid. Later on, dose of MMI was titrated and methimazole (MMI) was continued till date.

DISCUSSION

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. To date, we have found 50 cases regarding the conversion of Hashimoto's thyroiditis (HT) to Graves' disease (GD) through literature searches using PubMed and EMBASE. It is also stated that autoimmune destruction initially produces a hypothyroid state, but the stimulatory effect of thyrotropin receptor-stimulating antibodies (TSAb or TSI) and thyroid destruction may alter and subsequently create a hyperthyroid state (6). A few other 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, thus producing 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. One of the possible mechanisms for conversion is an environmental trigger in a genetically susceptible individual, which may 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 (9). 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 (10).

Occurrence of GD 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 with 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 an autoimmune switch by an external stimulus in genetically susceptible individuals (9).

One limitation in this case was the lack of assessment for thyroid receptor antibodies (TRAb) during the initial hypothyroidism diagnosis. Levothyroxine therapy was initiated based on clinical features and biochemical evidence. Previous studies indicate that some Graves' disease patients may initially present with transient hypothyroidism linked to positive TRAb. Despite this, the later emergence of overt clinical hyperthyroidism, alongside positive thyroid-stimulating immunoglobulin (TSI) and TRAb levels, as well as increased uptake on thyroid scintigraphy, suggests a progression from Hashimoto's thyroiditis to Graves' disease.

CONCLUSION

The conversion of Hashimoto's thyroiditis to Graves' disease remains an underrecognized clinical phenomenon. This case illustrates that, although rare, prolonged hypothyroidism may be followed by an immunological shift leading to recurrent hyperthyroidism mediated by stimulating antibodies. Further research is required to understand the precise pathophysiological mechanisms underlying this transition. Further research on a large scale is needed to evaluate the interchangeability of the condition.

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