A Review on Hashimoto’s Thyroiditis

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Abstract

Hashimoto’s thyroiditis (HT) is an autoimmune thyroid disorder first described by Japanese physician Haraku Hashimoto in 1912 characterized by lymphocytic infiltration of the thyroid parenchyma and is influenced by immune system instability. The onset of autoimmunity may be influenced by innate and acquired immune responses. Thyroid autoantibodies (TAbs) are the primary biochemical feature. Epidemiological studies show AITD (autoimmune thyroid disease) risk is higher in women and is age-related. Risk factors include high iodine consumption, selenium insufficiency, infectious disorders, and specific medications. Genetic predisposition and environmental factors also contribute to HT. Pregnancy and sex steroids play a role in the development of autoimmune thyroiditis, with older women being more susceptible. The immune system is modified during pregnancy, with progesterone playing a significant role. About 20% of postpartum thyroiditis patients eventually develop HT. The symptoms include dysphonia, dyspnea, and dysphagia, with primary hypothyroidism causing greater systemic symptoms. Diagnosis involves circulating thyroid-specific antibodies, ultrasound examination, increased thyroid stimulating hormone, and normal serum thyroid hormone levels. Ultrasonography is crucial for diagnosing Hashimoto’s thyroiditis, distinguishing it from other thyroid disorders like Graves’ disease (GD). The treatment comprises levothyroxine, which effectively lowers thyroid volume, as well as vitamin D deficiency and replacement. Autoimmune thyroiditis (AIT) surgery has traditionally been reserved for people who have discomfort or compressive symptoms from goitre or co-existing malignant thyroid nodules. Thyroidectomy has lately been advocated as a treatment option for decreasing TPOAbs, as the presence of such antibodies is linked to a worse quality of life even in euthyroid patients.

Keywords: Hashimoto’s thyroiditis (HT), Autoimmune thyroid disease (AITD), Autoimmune thyroiditis (AIT) Vitamin D, Levothyroxine

Introduction

HT was first described by a Japanese physician, Haraku Hashimoto, in 1912 an autoimmune disease of thyroid, first described by Hakaru Hashimoto (1912), a surgeon in Fukuoka and he stated that thyroid histologic investigation revealed characteristics that were entirely distinct from the typical colloid goitre.

Hashimoto proposed the term “struma lymphomatosa” (lymphomatous goitre) 1 and claimed that this illness differs from Riedel thyroiditis (RT) and Grave disease (GD). 2 Autoimmune thyroid disorders (AITD) are brought on by immune system instability that results in an immunological attack on the thyroid. Graves’ disease (GD) and Hashimoto’s thyroiditis (HT), both of which are characterized by lymphocytic infiltration of the thyroid parenchyma, are the two primary clinical manifestations of the AITD. Thyrotoxicosis and hypothyroidism are the clinical signs of GD and HT 3. The onset of autoimmunity may be influenced by the activation of innate and acquired immune responses, which can be brought on by an infection, an inflammatory reaction, or tissue damage. These findings imply that sterile thyroid damage alone, without the presence of infection, may be sufficient to cause thyroid dysfunction. Thyroid autoantibodies (TAb), which are directed against the two main thyroid antigens thyroid peroxidase (TPO) and thyroglobulin (Tg), are the primary biochemical feature 4. Doppler sonography or ultrasonography is a helpful method for identifying concurrent cases of Hashimoto’s thyroiditis 5. Thyroid ultrasonography has been found to be a useful diagnostic tool in research between Hashimoto’s thyroiditis and other conditions such as vitamin D insufficiency 6. The research revealed that levothyroxine therapy efficiently lowers thyroid volume, particularly in hypothyroid kids and adults with goitre brought on by AIT. Future study is required, although it is advised for both euthyroid and hypothyroid children with AIT. 7

Epidemiology:

According to the epidemiological studies AIT risk is higher in women than in men, hypothyroidism caused by AIT is age-related; and the mean incidence and prevalence of spontaneous hypothyroidism as a result of AIT were 3.5-5/1000 in women (mean age 57 years) and 0.6–1/1000 in men. 8

Risk:

The collapse of immunological tolerance, which leads to an autoimmune attack on the thyroid itself, is assumed to be the
root cause of HT. This breakdown is thought to be a result of a combination of hereditary predisposition and environmental risk factors.

The onset of autoimmune thyroiditis is associated with high iodine consumption, selenium insufficiency, pollutants like tobacco smoke, infectious disorders such chronic hepatitis C, and specific medications.  

**Genetic predisposition:**

Tg gene is found on chromosome 8q24, and there is a link between this area and HT and autoimmune thyroid disease. (11) Following precise mapping of this region, the Tg gene was discovered to be one of the primary thyroid specific susceptibility genes, connected and associated with autoimmune thyroid disease.  

**Diet:**

An excessive iodine intake is linked with a higher AIT prevalence.  

Low selenium levels in the body may associated with immune dysfunction, a reduced selenium consumption is considered as one of the risk factor for AITD development.  

Another dietary component that may play a role in HT is vitamin D, whose serum levels are linked to sun exposure. Although Lower serum levels of vitamin D were seen in HT subjects. May be linked to metabolic abnormalities in hypothyroidism, particularly because thyroid dysfunction is negatively associated with vitamin deficiency severity.  

The role of smoking and alcohol in the etiopathogenesis of HT is still debated, and no convincing data is known so far, though it appears that moderate alcohol use may be protective against HT.  

**Pregnancy and sex steroids:**

Women are more likely to develop AIT than men, sex steroids play a pathogenetic role in the condition. The presence or absence of oestrogen, however, presumably has little bearing because older women may be more susceptible to HT than younger women.  

Several mechanisms modify the immune system during pregnancy. The maternal fetal interface serves as a local locus of immunological advantage due to these elements together.  

Additionally, progesterone has a significant function in modulating the immune system after being released by the placenta and about 20% of postpartum thyroiditis patients eventually develop the characteristic HT.  

**Drugs:**

Women who already have high AbTPO levels appear to be at risk of hypothyroidism, and IFN-alpha therapy may cause the beginning of AIT. It may be toxic to thyroid cells or elicit immunological reactions that are harmful, leading to autoimmune hypothyroidism.  

**Symptomology:**

HT is distinguished by local and systemic symptoms such as dysphonia, dyspnea, and dysphagia. Primary hypothyroidism, which occurs virtually invariably in HT and affects most organs and tissues with significant variability, causes greater systemic symptoms. Painless thyroiditis, painful thyroiditis, postpartum thyroiditis, and Hashimoto’s encephalopathy are among the clinical variants identified.  

Painless thyroiditis is so termed because the patient experiences no neck pain, and its principal feature is a transitory episode of hypothyroidism that returns to euthyroidism.  

The name Painful Thyroiditis refers to the progressive, intense, and painful nature of the condition unbearable discomfort in one or both lobes of the thyroid.  

An important clinical variation is Hashimoto’s encephalopathy, which manifests as subacute cognitive decline, myoclonus, behavioural abnormalities, and seizures.  

**Diagnosis**

AIT diagnosis is determined by various factors including circulating thyroid-specific antibodies, ultrasound examination of hypo echogenic and heterogeneous gland parenchyma, increased thyroid stimulating hormone, and normal or low serum thyroid hormone levels.  

The diagnosis of euthyroid HT is based on the presence of TPO Abs and / or typical sonographic appearance of the thyroid gland but normal serum TSH and T4 levels.  

**Pathophysiology**

HT pathogenesis is linked to autoantibodies and lymphocytic infiltrates, including B and T cells in thyroid tissue. B cell dysfunction and T cell dysfunction disrupt immune homeostasis suggesting that cellular and humoral immunity play a key role in the pathogenesis of HT.  

**Cellular immunity**

CD8+ T lymphocytes are detected in autoimmune thyroiditis (HT) against thyroglobulin and TPO, although only a small percentage (2-3%) are specific to thyroid antigens. Cell death in HT is caused by both cytotoxicity and apoptotic mechanisms. A population-specific CD8+ cell, known as “Suppressor T cells,” can suppress damaging immune responses. T regulator cells (Treg) function in T suppressor cells by reducing immunological responses via cytokine synthesis. Recent research has highlighted on the involvement of Treg cells in HT, with Helios and PD-1 being key regulators of Treg cell peripheral tolerance and autoimmunity.  

**Humoral immunity**

Humoral immunity is an important characteristic of thyroid disease (HT), with most patients expressing specific autoantibodies for thyroid and thyroid protein (TPO). Increased serum levels of Th1 cells, IL-17, IL-22, and IL-12 cytokines can all have an effect on HT. Circulating exosomes contribute to the pathophysiology of HT by influencing biological activity and generating antigen presentation, inflammatory activation, autoimmune diseases, and tumour metastasis. HT is frequently accompanied with other autoimmune illnesses, implying a probable poly-autoimmune aetiology.  

Recently, a variant of HT called IG4 thyroiditis has been identified and is part of a systemic autoimmune disease characterized by the presence of IG4-positive cells.
**Follicular helper T - cells**

Follicular helper T cells (Tfh) are a newly identified subset of T helper cells involved in promoting antigen-specific B cells through IL-21 production they express CXCR5 and ICOS protein, and have been found in thyroid tissue of HT patients, indicating their involvement in disease pathogenesis.

**DNA fragments and micro RNA**

In vitro thyroid cell damage and genomic DNA release can result in an inflammatory response and impaired thyroid protein activity. Histone H2B, when attached to genomic DNA, activates innate immunity, resulting in thyroid autoimmunity, implying that sterile thyroid damage triggers immunity.

MicroRNAs (miRNA), which are tiny noncoding RNA sections, have also been linked to thyroid immunity pathogenesis. Several miRNAs have been found to regulate innate and adaptive immune responses.

**Treatment:**

The study found that levothyroxine treatment effectively reduces thyroid volume, especially in hypothyroid children and adolescents with goitre due toAIT. It is recommended for both euthyroid and hypothyroid children with AIT, though future research is needed.

The amount of LT4 needed to normalise serum TSH is determined by the amount of residual endogenous thyroid function present as well as the patient's weight, particularly lean body mass. The thyroid gland is estimated to produce 85 to 100 mcg of T4 per day and 5 to 6.5 mcg of T3 per 24 hours, with the remaining daily production of 26.5 mcg/day of T3 resulting from peripheral conversion of T4 to T3 by type 1 and type 2 deiodinases in patients with a preserved degree of endogenous thyroid function.

According to NHANES III (third national health and nutrition examination survey) data, the median TSH for adults aged 30-39 years is 1.2 mIU/ml, with the 2.5 and 97.5 percentiles ranging from 0.42 to 3.56 mIU/ml, respectively. TSH levels of 4-6 mIU/ml may be appropriate for older people. The best period for making judgements on LT4 dose adjustments is 6-8 weeks after starting therapy or changing the dose, to provide enough time for the hypothalamus-pituitary-thyroid axis set point to be re-established.

The significance of glucocorticoids has been called into doubt, as they may regulate thyroiditis and acutely improve thyroid function, despite the hazards associated with high doses and long therapy. Advantages However, prednisolone can be used for a brief period of time in Ig-G4 disease patients.

As several selenoproteins are involved in thyroid function, selenium plays an important role in human thyroid hormone homeostasis. Oral administration of selenium in the form of selenomethionine would be beneficial in HT patients with selenium deficiency and should protect the thyroid gland from the autoimmune reaction.

When clinically indicated, patients with HT may benefit from screening for vitamin D deficiency and supplementation, as well as monthly monitoring of calcium and 25[OH]D levels if necessary. The levels of AbTPO and AbTg significantly decreased following six months of vitamin D administration.

**Surgery:**

Surgery for HT has typically been reserved for individuals who come with pain or compressive symptoms related to goitre or co-existing malignant thyroid nodules. Thyroidectomy, however, has lately been proposed as a therapeutic approach for lowering TPOAbs, as the existence of such antibodies is associated with a worse quality of life even in euthyroid patients.

Thyroidectomy may result in problems. Hypocalcemia, wound infection, hematoma, recurrent laryngeal nerve (RLN) damage, and Horner's syndrome are the most common postoperative sequelae.

Hypocalcemia is a significant postoperative complication of thyroid surgery that can cause severe symptoms and lengthen hospitalisation.

**Dietary modifications:**

Dietary changes are a non-invasive strategy that can give quantitative results. To minimise thyroid inflammation, anti-inflammatory substances such as vitamin D, antioxidants, monounsaturated and polyunsaturated fatty acids, magnesium, and zinc are essential. Thyroid hormone synthesis and metabolism are aided by iodine and selenium. Because of the high prevalence of anaemia and cardiovascular illness in this group of Hashimoto's thyroiditis patients, an adequate intake of iron, folic acid, and vitamin B12 is also essential. Gluten and lactose should be avoided in the presence of food intolerances or disorders such as celiac disease, according to recent research. One of the fundamentals of a well-balanced diet is to restrict pro-inflammatory foods such as saturated fats, sweets, and refined carbs.

**Conclusion:**

Hashimoto's thyroiditis (HT) is an autoimmune condition characterized by the infiltration of lymphocytes into the thyroid tissue, resulting in hypothyroidism. The onset of HT is influenced by genetic factors, environmental triggers, and hormonal changes, particularly in women.

Crucial diagnostic tools such as ultrasonography and specific antibodies aid in identifying HT. The pathophysiology involves both cellular and humoral immunity, with significant roles played by CD8+ T lymphocytes, B cells, and follicular helper T cells. The complexity of HT is contributed to by genetic elements, environmental factors, and dietary components.

Treatment options encompass levothyroxine therapy, adjusted based on the patient's weight and remaining thyroid function. Additionally, benefits may arise from selenium supplementation and vitamin D administration. Surgery, usually reserved for symptomatic cases, could be considered to enhance quality of life.

Dietary adjustments, emphasizing anti-inflammatory substances and avoiding pro-inflammatory foods, can complement HT management. Regular monitoring, especially during pregnancy and hormone therapy, is crucial. In essence, a comprehensive approach, taking into account genetic, environmental, and lifestyle factors, is essential for comprehending and addressing Hashimoto's thyroiditis.

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