ECRONICON OPEN ACCESS

EC ENDOCRINOLOGY AND METABOLIC RESEARCH

Mini Review

Autoimmune Chronic Thyroiditis: A Concise Review on Pathogenesis, Clinical Signs and New Strategy Therapy

Francesco Lippi* and Antonietta Picone

Center for Thyroid Diseases, School of Endocrinology, University of Pisa, Italy

***Corresponding Author:** Francesco Lippi, Center for Thyroid Diseases, School of Endocrinology, University of Pisa, Italy.

Received: April 16, 2019; **Published:** May 02, 2019

Abstract

The autoimmune chronic thyroiditis or Hashimoto's thyroiditis (HT) is an inflammatory autoimmune disease of the thyroid gland characterized by a lymphocytic infiltration. This pathology is frequently silent, often hands to a gradual but progressive and irreversible hypo-function. It is the most frequent cause of hypothyroidism in the guilty ones of the world to enough contribution of iodine. The greatest incidence is in the women and was calculated around 3.5 cases for 1000 inhabitants. The etiology seems to be related to the genetic abnormalities or failure of immunoregulatory genes or thyroid specific genes, or for environmental factors or infections, or other factors. HT is characterized by a direct lymphocytic T-cell attack on the thyroid gland, leading to thyroiditis and subsequent exposure of thyroid antigen (thyroperoxidase and thyroglobulin) against which antibodies are then produced (TgAbs and TPOAbs). The therapy of HT can be different in relationship to the thyroid function. In many cases no treatment was required because the thyroid function is normal. If subclinical or clinical hypothyroidism is demonstrated the levothyroxine therapy is mandatory. In all cases selenium, and vitamin D can be used as antioxidant agents and seems to reduce the lymphocytic infiltration and antibodies title.

Keywords: *Hashimoto; Hashimoto's Thyroiditis; Autoimmune Chronic Thyroiditis; TSH; TgAbs; TPOAbs; Hypothyroidism; Levothyroxine; Selenium; Vitamin D; Pregnancy*

Introduction

Hashimoto's Thyroiditis (HT) or autoimmune chronic thyroiditis is an inflammatory disease of the thyroid, characterizes by a lymphocytic chronic infiltration. When described over century ago was described as a pronounced lymphoid goiter affecting predominantly women (1:10). In addition to this classic form, several other clinico-pathologic entities are now included under the term HT: fibrous variant, IgG4-related variant, juvenile form, Hashitoxicosis and painless thyroiditis (sporadic or post-partum) [1]. The greatest incidence of HT is in women and it is calculated around 3.5 cases of 1000 inhabitants a year [2].

Etiology

At the base of the pathology there is an inflammatory autoimmune processes that bring to the destruction of the thyroid follicles, caused both from a cells-mediate mechanism and from organ specific antibodies. The exact cause of HT is not known, but many factors are believed to play a role [3]. They include genetic susceptibility, environmental factors, some drugs, iodine and selenium, infections, molecular mimics and immune system defects [4,5]. Once activated the lymphocytic T helper it produces different cytokines that perpetuate and the inflammatory process they make autoimmune chronic [6] and T-cell and B-cells play a pathogenic role. Thyroglobulin antibodies (TgAbs) and thyroid peroxidase antibodies (TPOAbs) are commonly associated with HT and are considered diagnostic for this disease. Therefore, both the inflammatory process and the lymphocytic infiltration lead to a reduction of the synthesis of the thyroid hormones

(hypothyroidism). Sometimes in some occasions we can also be found some antibodies anti thyroid-stimulating-hormone (TSH) receptor blocking (TSHR blocking Abs) responsible for the atrophy variant (idiopathic myxedema) responsible for the condition of transient hyperthyroidism (Hashitoxicosis) due to the relapse of thyroid hormones from the destroyed thyroid cells [9].

Clinical manifestations

A part the classical form as a pronounced lymphoid goiter, described over century ago, in addition several other clinico-pathologic entities are now included under the term of HT: fibrous variant, IgG4-related variant, juvenile form, Hashitoxicosis, and painless thyroiditis (sporadic or post-partum) [1].

A particularly attention have to doing in pregnant woman with HT. In fact, the TSH level at the beginning of pregnancy should be maintained between 1.5 mIU/L to 2.5 mIU/L. The active surveillance of TSH during pregnancy is justified by the evidence that about 20% of euthyroid women show a TSH level more than 4.0 mIU/L throughout gestation [25,26]. In these cases, we suggest to start the treatment with low doses of Levothyroxine [27]. In fact, the thyroid dysfunction in pregnancy with a TSH level more than 4.0 mIU/L can lead to a reduced intelligent quotient (IQ) in the off-spring [28,29].

Occasionally, patients suffer from more than one autoimmune disease: polyendocrinopathy [7]. The autoimmune polyglandular syndromes [8] was classified in Type I or Whitaker syndrome (mucosal and cutaneous Candida infections, Addison's diseases, hypoparathyroidism and other multiple autoimmune presentations), Type II (Schmidt's syndrome) with Addison's disease, hypothyroidism or 1A diabetes as well as pernicious anemia, primary hypogonadism, vitiligo, celiac disease and myasthenia gravis, and Type III (the most common) with autoimmune thyroid disease, myasthenia or thymoma, Sjogren's syndrome, pernicious anemia, idiopathic thrombocytopenia purpura, Addison's disease, insulin-dependent-diabetes, vitiligo, autoimmune hemolytic anemia and systemic lupus erythematosus.

The diagnosis is based on evidence of thyroid auto-antibodies production like the most common is TPOAbs but in a low percentage of patients (5 - 10%) we can observe the absence of thyroid auto-antibodies [11] and the evidence of thyroid ultrasound modifications. Ultrasonography is an useful and essential tool to make this diagnosis based on the characteristics of the disease. In the differential diagnosis of thyroid nodules, ultrasound-guided fine-needle biopsy is an effective method to distinguish Hashimoto's thyroiditis from other thyroid disorders [10]. The typical picture in fact it's peculiar with a markedly hypoechoic pattern with poor intra-thyroidal vascularization.

Treatment

Normal thyroid function can be represented only in a little percentage of patients with HT and in this case we can decide if treat or not the patient. If euthyroid status is present, the largest part of authors agree to not to treat HT using Levothyroxine but only observe the evolution of the disease.

In other cases, most authors [12] in presence of normal thyroid function suggest to use selenium for maintaining immune-endocrine function, metabolism and cellular homeostasis [13]. The thyroid gland is characterized by a high concentration of selenium, which is incorporated in seleno-proteins [14]. Some of these have an important antioxidant activity, contributing to the antioxidant defense in the thyroid by removing oxygen free radical generated during the production of thyroid hormones [15]. In most articles published using a supplementation of 200 μg of sodium-selenite per day or selenomethionine was demonstrated a reduction after 3 - 6 months of the level of Abs (ranging from 40 - 55.5%) [16,17]. In fact, in the low population selenium status (almost 2-fold) is associated an increase prevalence of thyroid disease. The prevalence of pathological thyroid conditions (hypothyroidism), subclinical hypothyroidism, autoimmune thyroiditis and enlarged thyroid) was significantly lower in the adequate-selenium county than in the low-selenium county [18]. In summary selenium supplementation as selenomethionine would be beneficial in HT patients however chronic ingestion of large amount of selenium may be have adverse effects in human health [19].

The Vitamin D is a steroid hormone mainly produced in the skin that play an important role in the regulation of calcium homeostasis and bone density [20]. Vitamin D deficiency is widely prevalent worldwide. In adults vitamin D deficiency has been implicated in numerous health conditions including osteoporosis, cancer, diabetes, and autoimmune diseases [21]. Several studies have shown the correlation between vitamin D deficiency and thyroid autoimmunity [22,23]. The vitamin D is considered to be one of the natural immune modulators and a regulator of various immune-mediated process [22]. The mechanism seems related to the inhibition of the production of interleukin (IL)-13 and IL-23 and enhancing the release of IL-10, also leads to a shift from a pro-inflammatory to a more tolerogenic immune status and inhibits the production of cytokines (IL-2 and interferon-ɣ). The vitamin D seems to promotes the production of anti-inflammatory Th2 cytokines (IL-3, IL-4, IL-10) shifting the balance from immunoregulation and finally inhibits B-cells proliferations and differentiation into plasma cells, IgG or IgM and also induces B-cells apoptosis [24]. Also, the iron deficiency impairs thyroid metabolism, in particular in patients with autoimmune gastritis and/or celiac disease in which the iron absorption seems to be reduced. In two-thirds of women with persistent symptoms of hypothyroidism despite appropriate levothyroxine therapy, restoration of serum ferritin above 100 µg/l ameliorated symptoms [30].

In the prevalence of patients with HT the most common laboratory findings demonstrate an elevated circulating TSH with normal thyroid hormones (FT4 and FT3) subclinical or (low level of FT4) clinical hypothyroidism. Conventional treatment occurs with Levothyroxine at the recommended dose of 1.6 to 1.8 mcg/kg/day [11]. The thyroxin (T4) converts to triiodothyronine (T3) which is the active form of the thyroid hormone in the human body. The purpose of the hormone-therapy is to normalize the circulating TSH level with a first control after 45 - 60 days from the therapy start and then every 4 - 6 months.

In rare cases of patients with HT with increasing goiter during Levothyroxine therapy or if multinodular goiter with local compression signs we can suggest total thyroidectomy.

Conclusions

Hashimoto's thyroiditis is an autoimmune chronic disease characterized by a lymphocytic infiltration. This pathology is frequently silent, often hands to a gradual but progressive and irreversible hypo-function. The etiology in now unclear and seems to be related to multifactor as genetic susceptibility, environmental factors, bacterial or viral infection and immune system defects. The pathology is characterized by a lymphocytic infiltration in to the thyroid gland that lead to the TgAbs and TPOAbs formation and sometimes TSHR blocking Abs that lead to the atrophy variant.

Some patients can't have any evidence of the disease or can present transient hyperthyroidism (Hashitoxicosis) followed by a normal thyroid function and then with hypothyroidism (subclinical or clinical). However, the majority of patients present a classical hypothyroid signs. In all cases we suggest to use selenium and vitamin D supplementation for they ability as antioxidant agents to reduce the TPOAbs and Tg Abs. Also, the iron therapy seems to be adequate to reduce the persistent symptoms of hypothyroidism despite appropriate Levothyroxine therapy. The Levothyroxine therapy is mandatory in patients with HT and subclinical or clinical hypothyroidism. The recommended dose is from 1.6 to 1.8 mcg/Kg/day to normalize the circulating TSH level during therapy.

A particular attention has to be demonstrate for pregnant women with a closed control of circulating TSH levels. In fact, the thyroid dysfunction in pregnancy with a TSH level more than 4.0 mIU/L can lead to a reduced intelligent quotient (IQ) in the off-spring.

For this reasons we hope that in the future a particular attention could be recognized in a family in which at least one member presents an autoimmune chronic diseases and also in all women before pregnancy measuring the TSH level and the TgAbs or TPOAbs. Therefore, we suggest having a close collaboration between the specialist endocrinologist and other specialists as gynecologists and general medicine doctors.

Bibliography

1. Caturegli P., *et al*. "Hashimoto thyroiditis: clinical and diagnostic criteria". *Autoimmunity Reviews* 13.4-5 (2014): 391-397.
2. Weetman A and DeGroot LJ. "Autoimmunity to the thyroid gland". In F De Groot LJ., *et al*. editors. Endotext. South Darmouth (MA) (2000).
3. Kust D and Maresa N. "The impact of familiar predisposition on the development of Hashimoto's thyroiditis". *Acta Clinica Belgica* 20 (2018): 1-5.
4. Merril SJ and Minucci SB. "Thyroid autoimmunity: an interplay factors". *Vitamins and Hormones* 106 (2018): 129-145.
5. Biddal S., *et al*. "Recent advances in understanding autoimmune thyroid disease: the tallest tree in the forest of polyautoimmunity". *F1000 Research* 6 (2017): 1776.
6. Kristensen B. "Regulator Band T cell responses in patients with autoimmune thyroid disease and healthy controls". *Danish Medical Journal* 63.2 (2016): B5177.
7. Rojas-Villarraga A., *et al*. "Introducing polyautoimmunity secondary autoimmune diseases no longer exist". *Autoimmune Diseases* (2012): 254319.
8. Eisenbarth GS and Gottileb PA. "Autoimmune polyendocrine syndromes". *New England Journal of Medicine* 350.20 (2004): 2068-2079.
9. Tanja D., *et al*. "Thyrotropin Receptor Blocking Antibodies". *Hormone and Metabolic Research* 50.12 (2018): 853-862.
10. Wu G., *et al*. "Ultrasonography in the diagnosis of Hashimoto's thyroiditis". *Frontiers in Bioscience* 121 (2016): 1006-1012.
11. Mincer DL and Jialal I. "StatPearls [Internet]". Treasure Island (FL): StatPearls Publishing (2019).
12. Ventura M., *et al*. "Selenium and Thyroid Disease: From Pathophysiology to Treatment". *International Journal of Endocrinology* (2017): 1297658.
13. Duntas LH and Benvenga S. "Selenium: an element for life". *Endocrine* 48.3 (2015): 756-775.
14. Dikinson RC and Tomlinson RH. "Selenium in blood and human tissues". *Clinica Chimica Acta* 16.2 (1967): 311-321.
15. Sarnac L., *et al*. "Why is the thyroid do prone to autoimmune disease? *Hormone Research in Pediatrics* 75.3 (2011): 157-165.
16. Gartner R., *et al*. "Selenium supplementation in patients with autoimmune thyroiditis decreases thyroid peroxidase antibodies concentrations". *Journal of Clinical Endocrinology and Metabolism* 87.4 (2002): 1687-1591.
17. Duntas LH., *et al*. "Effects of a six months treatment with seleniomethionine in patients with autoimmune thyroiditid". *European Journal of Endocrinology* 148.4 (2003): 389-393.
18. Wu Q., *et al*. "Low Population Selenium Status Is Associated With Increased Prevalence of Thyroid Disease". *Journal of Clinical Endocrinology and Metabolism* 100.11 (2015): 4037-4047.
19. Lionitris L and Mazakopakis E. "A concise review of Hashimoto thyroiditis (HT) and the importance of iodine, selenium, vitamin D and gluten on the autoimmunity and dietary management of HT patients. Points that need more investigation". *Hellenic Journal of Nuclear Medicine* 20.1 (2017): 51-56.

20. Caprio M., *et al*. "Vitamin D: not just the bone. Evidence for beneficial pleiotropic extraskeletal effects". *Eating and Weight Disorders* 22.1 (2017): 27-41.

21. Haimi M and Kremer R. "Vitamin D deficiency/insufficency from childhood to adulthood: insights from a sunny control". *World Journal of Clinical Pediatrics* 6.1 (2017): 1-9.

22. Mazokopakis EE and Kotsiris DA. "Hashimoto's autoimmune thyroiditis and vitamin D deficiency. Current aspects". *Hellenic Journal of Nuclear Medicine* 17.1 (2014): 37-40.

23. Kivity S., *et al*. "Vitamin D and autoimmune thyroid diseases". *Cellular and Molecular Immunology* 8.3 (2011): 243-247.

24. Hewison M. "An update on vitamin D and human immunity". *Clinical Endocrinology* 76.3 (2012): 315-325.

25. Negro R., *et al*. "Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications". *Journal of Clinical Endocrinology and Metabolism* 91.7 (2006): 2587-2591.

26. Glinoer D., *et al*. "Risk of subclinical hypothyroidism in pregnant women with asymptomatic autoimmune thyroid disorders". *Journal of Clinical Endocrinology and Metabolism* 79.1 (1994): 197-204.

27. Negro R., *et al*. "A 2018 Italian and Romanian survey on subclinical hypothyroidism in pregnancy". *European Thyroid Journal* 7 (2018): 294-301.

28. Lazzarus JH., *et al*. "Antenatal thyroid screening and childhood cognitive impairment". *New England Journal of Medicine* 366.17 (2012): 493-501.

29. Hales C., *et al*. "Controlled antenatal thyroid screening 2: effects or treating maternal sub-optimal thyroid function on child cognition". *Journal of Clinical Endocrinology and Metabolism* 103.4 (2018): 1583-1591.

30. Rayman MP. "Multiple nutritional factors and thyroid disease, with particular reference to autoimmune thyroid disease". *Proceedings of the Nutrition Society* 78.1 (2019): 34-44.

Volume 4 Issue 3 May 2019