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HASHIMOTO THYROIDITIS IN PAEDIATRIC POPULATION- AN OVERVIEW

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ABSTRACT

The most frequent cause of goitre and acquired hypothyroidism in children and teenagers is Hashimoto's thyroiditis (HT). An imperfection or error in immunoregulation leads to a cascade of events that develops from thyroid lymphocyte infiltration to thyroid follicular cell damage caused by T cells and cytokines and apoptotic cell death. Approximately 70% of illness risk is linked to genetic predisposition, with environmental variables also contributing to disease onset in vulnerable individuals. The main reasons for referral in children and adolescents with HT include goitre, hypothyroid symptoms, and outcomes that occur while treating separate disorders or for high-risk groups. Children and adolescents with HT may not have any symptoms. Thyroid hormone replacement is the preferred medical approach for treating Hashimoto thyroiditis. Levothyroxine sodium, taken orally, is the preferred medication, typically for life. To prevent insufficient absorption, it shouldn't be administered along with calcium or iron supplements, aluminium hydroxide, or proton pump inhibitors.

Keywords: Hashimoto thyroiditis; autoimmune thyroiditis; thyroid disorders in pediatrics; thyroid diseases; goiter.

1. INTRODUCTION

Hashimoto thyroiditis (HT), It is also known as chronic lymphocytic thyroiditis and chronic autoimmune thyroiditis, and it is an autoimmune condition in which thyroid cells are destroyed by immunological processes mediated by cells and antibodies [1]. Antithyroid antibodies that are produced as a result of the condition target the thyroid tissue, leading to progressive fibrosis [1]. Cellular immune responses against thyroid autoantigens, which result in inflammation and decreased thyroid gland function, are the main contributors to the development of HT [2].

An error or defect in immunoregulation leads to a cascade of events that develops from lymphocyte infiltration of the thyroid to thyroid follicular cell damage caused by T-cells and cytokines, and finally to apoptotic cell death [3]. Approximately 70% of illness risk is linked to genetic predisposition, with environmental variables also contributing to disease onset in vulnerable individuals [3].

In places of the world where iodine is abundant, HT is the most common kind of thyroiditis in children [4] and the most frequent reason for paediatric thyroid illness. In the US and other regions of the world where appropriate iodine consumption is available, Hashimoto is the most frequent cause of hypothyroidism beyond the age of six [1]. Adolescence is the most typical age for presentation, however the disease can strike at any time, sometimes even in infants as young as one year old [5]. Monozygotic twins showed a higher concordance of Hashimoto thyroiditis than dizygotic twins, according to twin studies. Furthermore, monozygotic twin concordance rates are 55%, compared to just 3% for dizygotic twins, according to Danish research [6].

According to genetic susceptibility, age and gender, ethnicity, iodine status, the existence of other autoimmune diseases or genetic syndromes, and the diagnostic criteria utilised, an approximate incidence in paediatrics was found to be between one and two percent [7]. Children between the ages of 6 and 16 are more likely to use it, as are women, Caucasians, and nations where iodine deficiency is a problem. Additionally, type 1 diabetes, celiac disease, Addison's disease, autoimmune hypoparathyroidism, Down syndrome, Noonan syndrome, and Turner syndrome are more frequently associated with it in children [7].

It is unclear what causes Hashimoto thyroiditis to begin with [8]. Most individuals produce antibodies to a variety of thyroid antigens, with anti-thyroid peroxidase being the most prevalent (anti-TPO). Several also develop antibodies that inhibit the TSH receptor and anti-thyroglobulin (anti-Tg) (TBII). These antibodies cause thyroid tissue injury, which ultimately results in inadequate thyroid hormone production [9,10]. It can segment type 1 DM and autoimmune adrenal insufficiency from Polyglandular Autoimmune Syndrome type 2 [11]. Numerous additional autoimmune illnesses, including celiac disease, adrenal insufficiency, and pernicious anaemia, are associated with Hashimoto thyroiditis. The development of Hashimoto thyroiditis and vitamin D insufficiency may be related, according to research by Mazokopakis et al. [12].

Children and adolescents with HT may not have any symptoms, and goitre, hypothyroid symptoms, and outcomes that occur while treating separate issues or for high-risk groups are the main reasons for referral [13]. In the numerous paediatric studies, thyroid function at presentation might vary significantly, ranging from euthyroidism to overt hypothyroidism or, sometimes, hyperthyroidism [14].

Children with HT have the same hyperthyroidism-related clinical signs and symptoms as adults, including goitre, tachycardia, tremor, weight loss, restlessness, warm, moist skin, ophthalmopathy, and growth acceleration, delayed or precocious puberty [15].

Thyroid hormone replacement is the preferred medical approach for treating Hashimoto thyroiditis. Levothyroxine sodium, taken orally, is the preferred medication, typically for life. To prevent insufficient absorption, it shouldn't be administered along with calcium or iron supplements, aluminium hydroxide, or proton pump inhibitors. Combining liothyronine (T3) and levothyroxine to more precisely resemble the physiology of thyroid hormones is one frequent prescription, more so among patients than physicians [16]. The evidence in favour of an autoimmune/anti-inflammatory diet is weaker. Morbidity related to Hashimoto thyroiditis is typically brought on by a failure to diagnose hypothyroidism, to start L-thyroxine replacement therapy in sufficient quantities, or by a patient's failure to take the prescribed medication. Patients with Hashimoto thyroiditis are more likely to develop papillary thyroid cancer [17,18]. Undoubtedly, a prospective study by Silva de Morais et al. revealed that patients with Hashimoto thyroiditis who were undergoing a thyroid nodule screening had a higher likelihood of developing cancer than did people without the condition [19]. Additionally, a study by Machens et al. increased the likelihood that Hashimoto thyroiditis is related to both follicular and papillary thyroid cancer in addition to papillary thyroid cancer [20].

The prognosis for Hashimoto thyroiditis is generally excellent, with patients having normal lives with prompt diagnosis, timely introduction of levothyroxine replacement therapy, indicated patient follow-up care, and assessment of additional concomitant comorbidities.

2. HISTORY OF DISEASE

Hashimoto first identified four people with struma lymphomatosa, a persistent thyroid condition, in 1912. These patients' thyroid glands displayed fibrosis, parenchymal shrinkage, diffuse lymphocytic infiltration, and a change in eosinophilia in some acinar cells. Since Hashimoto's initial description of this condition, clinical and pathologic studies of it have frequently been published. The condition has also been referred to as lymphocytic thyroiditis, chronic Recent cases of autoimmune thyroiditis, lymphadenoid goitre, and thyroiditis all occurred [21].

The condition typically manifests a painless, broad enlargement of the thyroid gland in a young or middle-aged woman. It frequently goes hand in hand with hypothyroidism. For many years, the condition was assumed to be rare, and the pathologist or the surgeon performing the thyroidectomy would often make the diagnosis. The prevalence of recognition has increased significantly as a result of the increased usage of needle biopsies and antibody serologic testing, and there is cause for concern that this trend may continue. It is currently one of the most prevalent thyroid conditions [22].

An increase in the amount of plasma gamma globulin, as determined by Fromm et al. [23]. The earliest indication of an immunologic abnormality in this illness was the symptom. This finding, together with anomalies in the serum flocculation test results, led researchers to hypothesise that the sickness might be related to a lingering immune reaction. Witebsky and Rose [24] showed that giving rabbits a vaccine containing rabbit thyroid extracts led to thyroid gland changes comparable to those seen in Hashimoto's thyroiditis. Additionally, thyroglobulin-specific antibodies were found in the animal blood. Following that, Roitt et al. [25]. It was observed that a precipitate was formed after a human thyroid gland extract was added to a patient's serum who had Hashimoto's thyroiditis. As a result, the serum appeared to have antibodies against a component of the human thyroid, and these antibodies may be to blame for the development of the sickness. New theories about how autoimmunity promotes disease were directly impacted by these preliminary findings [21].

3. PATHOPHYSIOLOGY

Hashimoto disease is typically characterised by lymphocyte infiltration and fibrosis, and it is thought to have an autoimmune aetiology. The present diagnosis is supported by clinical signs that are consistent with elevated TSH levels and normal to low thyroxine levels observed in the laboratory. The fact that there is little evidence that antithyroid peroxidase (anti-TPO) antibodies contribute to the onset of autoimmune thyroid disease is significant (AITD). In addition to fixing complement, anti-TPO antibodies have been shown to attach to and kill thyrocytes in vitro. There hasn't yet been any evidence in human studies linking the severity of the illness to the number of anti-TPO antibodies found in the blood [26].

Fibrosis might be completely absent, barely perceptible, moderately prevalent, or severe, as in subacute or Riedel's thyroiditis. Hashimoto's thyroiditis does not feature granulomas or large cells

from foreign bodies, in contrast to subacute thyroiditis. Children tend to have less obvious oxyphilia, fibrosis, and epithelial cell hyperplasia. IgG deposits that are dense can be spotted along the basement membrane using electron microscopy [17].

4. SYMPTOMS AND PRESENTATION

Goitre, hypothyroid symptoms, discoveries made while treating unrelated illnesses or high-risk populations, and the possibility that children and adolescents with HT may not be displaying any symptoms at the time of diagnosis are the main reasons for referrals. There is a wide range of thyroid function at presentation in many paediatric studies, from euthyroidism to overt hypothyroidism or, in rare cases, hyperthyroidism. At the time of HT development, subclinical hypothyroidism or, less commonly, subclinical hyperthyroidism have also been reported in children and adolescents [27,28].Myxedema is the most well-known skin feature associated with hypothyroidism and is an edema-like skin condition caused by increased glycosaminoglycan deposition. However, this is uncommon and only occurs under dire situations. Skin might become dry and scaly, especially on the extensor surfaces, palms, and soles. Histological analysis revealed epidermal thinning. Pale skin is a result of water retention brought on by increased cutaneous mucopolysaccharides [29]. Reduced pulmonary and cardiac reserve as well as lowered muscle strength or greater muscle exhaustion are likely linked to tiredness, exertional dyspnea, and exercise intolerance. It has been demonstrated that the endurance of hypothyroid rats is reduced. This group has undergone biochemical alterations that have resulted in decreased muscle increased utilisation of glycogen stores, increased oxidation of pyruvate and palmitate, and decreased mobilisation of fatty acids. Myopathy and muscular weakness are significant traits [28].

Subclinical manifestations are another possibility. Constipation, exhaustion, dry skin, and weight gain are examples of early symptoms. More severe signs and symptoms may include cold intolerance, decreased sweating, nerve deafness, peripheral neuropathy, decreased energy, depression, dementia, memory loss, muscle cramps, joint pain, hair loss, apnea, menorrhagia, and pressure symptoms in the neck from goitre enlargement like hoarseness of voice [28].

Age of the child appears to have the greatest influence on thyroid function patterns at HT presentation, with cases of early HT presentation being more likely to have significant gland dysfunctions [29].

5. EVALUATION

Measuring blood TSH levels is the most reliable initial screening procedure for the presence of primary hypothyroidism. If the TSH is elevated, the serum free thyroxine (fT4) concentration test will help doctors decide whether the kid has overt (low fT4) or subclinical (normal fT4) hypothyroidism. AIT can be identified when serum levels of Tg Abs and/or TPO Abs are high enough. Measuring TSH receptor blocking Abs should be taken into account in adolescent girls with severe hypothyroidism due to the persistence of this Ab population in some patients and its link to an increased risk of producing children with TSH receptor blocking Ab-induced congenital hypothyroidism [30].

Imaging techniques (thyroid ultrasound and/or thyroid uptake and scan) may be performed if thyroid Ab tests are negative or if a nodule is palpable, but they are rarely necessary. Before Abs, reports of the existence of uneven echogenicity on ultrasonography examination have been made. The typical pattern of intermittent uptake of radioactive iodine found in adults is also uncommon in children [31].

6. MANAGEMENT

Thyroid hormone replacement is the cornerstone of hypothyroidism treatment. For those with severe, persistent hypothyroidism, slow LT4 correction is recommended to lessen the risk of unfavourable side effects (deterioration in school performance, short attention span, hyperactivity, insomnia, and behaviour difficulties). The replacement dose needs to be gradually raised in these patients over a few weeks to months. Children who are significantly hypothyroid should also be closely watched for complaints of a severe headache when treatment is started because pseudotumor cerebri is a rare occurrence. Children with moderate hypothyroidism, on the other hand, can begin total replacement straight immediately without much danger of adverse side effects [32,33]. It is disputed whether or not to treat subclinical hypothyroidism in children and teenagers (normal fT4, high TSH).Every time the serum TSH concentration is >10 mU/L Medication has been recommended for people, especially those over 60 years old, in whom there is a significant risk of developing overt hypothyroidism; if TSH is in the range of 6–10 mU/L, case-by-case treatment is advocated. Children with subclinical hypothyroidism caused by AIT had a high possibility of remission, according to long-term follow-up research. As a result, it is fair to reevaluate thyroid function in if the patient is asymptomatic and there is no strong family history of hypothyroidism, 6 months. But some

originally healthy individuals will later become hypothyroid. As a result, regular follow-up is required [33,34].

The evidence in favour of an autoimmune/anti-inflammatory diet is weak. The leaky gut syndrome, which occurs when the gut mucosa is injured, is thought to be the cause of the inflammation because it allows proteins that normally cannot via transporters in the stomach mucosa, enter the circulation. According to one explanation, antibodies are produced against the antigens as a result of a process mimicking molecular mimicry. Unfortunately, there is a chance that the antigen will cause antibodies to develop against thyroid peroxidase because of its strong structural similarity. The idea behind an autoimmune diet is to improve gut health and lessen the severity of the autoimmune reaction. Before it is included in the guidelines, more study on this subject is necessary [35].

7. PROGNOSIS

According to a very recent prospective study that sought to examine the long-term outcome of HT in the children presenting with overt hyperthyroidism, a definitive resolution of hyperthyroidism is typically seen on average eight months after Htx diagnosis, even though there is a great deal of variation between subjects. Non-pharmacological treatments were never required, according to that report, and managing children with Htx may require a lengthy clinical and biochemical follow-up. The hyperthyroid phase of Htx in children is always followed by a permanent resolution, free from relapses or protracted euthyroidism or hypothyroidism [36]. While the remaining 50% of cases were reported to continue or become euthyroid after 5 years of follow-up, the natural history of HT in children with biochemical and/or clinical euthyroidism appears to be characterised by a trend towards gradually declining thyroid function in around 50% of instances. It is possible to consider goitre, greater levels of thyroglobulin autoantibodies (Abs), a progressive increase in thyroid peroxydase Abs and TSH, and other conditions as potential risk factors for the development of hypothyroidism in the future [37]. The final possible, albeit unusual, outcome of HT is the conversion to GD. The initiation of hyperthyroidism may actually be preceded by an HT diagnosis, with either hypothyroidism or euthyroidism, in at least 3,7% of children and adolescents with GD, according to a recent retrospective epidemiological study. When GD appears, TSH receptor Abs' biological activity switches from being largely thyroid-blocking antibodies during the hypothyroid phase to thyroid-stimulating antibodies. One mechanism that explains the transformation from HT to GD is the altered physiologic activity of TSH receptor Abs [38,39].

8. CONCLUSION

The most frequent thyroid condition in children is Hashimoto thyroiditis. A still poorly known immunoregulatory dysfunction or deficiency, as well as a chain of events that go from thyroid lymphocyte infiltration to thyroid follicular cell injury and apoptosis, are what produce the illness. The thyroid functions of all children and teenagers with HT, whether initially euthyroid or with subclinical hypothyroidism, should be routinely evaluated for hypothyroidism. Most individuals who are not receiving therapy when they initially present might subsequently. Levothyroxine therapy may improve antibody titers and the clinical course of the disease. Randomized controlled studies are required for large paediatric patient series.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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