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Hashimoto's disease - the role of factors and diet in the course of the disease

Choroba Hashimoto – rola czynników i diety w przebiegu choroby

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ABSTRACT

Introduction: Hashimoto's disease is an autoimmune disorder that develops as a result of a pathological reaction of the patient's immune system, which consequently destroys the body's own healthy cells and tissues. Genetic, environmental and immunological factors influence its development. The disease may initially be asymptomatic. The exact aetiology of the disease is unknown. The worldwide incidence is approximately 10-12%.

Purpose: This paper aims to present the influence of genetic factors, environmental factors, trace elements, and diet on the development and course of Hashimoto's disease based on the current state of knowledge.

Conclusions: Hashimoto's disease is a multifactorial disease, but the relevance of all factors presented in the development and progression has not yet been confirmed. To date, a special diet for patients has not been created. Further research is needed to better understand the pathogenesis of the disease in order to help patients control HT.

Methods: Data for the article were retrieved using PubMed setting the time descriptors to 2013-2023.

Keywords: Hashimoto's disease, autoimmune disease, factors, trace elements, diet, coeliac disease.

INTRODUCTION

The thyroid disease Hashimoto's thyroiditis (HT) now classified as an autoimmune thyroid disorder (AITD). It was first described by Dr Hakaru Hashimoto in 1912. [1]. It is one of the most common thyroid diseases and a cause of hypothyroidism of the thyroid gland. It is also called lymphocytic thyroiditis and chronic autoimmune thyroiditis [2]. It is the most common autoimmune disease worldwide [1].

In HT, anti-thyroid antibodies - anti-thyroperoxidase antibody (anti-TPO) and usually anti-thyroglobulin antibody (anti-Tg) - are produced by immune processes. They attack the thyroid tissues, causing fibrosis, so that the function the thyroid gland performs in the human body is disrupted, which is also accompanied by lymphocyte infiltration. Gradually, hypothyroidism may develop [1,2]. There are 2 clinical forms - with goiter present and atrophic. Initial physical symptoms include weight gain, constipation, feeling cold and dry skin. In the course of HT, cardiovascular disease may develop. Thyroid hormones are responsible for regulating the rate of basal metabolism, and in the course of Hashimoto's disease, mood disorders may occur, negatively affecting quality of life [3]. A significant increased risk of future thyroid cancer has been observed in HT patients. Based on a recent trend, there is an increasing incidence [2]. The overall incidence of HT is approximately 10-12% [2,3]. The disease affects women much more frequently than men, in the middle age range [3]. The exact aetiology of the disease is unknown, and more robust research is needed to understand in more detail the causes of HT development. Genetic susceptibility, environmental factors as well as trace elements play a major role in the pathogenesis [1,2].

GENETIC FACTORS

Specific loci are associated with Hashimoto's disease, i.e. HLA-DR, immune regulatory genes - CD40, CTLA-4, PTPN22, FOXP3 and CD25, recombinant interleukin-2 receptor alpha (IL2RA), as well as thyroid-specific thyrotropin hormone receptor and receptor for thyroglobulin [1]. The loci shown can impair peripheral immune tolerance and also disrupt T-lymphocyte regulation [2]. Tyr-26, Tyr-30, Lys71, or Arg74 can cause structural changes in pockets, which can affect selection, and also cause pathogenic peptides to bind to the affected pockets, increasing the risk of Hashimoto's disease. CTLA-4 and PTPN22 are major negative regulators of immune function. Polymorphisms of these genes are strongly associated with HT [1].

It is now known from many analyses that dozens of genes are involved in the pathogenesis of HT, the effects of which combine to give an overall picture of the disease [4]. The course of each patient may vary, so each patient must be approached strongly on an individual basis. In addition to the well-known genetic factors in this disease entity, there are also so-called private genes that contribute to the development of HT, but there is not enough information to fully describe their significance [4]. A variant of the thyroglobulin gene has

been discovered that is associated with skipping coding sequences - exons . It is not yet fully known whether the variant presented encodes a thyroglobulin that damages thyroid cells and leads to autoimmunity, or whether it induces an immune response through alternative mechanisms.

In a study in HT patients where the disease was autosomal dominantly inherited with this gene variant, autoantibodies against both thyroglobulin and thyroid peroxidase were detected. In contrast, in another family with autosomal dominant inheritance Hashimoto's disease was also present, where the mutation was in the gene encoding tumour necrosis factor alpha-induced protein 3 - A20. There is a possibility that A20 deficiency will result in autoimmune as well as inflammatory diseases. Due to the effect of A20 on the regulation of immune responses including mainly T helper 17 (Th17) lymphocytes [4].

ENVIRONMENTAL FACTORS

In genetically susceptible individuals, environmental factors can lead to the induction of thyroid autoimmunity. This process is influenced by infections, diet, especially iodine, stress and pregnancy. Excess iodine directly inhibits hormone synthesis causing induction of thyroid autoimmunity, due to increased immunogenicity of thyroglobulin and possible release of oxygen free radicals. The increase in oxygen free radicals increases the expression of an adhesion molecule inside the cell. The autoimmune response is exacerbated by smoking, hepatitis C, and selenium deficiency [1]. Some drugs currently used in oncology, i.e. interferon-alpha, due to the specificity of their action, may contribute to autoimmune thyroid dysfunction [3]. According to a cohort study in Denmark, which found that there is a 2% increased risk of HT in women born in the summer months compared to other seasons. A cause for this could not be found, but the influence of infectious factors or vitamin D concentrations is suspected [4].

The intestinal microbiota plays an important role in metabolic processes, influences immune processes and enables homeostasis. Maintaining the intestinal flora in a good, unaltered state relative to the physiologically occurring state influences the proper functioning of the gastrointestinal tract. Altered intestinal microflora as a result of intestinal dysbiosis or overgrowth of resident bacteria may contribute to the development of inflammatory, autoimmune diseases including Hashimoto's disease [3,4]. A balanced diet is the basis for well-being, as well as for a properly functioning body. Fat-free foods, fibre, as well as

antioxidants influence the correct composition of the microbiota, thereby reducing the risk of developing HT [2].

TRACE ELEMENTS

Iodine

Iodine is very important in diseases in the field of endocrinology, in particular the thyroid gland [2]. This element is essential for the synthesis of thyroid hormones [6]. Iodine is taken up from the blood by thyroid epithelial cells and, via hydrogen peroxide, the iodination of tyrosine takes place. Under the influence of the specific catalyst thyroid peroxidase (TPO), triiodothyronine (T3) and thyroxine (T4) are formed [2]. The absorption of iodine supplied with food takes place in the stomach, duodenum and jejunum. There are approximately 15-20 mg of iodine in the thyroid gland [6]. It is common to supply iodine with salt. The WHO recommended daily intake for an adult is 150 µ/day [3].

Studies confirm that too high a dietary iodine supply increases the risk of autoimmune thyroid diseases including Hashimoto's Disease. When high doses of iodine are consumed over a long period of time, thyroglobulin immunogenicity may be increased, resulting in the activation of pathways leading to apoptosis and destruction of thyroid tissue and the onset of oxidative stress [2]. Excessive iodine consumption additionally generates the Wolff-Chaikoff effect, which involves a temporary reduction in thyroid hormone synthesis within 24 h of supplying the excess [6]. The main sources of iodine include, among others, seafood, seaweed, fish, milk fruits and vegetables [3]. The iodine content of food depends on the amount of iodine in the soil, so there are differences depending on geographical location . Iodine deficiency, in turn, can lead to thyroid goitre, thyroid nodules and metabolic disorders due to the inability of the thyroid gland to synthesise hormones [6].

Selenium

Selenium is a very important micronutrient in the body's metabolic processes, the largest reservoir of which is the thyroid gland. Its role mainly relates to immune processes [2]. It has anti-inflammatory and antioxidant properties [3]. SELENOS is a susceptibility gene for the occurrence of HT, is responsible for encoding specific proteins whose function is to trigger an immune inflammatory response, and is also important in the occurrence of

oxidative stress [2]. In the body, selenium co-forms proteins - selenoptoreins, which are involved in the formation of antioxidant enzymes, i.e. glutathione peroxidase, iodothyronine deiodinase and thioredoxin reductase [3,5]. They play an important role in hormone metabolism and antioxidant action against free radicals that are formed during thyroid hormone synthesis. There is a significant proportion of Se deficient individuals worldwide. Toxic levels of this element are very close to the recommended values, so caution should be exercised with any supplementation. Excess can cause endocrine alterations in hormone synthesis, or increase the risk of developing type 2 diabetes.

Selenium supplementation in the form of selenomethionine is recommended along with maintaining adequate iodine levels in patients with Hashimoto's disease. In food, this element is most commonly found in protein-bound form e.g. in meat, eggs, fish, and mushrooms and Brazil nuts are particularly rich in selenium [3]. Studies have shown that selenium deficiency causes an increase in the volume of the thyroid gland, and can induce hypothyroidism and HT. Low selenium levels increase the risk of antithyroid antibodies [5]. In recent years, a study was presented that proved the beneficial antioxidant effect of selenium in patients with Hashimoto's disease, additionally proving that selenium supplementation had a similar effect on thyroid-specific antibodies as vitamin C. Some studies do not show arguments for the efficacy of selenium to prevent the progression of hypothyroidism, so further research in this direction is needed [3].

Iron

Iron enables the activation of human thyroid peroxidase (TPO), a haem enzyme that catalyses the thyroid hormone synthesis reaction. As a result of iron deficiency, iodine regulation of thyroglobulin and coupling of iodotyrosine molecules is impaired and, consequently, the body produces less T3 and T4, disrupting overall thyroid function [2]. In food, iron is found in two forms: haemic and non-haemic. Sources of the first form include red meat, poultry, fish and eggs. In contrast, the non-haemic form is found in legumes, cereals, vegetables and fruits . Among HT patients, iron deficiency is quite common due to co-morbidities such as autoimmune gastritis or coeliac disease, which contribute to iron loss during the course of the disease [3]. Iron deficiency is found in up to 60% of HT patients. It is quite common for iron deficiency to occur together with iodine among the patients studied [6].

Magnesium

The element is a component of over 300 enzymes in the human body, responsible for all kinds of metabolic processes. Sources of magnesium include vegetables, legumes, spinach, nuts and whole-grain products. Reduced levels of this element contribute to a number of diseases; according to research, there is not yet sufficient evidence to confirm that it is important in the course of Hashimoto's disease. It is recommended that serum levels be determined in patients with the diagnosis. One study reports that low serum magnesium levels increase the incidence of a positive antithyroid antibody test and, at the same time, the risk of hypothyroidism and HT [3].

Zinc

Zinc is a micronutrient that is important for immune function. It is a component of about 750 transcription factors and about 2000 enzymes catalysing metabolic reactions in the human body of all classes - hydrolases, transferases, oxidoreductases, ligases, lyases and isomerases. Which speaks to its important role in cellular processes i.e. growth, development and DNA synthesis [7]. It promotes the synthesis of hypothalamic thyrotropin-releasing hormone and thyrotropin. It also acts as a factor that regulates the expression of thyroid hormones [2]. Low zinc concentrations affect thyroid hormone metabolism and thyroid structure. T3 and T4 levels are reduced. Deficiency is associated with impaired immune function [7]. Sources of this element include meat, eggs fish and sunflower seeds. There is a reciprocal relationship based on research, as hypothyroidism leads to zinc deficiency and low levels of zinc in the body can lead to hypothyroidism [6]. One should also be wary of too much zinc due to its immunosuppressive effects. High doses cause inhibition of lymphocyte function and INF-gamma production [8].

Vitamin D

Vitamin D levels in the body are associated with TNF alpha, IL-5 and IL-7, all of which are involved in the inflammation-induced immune response, which speaks to its importance in the pathogenesis of Hashimoto's disease. The greater the vitamin D deficiency, the greater the risk of HT [2]. Studies indicate that vitamin D has a proliferative, differentiating and also immunomodulatory function, which supports its use in patients with

Hashimoto's disease, as it causes a decrease in antithyroid antibodies and an increase in HDL cholesterol. This indicates that vitamin D supplementation may slow the development of hypothyroidism-related diseases, while also reducing the risk of cardiovascular disease. Vitamin D is synthesised by the skin as a result of exposure to sunlight or can be supplied with food, i.e. fish, eggs and dairy products [3].

Diet

A balanced diet is an essential element for the body to function properly and maintain homeostasis. Diverse dietary habits, may result in an increased risk of inflammatory diseases of immune origin, including autoimmune diseases. The role of the micronutrients presented and the function of the normal microbiota in the course of HT are known. At this point, however, it is not possible to clearly delineate appropriate dietary habits in patients with Hashimoto's disease [3].

Based on studies, it has been found that saturated fatty acids present in animal fats may contribute to the development of an inflammatory response in the body, by activating pro-inflammatory factors and consequently inducing inflammatory mediators. In addition, such a diet increases TSH levels, which causes thyroid dysfunction and can induce hypothyroidism in this organ. It has also been proven that in patients with HT, the consumption of red meat in the daily diet is common. These individuals had a higher risk of developing thyroid autoimmunity and it has been found that following a Mediterranean diet has a protective effect [3,12,15]. The consumption of vegetables, legumes, nuts and fruit, the so-called anti-inflammatory diet, which is rich in phytosterols and polyphenols, is associated with a negative result of anti-thyroid peroxidase antibodies and/or anti-thyroid antibodies [3,15].

Some studies over the years have referred to the use of a gluten-free diet in patients with Hashimoto's disease. It has been suggested that there is a relationship between the use of gluten-containing foods and the development and even progression of HT [3,8]. Coeliac disease (CD) is an autoimmune disease that occurs in response to gluten consumption. Gluten is a group of proteins found in wheat, barley, rye and oats [9,10]. As a result of gluten ingestion, inflammation forms, villi atrophy occurs and the absorption of micronutrients including Fe is impaired. Iron deficiency impairs thyroid function due to reduced thyroid peroxidase (TPO) activity [11,12]. It is often asymptomatic and therefore underdiagnosed.

When the symptomatic form is present, the most characteristic symptoms include gastrointestinal disorders, malabsorption, weight loss and developmental delay in children [12,13]. Serological tests, i.e. tissue transglutaminase and antibodies to gliadin peptide, are important in the diagnosis. The best treatment for this disease is a gluten-free diet (GFD) for life. [10]

A common substrate for the co-occurrence of Hashimoto's disease and celiac disease is genetic factors. Coeliac disease can be diagnosed either before or after the diagnosis of autoimmune disease [10]. Both diseases are HLA-coupled [11,13]. The prevalence of CD in patients with autoimmune thyroid disease is increasing [10,12]. When a patient requires a gluten-free diet and has Hashimoto's disease, one should also be aware of the possibility of magnesium and vitamin D deficiencies and other trace elements important in HT [14]. Close dietary control of such patients is necessary [9,11]. Despite many studies, it is not possible to clearly state the most appropriate diet as the golden mean for patients with Hashimoto's disease; each diet has supporting factors, but not enough scientific evidence to be able to choose the most appropriate one. Providing all the necessary nutrients with food or possibly supplementing them promotes proper functioning of the body. Many more years and studies are needed to fully assess the impact of dietary habits on the development, course and possible progression of the disease [3,15].

CONCLUSION

The incidence of Hashimoto's disease has increased significantly over the years. It is recognised as the most common autoimmune disease worldwide and has been described as the leading cause of hypothyroidism. The sources of development and prevention of HT are not yet fully understood. On the basis of numerous meta-analyses and scientific studies published in recent years, this paper presents the influence of factors that may affect Hashimoto's disease. Due to the existence of correlations concerning food deficiencies and the validity of supplementation of certain trace elements, continuous diagnostic control is necessary, as well as cooperation between doctors from different disciplines, i.e. endocrinology and dietetics, in the case of HT development. These factors may contribute to lowering autoantibody levels, improving thyroid function and preventing metabolic disorders in patients. Despite the recommendation of an anti-inflammatory diet in patients and the suggestion of a possible effect of a gluten-free diet in Hashimoto's patients, there is not enough evidence to support

this. New research is needed into the role of micronutrients as well as diet in the development and progression of Hashimoto's disease.

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