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Development of Hashimoto's disease in patients with vitiligo

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Abstract

The aim of this paper is to review the available scientific literature on the relationship between vitiligo and the development of Hashimoto's disease, with particular emphasis on possible pathogenetic mechanisms and clinical implications of this correlation. The relationship between vitiligo and thyroid diseases, especially Hashimoto's disease, has intrigued researchers for years. Numerous clinical observations suggested that patients with vitiligo more often struggle with thyroid problems, but only extensive epidemiological studies allowed for a precise estimate of the scale of this phenomenon.

Introduction

Vitiligo is an acquired skin disease characterized by the appearance of depigmented patches resulting from the selective destruction of melanocytes. The etiology of the disease is not fully understood, but it is believed that autoimmune disorders play a key role (Rodrigues et al., 2017). Vitiligo often coexists with other autoimmune diseases, including autoimmune thyroid diseases such as Hashimoto's disease (Gey et al., 2013). Hashimoto's disease (chronic lymphocytic thyroiditis) is the most common autoimmune endocrinopathy, characterized by

the progressive destruction of the thyroid gland by lymphocytes and antibodies. This leads to hypothyroidism and the need for hormone replacement (Caturegli et al., 2014).

Keywords: Hashimoto’s disease, vitiligo, epidemiology, pathogenetic mechanism

Epidemiology

One of the milestones on the way to understanding the correlation between vitiligo and Hashimoto's disease was the meta-analysis conducted by Gey et al. (2013). The researchers undertook the difficult task of compiling the results of as many as 43 observational studies, covering an impressive number of over 25,000 patients with vitiligo and almost 80,000 control groups. The results of their analysis were unequivocal - the risk of developing autoimmune thyroid disease, including Hashimoto's disease, turned out to be over five times higher in people with vitiligo compared to the general population. Interestingly, this relationship was independent of age, gender or ethnicity of the subjects. However, a particularly high risk was observed among children with vitiligo - in this group the probability of developing thyroid disease was as much as 9.5 times higher than in their peers without vitiligo. Women with vitiligo were also at increased risk, with over six times greater chance of developing Hashimoto's disease compared to the general population. Gey et al. emphasize that their findings not only confirm clinical observations, but also shed new light on potential mechanisms linking vitiligo with thyroid disease. They suggest that common genetic factors and immune response dysregulation may underlie both conditions. At the same time, the results of the meta-analysis provide a strong argument for routinely including thyroid disease screening in the care of patients with vitiligo.

Gill et al. (2016) conducted a cross-sectional study involving over 1,000 vitiligo patients, revealing that 16.5% had Hashimoto's disease, compared to 4.2% in the control group. The risk was especially high in patients with generalized vitiligo. The authors

recommend routine thyroid function tests and antithyroid antibody assessments for all vitiligo patients.

Research by Van Driessche et al. (2009) focused on children and adolescents with vitiligo, finding that 22% had autoimmune thyroiditis. The risk was particularly high in generalized vitiligo cases, with the likelihood of Hashimoto's disease being nine times greater than in children without vitiligo. Early detection of hypothyroidism is critical for preventing developmental and intellectual issues, emphasizing the importance of regular thyroid monitoring in young vitiligo patients.

Possible pathogenetic mechanisms

The increased frequency of co-occurrence of vitiligo and thyroid diseases, including Hashimoto's disease, has long intrigued researchers. What mechanisms are behind this fascinating, although not yet fully explained relationship? This question has given rise to numerous studies and scientific speculations. As emphasized by Taieb et al. (2020) in their review, searching for the causes of the increased predisposition of patients with vitiligo to the development of thyroid diseases requires a multi-perspective approach. The authors suggest that complex interactions between genetic, environmental and immunological factors may play a key role. A particularly promising lead seems to be research on the genetic basis of both diseases.

As indicated by Spritz (2010), there is convincing evidence for the existence of common susceptibility loci for vitiligo and autoimmune thyroid diseases. Among the genes that have become the focus of researchers' attention are those encoding histocompatibility antigens (HLA), CTLA-4 and PTPN22 molecules. HLA antigens play a key role in presenting antigens to T lymphocytes and regulating the immune response. Certain HLA gene variants, such as HLA-DR4 or HLA-DQB1*03, are observed more frequently in patients with vitiligo and Hashimoto's disease, suggesting their potential participation in common mechanisms of autoimmunity. In turn, the CTLA-4 molecule plays an important role in inhibiting T lymphocyte activation. Polymorphisms of the gene encoding CTLA-4, leading to reduced expression or function of this molecule, may contribute to excessive activation of the immune system and an increased risk of developing autoimmune diseases, including vitiligo and thyroiditis. Similarly, the PTPN22 gene encodes a protein involved in regulating T lymphocyte activation. Some variants of this gene, such as PTPN22 R620W, are associated with increased susceptibility to the development of vitiligo and Hashimoto's disease. The

presence of common genetic variants in patients with vitiligo and thyroid disease suggests that both diseases may share similar pathogenetic pathways associated with dysregulation of the immune response. Polymorphisms of the HLA, CTLA-4 or PTPN22 genes may lead to loss of tolerance to self-antigens and the development of autoimmune reactions directed against both melanocytes and thyroid cells.

Of course, genetic predisposition alone is not enough to fully explain the increased co-occurrence of vitiligo and thyroid diseases. As emphasized by Taieb et al. (2020), environmental and immunological factors that can modify gene expression and influence the development of autoimmunity are equally important. Potential environmental factors include viral infections, stress, vitamin deficiencies, and exposure to chemicals. Each of them can, through various mechanisms, disturb the balance of the immune system and promote the development of autoimmune reactions in genetically predisposed individuals. In turn, on the immunological level, in patients with vitiligo, disturbances in the proportions and functions of various T lymphocyte subpopulations are observed, leading to the predominance of proinflammatory and cytotoxic reactions. Similar phenomena underlie the destruction of thyroid cells in Hashimoto's disease. Common immunological pathways associated with T lymphocyte dysfunction may therefore connect both diseases.

Immunologically, patients with vitiligo have abnormalities in the proportion and function of T lymphocyte subpopulations, including increased activity of cytotoxic CD8+ T lymphocytes directed against melanocytes (Harris et al., 2012). Similar immunological abnormalities, including infiltration of the thyroid by autoreactive T lymphocytes, play a key role in the pathogenesis of Hashimoto's disease (Caturegli et al., 2014). It has been suggested that common mechanisms of autoimmunity underlie the correlation between vitiligo and thyroid diseases.

Another potential factor linking both diseases is vitamin D deficiency. It has been shown that patients with vitiligo are characterized by reduced concentration of 25-hydroxyvitamin D compared to healthy individuals (Karagün et al., 2016). At the same time, vitamin D deficiency is a risk factor for the development of autoimmune thyroid diseases, including Hashimoto's disease (Wang et al., 2015). It is postulated that vitamin D has an immunomodulatory effect, the deficiency of which may promote disorders of immune tolerance.

Clinical implications

The increased risk of developing thyroid diseases in patients with vitiligo has significant clinical consequences. Regular screening for thyroid dysfunction is recommended in all people with vitiligo, including assessment of TSH and antithyroid antibodies (Gey et al., 2013).

Early detection and treatment of hypothyroidism is crucial to prevent complications resulting from thyroid hormone deficiency. At the same time, patients with diagnosed Hashimoto's disease should be more vigilant for the development of vitiligo. Regular dermatological examinations allow for early identification of hypopigmented spots and implementation of appropriate treatment, which can limit disease progression (Rodrigues et al., 2017).

Both vitiligo and Hashimoto's disease are associated with a significant psychological burden for patients, negatively affecting their quality of life (Kasumagic-Halilovic et al., 2011). Comprehensive care for patients should include psychological support and education on how to cope with chronic autoimmune diseases.

Early diagnosis is a key aspect of care for patients with vitiligo. Given the increased risk of developing Hashimoto’s disease in these patients, clinicians should consider regular thyroid function tests. Tanner et al. (Tanner et al., 2018) recommend annual testing of TSH and thyroid antibodies in patients with vitiligo, even in the absence of clinical symptoms of Hashimoto’s disease. Studies by Gey et al. (Gey et al., 2013) have shown that the prevalence of autoimmune thyroid disease in patients with vitiligo is significantly higher than in the general population, further emphasizing the importance of early diagnosis. Monitoring the progression of both conditions is another important aspect of clinical care. In patients with vitiligo who develop Hashimoto’s disease, close monitoring of the activity of both diseases is necessary. Studies by Colucci et al. (Colucci et al., 2015) suggest that the activity of one disease may influence the course of the other. In addition, Vrijman et al. (Vrijman et al., 2012) observed that patients with vitiligo and concomitant autoimmune thyroid disease may have more extensive skin lesions. Optimizing treatment is another clinical challenge. Treating one condition may affect the course of the other, which requires clinicians to take a holistic approach to therapy. Studies by Gey et al. (Gey et al., 2013) have shown that normalizing thyroid function can lead to improved skin condition in patients with vitiligo. On the other hand, some therapies used to treat vitiligo may affect thyroid function. For example, Silverberg et al. (Silverberg et al., 2018) observed that the use of JAK inhibitors in the

treatment of vitiligo may potentially affect thyroid function. Patient education plays a key role in the management of these diseases. Patients with vitiligo should be informed about the increased risk of developing Hashimoto's disease and other autoimmune diseases. Ezzedine et al. (2015) emphasize the importance of educating patients about risk factors, potential symptoms, and self-examination methods. A holistic approach to treatment is essential due to the common pathogenic mechanisms of both conditions. Immunomodulatory therapies may be beneficial in the treatment of both vitiligo and Hashimoto's thyroiditis. Studies by Craiglow and King (Craiglow & King, 2019) have shown promising results with JAK inhibitors in the treatment of vitiligo, and some reports suggest that they may also have potential in the treatment of autoimmune thyroid diseases. Interdisciplinary collaboration between dermatologists, endocrinologists, and immunologists is crucial to provide comprehensive care for patients. Antonelli et al. (2015) emphasize the importance of a multidisciplinary approach in the treatment of patients with comorbid autoimmune diseases. Finally, the psychological implications of the comorbidity of both diseases should not be overlooked. Both vitiligo and Hashimoto's disease can have a significant impact on the quality of life of patients. Krüger and Schallreuter's research (Krüger & Schallreuter, 2012) showed that patients with vitiligo often experience stress, anxiety and low self-esteem, which may be further exacerbated by the coexisting Hashimoto's disease.

Conclusions

A review of the available literature indicates a significant relationship between vitiligo and the development of Hashimoto's disease. Patients with vitiligo are characterized by a several times higher risk of developing autoimmune thyroid diseases compared to the general population. It is suggested that common genetic, environmental and immunological factors participate in the pathogenesis of both diseases.

The increased frequency of co-occurrence of vitiligo and Hashimoto's disease has significant clinical implications. Regular screening for thyroid dysfunction is recommended in all patients with vitiligo and dermatological vigilance in people diagnosed with Hashimoto's disease. Early diagnosis and appropriate treatment are crucial for preventing complications and improving the quality of life of patients. Further studies are necessary to fully explain the pathogenetic mechanisms underlying the correlation between vitiligo and Hashimoto's disease. A better understanding of these relationships may contribute to the development of new preventive and therapeutic strategies aimed at common links of autoimmunity.

Disclosure:

Author's contribution:

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Methodology: Jakub Paprocki, Anna Mataczyńska, Michał Paprocki;

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