Celiac Disease and the Thyroid

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Contributor: Christina Starchl

Celiac disease (CD) and autoimmune thyroid diseases (AITD) like Hashimoto's thyroiditis (HT) and Graves' disease (GD) frequently coexist, entailing numerous potential impacts on diagnostic and therapeutic approaches. Possible correlations might exist through gut microbiota, regulating the immune system and inflammatory responses, promoting autoimmune diseases, as well as shared cytokines in pathogenesis pathways, cross-reacting antibodies or malabsorption of micronutrients that are essential for the thyroid like iron or vitamin D. Vitamin D deficiency is a common finding in patients with AITD, but might protect from autoimmunity by wielding immunoregulatory and tolerogenic impacts. Additionally, vitamin D is assumed to be involved in the onset and progression of CD, presumably plays a substantial protective role for intestinal mucosa and affects the thyroid via its immunomodulatory effects. Iron is an essential micronutrient for the thyroid gland needed for effective iodine utilization by the iron-dependent enzyme thyroid iodine peroxidase (TPO). Despite being crucial for thyroid hormone synthesis, iron deficiency (ID) is a common finding in patients with hypothyroidism like HT and is frequently found in patients with CD.

Keywords: thyroid ; celiac disease ; Hashimoto's thyroiditis ; Grave's disease ; vitamin D ; iron

1. Introduction

A substantial number of patients with autoimmune thyroid diseases (AITDs) shows an increased prevalence of coexisting autoimmune diseases [1][2]. Celiac disease (CD) is an inflammatory disease of the small intestine with autoimmune traits [3] that entails intolerance to dietary gluten and might be associated with other organ autoimmunity [4]. The ingestion of gluten triggers chronic inflammation, which leads to villous atrophy, deprivation of brush-border proteins, as well as enzymes needed for the absorption of micronutrients such as iron [5]. In contrast, iron deficiency (ID) worsens preexisting thyroid dysfunction due to the decreased activity of the heme-dependent thyroid peroxidase (TPO) [6]. Diminished levels of iron, folate, vitamin B12, vitamin D, zinc and magnesium are a frequent finding in untreated CD. Deficiencies of various micronutrients frequently coexist and may compromise physical growth and neurological development, as well as raise the risk of morbidity and mortality [7]. Micronutrient deficiencies are associated with a lower quality of life, given various side effects including fatigue, weakness, headache, dizziness or shortness of breath [8][9]. Although a correlation would be biologically plausible, studies yielded conflicting results so far on the relationship of thyroid hormone balance and trace element levels.

Hashimoto's thyroiditis (HT) and Graves' disease (GD) are the major causes of hypo- and hyperthyroidism, being mediated by different immunological mechanisms [10]. HT is generally the most prevalent autoimmune disease, frequently clustering with other autoimmune endocrinopathies. The presence of TPO or thyroglobulin antibodies, as well as potentially elevated serum thyroid stimulating hormone (TSH) concentrations can help diagnose the disease. Further, in sonography, a hypoechoic and mostly undersized thyroid gland with inhomogeneous tissue and isolated scarred hyperechoic tissue defines HT. The main feature of GD is circulating TSH receptor stimulating antibodies that bind and stimulate the TSH receptor on thyroid cells, promoting hypertrophy and hyperplasia, eventually resulting in goiter. Patients are predominantly women and may also show high serum concentrations of antibodies against thyroglobulin and TPO [3].

Up to 30% of first-degree relatives of patients with CD and/or AITDs are afflicted by the other disease, respectively. The genes predisposing endocrine autoimmunity, such as diabetes type 1 or AITDs, namely DR2-DQ2 and DR4-DQ8 are substantial genetic parameters of CD, which is an HLA-linked disease as well [11]. CD and endocrine autoimmunity share a similar genetic background. Single nucleotide polymorphisms of several immunoregulatory genes have been found to be overlap susceptibility genes for both CD as well as monoglandular or polyglandular autoimmunity [12]. Genetic overlap between CD and other autoimmune disease may be of clinical relevance, but genetic screening is not yet sensitive nor specific enough to predict the disease onset and progression [13]. Nonetheless, patients with CD should be screened for type 1 diabetes or AITD and vice versa.

2. The Roles of Vitamin D and Iron

Celiac disease (CD) and autoimmune thyroid diseases (AITDs) like Hashimoto's thyroiditis (HT) and Graves' disease (GD) frequently coexist, entailing numerous potential impacts on diagnostic and therapeutic approaches. Accumulating data supports the existence of a significant thyroid-gut-axis, indicating effects of the gut microbiome not only on the immune system and the absorption of micronutrients, but also on thyroid function. Micronutrients such as iron and vitamin D often lack in CD, but also frequently in thyroid diseases, implicating intercorrelating mechanisms. This interconnected synergy can be easily disturbed by numerous events, including environmental factors, early infections, birth mode or eating habits.

There is a higher prevalence of coexisting thyroid and gut related disease, including HT and GD, as well as CD—and dysbiosis frequently co-occurs in this context, either. An altered microbiota is able to change the immune response as well as onset of autoimmune diseases and it is probably able to function as a reservoir for thyroid hormone medication. Supported by a proper composition of the gut microbiota which binds it to bacterial thyroid-binding hormone, patients could reduce hormone fluctuations and reduce their dosage of L-thyroxine. The role of microorganisms and microbiota in the development and progression of AITDs and CD is still controversial and needs to be further elucidated. However, increasing evidence suggests the importance of this thyroid–gut axis, which is thought to modulate autoimmune disorders. Patients often refer to changes in their quality of life and thyroid function in relation to dietary changes. Probiotics could represent a novel additional treatment option for patients with need for thyroid hormone substitution.

There is a clear link between the lack of micronutrients such as iron and vitamin D and CD, as well as AITDS. Iron deficiency is a common finding in CD, presumably as a result of permanent inflammation and villous atrophy. ID occurs often in thyroid diseases as well and deteriorates preexisting thyroid dysfunction, for example, through inhibiting the activity of heme dependent TPO. Studies still yield conflicting results, but a correlation between appropriate iron status and proper thyroid function appears to be clear.

Vitamin D is often lacking in patients with AITDs but might protect from autoimmunity by wielding immunoregulatory and tolerogenic impacts. Vitamin D deficiency is associated with AITDs such as HT and GD, but the correlations are controversial and require further studies. It is not entirely clear whether vitamin D deficiency can be considered a cause or rather a consequence of autoimmune diseases, even though studies point towards a rather causative role of vitamin D.

Future studies should try to examine if and how a gluten-free diet can prevent or delay the development of CD and endocrine autoimmunity of children at risk. The manifold consequences implicate the need for a higher awareness of interconnected thyroid and celiac disease and their common micronutrient deficiencies. There is a close relationship between CD and endocrine autoimmunity, which justifies broader immune genetic and endocrinological screenings of celiac patients.

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