



REVIEW ARTICLE

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Celiac disease and autoimmune thyroid diseases

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Abstract

Celiac disease (CD) is a disease that characterized with small intestinal injury by the ingestion of gluten, the major protein of wheat and similar grains in genetically predisposed persons. The clinical presentation may be seen in a wide spectrum from severe malabsorption syndromes to silent asymptomatic cases. Diagnosis of celiac disease requires the finding of a typical mucosal lesion from small bowel biopsy such as villous atrophy and crypt hypertrophy and recovery of the histological findings and clinical improvement after introduction of gluten free diet. The occurrence of antibodies supports the diagnosis of celiac disease. Prevalence of other autoimmune diseases, including autoimmune thyroid diseases, has been reported to be higher than controls. The coexistence of autoimmune thyroid disease and celiac disease may related to genetic predisposition. Thus evaluation of CD patients for thyroid disorders may improve CD patients' quality of life and may be important in their clinical management. Patients diagnosed with autoimmune diseases may develop other autoimmune disorders related with different organ systems in consequent years. Clinicians should be aware of this issue and evaluate patients' for concomitant endocrinopathies.

Keywords: Celiac disease, autoimmune thyroid diseases, management

Introduction

Celiac disease (CD) is a disease that characterized with small intestinal injury by the ingestion of gluten, the major protein of wheat and similar grains such as rye and barley, in genetically predisposed persons [1]. In Europe and USA approximately 1% of the population was diagnosed with celiac disease and the diagnosed population is approximately 15% of the affected population [2]. In Turkey, the tissue transglutaminase antibody positivity prevalence was reported as 1.3 % of healthy Turkish blood donors which was relatively high in comparison to the prevalence reported in Europe and USA [3].

The clinical presentation of celiac disease may vary according to different age groups. In adulthood the clinical presentation may be seen in a wide spectrum from severe malabsorption syndromes to silent asymptomatic cases [4]. The diagnosis of celiac disease requires the finding of a typical mucosal lesion from small bowel biopsy such as villous atrophy and crypt hypertrophy and recovery of the histologic findings and clinical improvement after introduction of gluten free diet. The occurrence of antibodies supports the diagnosis of celiac disease [4].

Nutritional therapy, gluten-free diet is the only accepted treatment for celiac disease. But in patients who are refractory to gluten free diet immunosuppressive therapies may be beneficial[5]. Several other autoimmune disorders are more prevalent in patients with celiac disease [6]. Ventura et al. reported that the prevalence of other autoimmune disease prevalence was 14% in patient with celiac disease and 2.8% in control group and longer duration of exposure to gluten resulted in higher autoimmune disease (Addison disease, pernicious anemia, autoimmune thrombocytopenia, sarcoidosis, type 1 diabetes mellitus and alopecia) prevalence [7].

Celiac Disease in Autoimmune Thyroid Diseases

The coexistence of autoimmune thyroid disease and celiac disease is supposed to be related to genetic predisposition [8]. Especially HLA DQ2 and DQ8 haplotypes of HLA antigens are over-expressed in many autoimmune diseases [9]. It was reported that inheritance of these haplotypes and immunological phenotype may explain the link between autoimmune thyroid disease and celiac disease [10-11]. Also, it was reported that polymorphisms in gene CTLA4 coding for a protein in the inhibition of activation of T cells lead to increment in thyroid antibody secretion and autoimmunity [12-13]. But, the exact pathogenesis of coexistence of autoimmune thyroid disease and celiac disease has not been explained yet [8]. In a study screening 83 patients with AITD, Collin et al. found three patient with asymptomatic celiac disease and one patient previously diagnosed with CD, the overall frequency was

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4.8% in AITD group and 0.4% in control group [14]. Valentino et al. found antibody positivity in five patients in 150 patients with AITD and frequency of CD was reported as 3.3%. In the same study after removal of gluten from diet improvement in hypothyroidism symptoms and required thyroxin dose reduction reported [15]. Berti et al. found that six of 172 (3.4%) AITD patient antibodies were positive; five of six patients underwent small bowel biopsy all of which showed total villous atrophy. In the same study antibody positivity was reported as 0.25% in 4000 blood donors. Increased frequency of celiac disease among AITD patients and importance of screening of AITD patients for CD is emphasized [16]. Larizza et al. screened 90 children and adolescents with AITD and found CD frequency as 7.8% [17]. In another study Meloni et al. found CD frequency as 4.4% [18]. Chang et. al. evaluated 111 patients with Graves' disease and found that CD prevalence was 4.5% in patients with Graves' disease and 0.9% in control group. According to these results screening for CD was recommended for patients with Graves' disease [19].

In Turkey, Guliter et al. found CD prevalence as 5.8% among 136 adult AITD patients and 0.8% in control group [20]. In pediatric age group, Sari et al. found eight of 101 (7.8%) AITD patients antibody positive; they recommended screening of children with AITD for CD [21].

Autoimmune Thyroid Diseases in Celiac Disease

As it has been previously described that several autoimmune diseases including autoimmune thyroid disease increase in patients with CD [7]. Sategna et al. screened 422 patients and 605 controls for autoimmune disease and found the prevalence of AITD 13.5% of the patient group and 2% of the control group. In the same study age at diagnosis for CD which is an indirect measure of gluten exposure was significantly higher in patients with both CD and AITD than in patients with CD alone. But in this study Sategna et al. didn't found any significant relationship between duration of gluten exposure and frequency of autoimmune diseases [22].

In other studies AITD prevalence was reported as 4-10% of patients with celiac disease and thyroid autoantibody positivity was reported in 10-15% of them [23-25]. Kowalska et al. reported that in pediatric age group in patients with celiac disease without gluten free diet the frequency of thyroid autoantibody positivity was 41% of the patient group and 3.6% of the control group. And also 11% of these patients had thyroid function disorders [26]. Sategna et al. screened 241 adult untreated CD patients and found that 39 (16.2%) patients in CD group and 8 patients (% 3.8) in the control group had euthyroid autoimmune thyroid disease. In the same study it was reported that thyroid disease was three fold higher in patient group than in controls. Hypothyroidism was diagnosed in 12.9% in patient group and 4.2% in control group and after one-year

of strict gluten withdrawal normalization of patients' subclinical hypothyroidism observed. Regarding hyperthyroidism there was no difference between groups [27].

Hakanen et al. found clinical autoimmune thyroid disease in 11 (13.9%) out of 79 CD patients; 3 patients diagnosed as Graves' disease and 8 patients diagnosed as autoimmune hypothyroidism. 8 patients (10.1%) diagnosed as subclinical hypothyroidism. Clinical AITD prevalence was 2.1% and subclinical AITD prevalence was % 3.3 in the control group. Also the study showed that thyroid gland volumes were smaller compared to the control group (8.3 vs. 10.3) in ultrasonography and moderate – severe hypoechogenicity was found in 73% of patients with CD compared to 42% of controls, both of which were statistically significant [28].

The Effect of Celiac Disease Treatment in the Course of Associated Autoimmune Thyroid Diseases

The early diagnosis and treatment of CD should be beneficial in reducing complications of CD such as malabsorption, infertility, osteoporosis and lymphoma [8, 29]. Treatment of CD leads to improvement in absorption from small intestine and may decrease the required thyroxin dose and other related medications [15].

It is not exactly known whether treatment of CD with gluten free diet changes the course of AITD. Literatures concerning this issue are confusing. As it has been previously mentioned, Sategna et al. reported clinical improvement in subclinical hypothyroidism with treatment of CD but they didn't find any correlation between gluten free diet and frequency of AITD [22]. In another study, Viljamaa et al. found no correlation between duration of gluten exposure and risk of autoimmune disorders in adults [30]. But on the other hand Ventura et al. reported that thyroid related antibodies tended to disappear from 14.4% to 2.2% with gluten free diet [7]. More studies are needed to clarify the role of gluten free diet in course of AITD.

Conclusion

Many patients with CD admit to clinicians with wide spectrum of nonspecific clinical signs and symptoms in adulthood. These nonspecific signs and symptoms lead to delay in diagnosis of CD and majority of cases remain undetected. Association between autoimmune thyroid disorders and celiac disease has been shown in numerous studies. Increased frequency of CD reported in AITD. Because of this evaluation of patients with AITD for signs and symptoms of CD may be beneficial in early diagnosis of CD and in reducing CD related complications. Also since autoimmune thyroid disorders increase in CD, evaluation of CD patients for thyroid disorders may improve CD patients' quality of life and may be important in their clinical management.

Patients diagnosed with autoimmune diseases may develop other autoimmune disorders related with different organ systems in consequent years. Clinicians should be aware of this issue and evaluate patients' for concomitant endocrinopathies.

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