CASE REPORT

# CELIAC DISEASE ASSOCIATED WITH GRAVES DISEASE

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**Abstract:** Celiac disease is an autoimmune enteropathy induced by gluten intake in genetically susceptible individuals. Celiac disease is known to be associated with autoimmune diseases. However the association celiac disease, Graves' disease and selective IgA deficiency are rarely found in children. A 4 years-old girl with celiac disease and selective IgA deficiency presented with diarrhea and growth acceleration. Thyroid tests showed hyperthyroidism with positive thyroid receptor antibodies, confirming the presence of Graves' disease. HLA typing showed the haplotype A23 851 A28 03 DRB1 * B3. Screening for other autoimmune disorders was negative. Treatment with carbimazole was started and the patient soon became euthyroïd. Carbimazole was stopped after 18 months of follow-up.

**Keywords:** celiac disease, Graves' disease, IgA deficiency, children

## Introduction

Celiac disease (CD) is an autoimmune enteropathy induced by ingestion of gluten in genetically predisposed subjects. It may be associated with other extra-intestinal manifestations and autoimmune diseases. Type 1 diabetes, autoimmune thyroiditis, Hashimoto's thyroiditis essentially, are related to celiac disease. (1,2) Hyperthyroidism is uncommon in the pediatric age range and particularly rare in young children. (3) Graves' disease (GD) is a specific form of hyperthyroidism. Autoimmune thyroid diseases, including GD and Hashimoto's thyroiditis, are due to complex interactions between environmental and genetic factors. (4,5) Celiac disease and autoimmune thyroid disease have similarities in pathogenesis. CD is associated with HLA-DR3, and such an association has been demonstrated in Graves' disease and Hashimoto's thyroiditis as well. Selective IgA deficiency (IgAD) is characterized by total IgA serum levels below 0.06 g/L and normal levels of IgM and IgG. Although the majority of IgAD individuals are asymptomatic, IgAD is associated with autoimmune disorders such as CD. Its frequency is raised and estimated to be about 1:40 among patients suffering from celiac disease. (6,7) We report the case of a girl who had CD associated with GD and selective IgA deficiency.

## Case Report

A one-year-old-girl with chronic diarrhea and failure to thrive was admitted to hospital. She was born from non-consanguineous parents and had a family history of thyroid disease. Serologic tests for celiac disease were performed. IgG class anti-gliadin and anti-reticulin antibodies were positive but IgA class of these antibodies were negative. Anti-endomysial and anti-transglutaminase antibodies of IgG class were negative. Total IgA levels were low [11.7 mg/dl (normal value between 80-450 mg/dl)]. Histopathological examination of the jejunal biopsy showed total villous atrophy grade 5. Patient was started a gluten-free diet, she was compliant with her diet and had a normal growth during the follow-up. At the age of 4 years and 6 months, she developed diarrhea with sweating, irritability, clammy hands and polyphagia. On physical examination, her weight was 17 kg, height was 111 cm. She was afebrile with regular pulse rate of 120/min with normal blood pressure. Bilateral exophthalmos was observed. Her bone age was 5 years by the Greulich –Pyle method. Serum thyroid stimulating hormone level (TSH) was less than 0.05 µUI / mL and free thyroxine (freeFT4) was 38ng/dL (7-19 ng/dL). Anti-thyroperoxidase antibodies were positive [77 IU/ml (< 35 IU/mL)], anti-thyroglobulin antibodies and anti-TSH receptor antibodies were negative. A thyroid nuclear scan revealed diffuse enlargement with markedly increased uptake of both thyroid glands. She was subsequently diagnosed with Graves' disease. HLA typing showed the haplotype A23 851 A28 03 DRB1 * B3 and the screening for other autoimmune disorders was negative. She was treated with carbimazole (10 mg/day) and propranolol (3 mg/kg/day). Rapid disappearance of clinical signs of hyperthyroidism was observed after a few weeks. A normal serum thyroid hormone level was obtained after 4 months. She had normal statural growth; thyroid function test showed hypothyroidism and carbimazole was stopped after 18 months of follow-up.

## Discussion

We report a rare pediatric observation of CD associated with GD and selective IgA deficiency. This association suggests a common pathophysiologic mechanism, including a genetic predisposition (HLA and non-HLA genes).Our patient had the HLA typing HLA DR3. HLA DR3 promotes the expression of multiple autoimmune diseases. (2) Screening for other autoimmune disorders was negative. Many autoimmune disorders are associated with CD. Autoimmune thyroid disease and CD have similarities in pathogenesis. There are some hypotheses that gluten may be the primary antigen which initiates the formation of anti-thyroid antibodies as well as antibodies directed against other endocrine glands. Several studies have indicated that impaired thyroid function in patients with untreated CD improves after the implementation of a gluten – free diet, and a drop in the titer of thyroid antibodies is observed. (8) The association of celiac disease and GD had been reported in the literature, with two children who also had Down syndrome. (9, 10) The first patient was 17 years old and had, in addition diabetes mellitus. In the second case, GD and CD were diagnosed in a 16 years old adolescent with Down syndrome presenting with chronic diarrhea, important delayed development and signs of hyperthyroidism.

Hyperthyroidism is uncommon in the pediatric age range and particularly rare in young children. The incidence of hyperthyroidism is 8 cases per 1,000,000 individuals aged 0-15 years per year as reported in the Danish population, and the lowest incidence 1 per 1,000,000 was found in children younger than 4 years. (11) The peculiarity of our case is the occurrence of

GD in a girl under 5 years. Diagnosis is confirmed by thyroid hormone determinations. TSH is undetectable in the serum (<0.3 mU/l) in all patients. Most children with hyperthyroidism have very high serum FT4 and FT3 concentrations. Thyroid gland is diffusely enlarged, and often homogeneous in thyroid imaging as was seen in our patient. (12)

Optimal treatment of Graves' disease in pediatric patients is still a matter of controversy. Anti-thyroid drugs, radioiodine and thyroidectomy are the three therapeutic options available. The use of anti-thyroid drugs as the initial treatment option in GD is well accepted. An average two years remission is achieved in about 30% of children treated with anti-thyroid drugs. However, the optimal treatment duration and the predictive marker of remission after anti-thyroid drug therapy are still controversial. (13)

Furthermore, it has also been shown that IgA class anti-transglutaminase react with thyroid tissue, and this bond could contribute to the development of thyroiditis in patients with celiac disease. (14) In our patient, IgA class anti-transglutaminase were negative since she had a selective IgA deficiency. Similarly, the combination of IgA deficiency and Graves' disease had been reported in the literature. (14)

**Conclusion**

The presence of several multiple conditions, as in our case, requires a close and continuous monitoring in order to detect the possible occurrence of other attacks in susceptible individuals and help to avoid diagnostic and therapeutic delay.

**Funding:** None

**Conflict of Interest :** None

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**DOI No.** 10.7199/ped.oncall.2015.39