

## Case Report: Hyperthyroidism, Iron-deficiency Anemia, and Celiac Disease

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**Abstract.** The objective was to report a case of a woman with celiac disease presenting with hyperthyroidism and iron-deficiency anemia. **Methods.** We report the clinical course of this patient and her laboratory findings. We highlight the important associations between hyperthyroidism, iron-deficiency anemia, and celiac disease. The literature is reviewed for the typical and atypical presentations of celiac disease in relation to hyperthyroidism and iron-deficiency anemia. **Results.** A 37-year-old woman presented with symptoms of hyperthyroidism and was found to have iron-deficiency anemia. During the work up for iron-deficiency anemia, she was diagnosed with celiac disease on small-bowel biopsy. After being placed on a gluten free diet, symptoms of hyperthyroidism improved without anti-thyroid medication. **Conclusion.** Our case demonstrates that routine screening for celiac disease should be highly considered for patients with both hyperthyroidism and iron-deficiency anemia. Treating celiac disease by gluten withdrawal may reduce morbidity and improve quality of life in patients with hyperthyroidism, anemia, and celiac disease.

**Keywords** • Celiac disease • Hyperthyroidism • Iron-deficiency anemia

### Introduction

Celiac disease is on the rise globally, particularly in the Western countries. Recent population screening studies have shown that the prevalence of celiac disease in Western countries approaches 1%.<sup>[1]</sup> The condition is greatly under-diagnosed due to its previously perceived rarity.<sup>[2,3]</sup> The incidence and failure to diagnose the condition can result in complications for the affected patient.<sup>[4]</sup> Many autoimmune diseases can be associated with celiac disease, including autoimmune thyroid disease. An association between thyroid disease and celiac disease has previously been described.<sup>[1,5,6,7,8]</sup> There is also an increased incidence of Graves' hyperthyroidism among patients with celiac disease, and researchers have recommended routine screening for celiac disease in patients with thyroid disorders.<sup>[9]</sup> In addition, patients with celiac disease sometimes present with iron deficiency anemia.<sup>[10,11]</sup> However, Graves' disease, iron deficient anemia, and celiac disease occurring in a single patient has not been reported before; we therefore report the

first case of Graves' hyperthyroidism associated with iron-deficiency anemia and celiac disease.

### Case Report

A 37-year-old woman with no significant past medical history presented to the endocrinology clinic with a one-year history of palpitations, tachycardia, anxiety, diarrhea, and a 20 pound weight loss. Clinical and biochemical findings were consistent with overt hyperthyroidism. Her TSH was 0.02 mIU/L (reference range 0.4-5.5 mIU/L), her free T<sub>4</sub> was 2.9 ng/dL (reference range 0.8-1.8 ng/dL), her T<sub>3</sub> was 388 ng/dL (reference range 60-181 ng/dL), and her thyroid uptake showed homogenous increased 24-hour uptake at 65%. Thyroid ultrasound showed a diffusely enlarged thyroid with no focal lesion.

The patient was started on methimazole, 10 mg bid, and propranolol, 40mg bid, for symptom control. She developed facial rash after starting methimazole, so it was discontinued after three weeks of treatment. Blood tests showed hemoglobin/hematocrit to be 10.9

**Table 1.** Results of Laboratory Tests

	At initial presentation	2 months after starting a gluten-free diet	7 months after starting gluten-free diet	12 months after gluten-free diet	Reference range
<b>TSH</b>	0.02 mIU/L	0.04 mIU/L	0.04 mIU/L	0.03 mIU/L	0.4-5.5 mIU/L
<b>Free T<sub>4</sub></b>	2.9 ng/dL	1.1 ng/dL	1.1 ng/dL	1.4 ng/dL	0.8-1.8 ng/dL
<b>Total T<sub>3</sub></b>	388 ng/dL	115 ng/dL			60-181 ng/dL
<b>Free T<sub>3</sub></b>			337 ng/dL	412 ng/dL	230-420 pg/dL
<b>Hemoglobin</b>	10.9 g/dL	14.4 g/dL	14.0 g/dL	14.0 g/dL	11.5-15.0 g/dL
<b>Hematocrit</b>	33.3%	41.4%	40.5%	40.1%	34.0-44.0%

g/dl/33.3% with a MCV of 68. Iron studies revealed iron-deficiency anemia. Her iron level was 32 µg/dL (reference range 40-175 µg/dL), transferrin saturation was 8% (reference range 15-50%), and total iron-binding capacity (TIBC) was 400 µg/dL (reference range 250-450 µg/dL).

The patient was referred to Gastroenterology Department for a work up for anemia and chronic diarrhea. She was found to have positive anti-gliadin antibodies and positive tissue transglutaminase IgG antibodies that are consistent with celiac disease. Endoscopic small bowel biopsies were suggestive of celiac disease. The patient was then placed on a gluten-free diet, which gradually improved her diarrhea and anemia.

Two months after she started a gluten-free diet, the patient was no longer anemic (hemoglobin/hematocrit was 14.4 g/dl/41.4%), and her symptoms improved. She remained clinically euthyroid, and a blood test showed a TSH level of 0.04 mIU/L, a free T<sub>4</sub> level of 1.1 ng/dL, and a T<sub>3</sub> level of 115 ng/dL. She remained clinically euthyroid except for occasional palpitations which were controlled by Toprol XL, 25 mg daily. Twelve months after adopting a gluten-free diet, she gained 4 lbs and blood tests showed a TSH level of 0.03 mIU/L, a free T<sub>4</sub> level of 1.1 ng/dL, and a free T<sub>3</sub> level of 412 ng/dL. See Table 1 for the summary of her laboratory test results.

## Discussion

Celiac disease or gluten sensitive enteropathy is an intolerance of dietary gluten that results in immunologically-mediated inflammatory damage to the small intestinal mucosal. The damage is characterized by inflammation, crypt hyperplasia, and villous atro-

phy.<sup>[1,7,12]</sup> Celiac disease patients cannot tolerate gluten. Classic symptoms include diarrhea, flatulence, abdominal pain, and weight loss. However, there is an increased incidence of subclinical or silent celiac disease in recent years.<sup>[13,7,14]</sup>

An increased prevalence of thyroid dysfunction and anemia has been reported in patients with Celiac disease. Iron-deficiency anemia can be an extra-intestinal marker of subclinical celiac disease.<sup>[13]</sup> Some authors have recommended that patients with iron-deficiency anemia be routinely evaluated for celiac disease.<sup>[10,11]</sup>

In addition, authors of previous studies recommend routine screening for celiac disease in patients with autoimmune thyroid disease. In a prospective study of 115 patients with Graves' hyperthyroidism by Ch'ng et al.,<sup>[9]</sup> the prevalence of celiac disease in patients with Graves' hyperthyroidism was found to be 4.5% as compared with 0.9% in age and sex matched controls.

Graves' disease, iron-deficient anemia, and celiac disease occurring in a single patient has not been reported before. In our case, the diagnosis of Graves' hyperthyroidism was based on elevated free thyroid hormones, suppressed TSH levels, and homogeneously increased iodine uptake.

Celiac disease was diagnosed by characteristic histological abnormalities on small bowel biopsy, positive antibodies, and a good response to a gluten-free diet. Iron deficiency anemia was based on low serum iron, a low transferrin saturation of 8%, and high TIBC.

Celiac disease and iron deficiency anemia are clinically important because early treatment of celiac disease may prevent or reverse extra-intestinal manifestations, including osteoporosis, anemia, and fa-

tigue, and may reverse some thyroid abnormalities. In this case, the patient's anemia significantly improved on a gluten-free diet. Her symptoms of hyperthyroidism also improved without antithyroid medication. This suggests that treating celiac disease may have reversed the patient's thyroid abnormalities.

Celiac disease should be considered in patients presenting with iron deficiency and hyperthyroidism. The diagnosis of celiac disease can be made based on a combination of serologic testing and pathology. The gold standard for diagnosing celiac disease is a small bowel biopsy sample by which the extent of the damage can be measured.<sup>[7,16]</sup>

The effective treatment for celiac disease is withdrawal of gluten from the diet. Withdrawal includes the avoidance of all foods containing wheat, rye, and barley. The withdrawal allows the small bowel mucosa and nutrient absorption to normalize.<sup>[7,12]</sup> Such dietary modifications may correct refractory anemia and hyperthyroidism. If celiac disease is not effectively treated, both benign and malignant complications may occur, such as malabsorption, osteoporosis, infertility, and lymphoma of celiac disease. These complications, however, can often be avoided by early diagnosis and compliance with a gluten-free diet.<sup>[1,7]</sup> In our case, the gluten-free diet reversed the iron-deficiency anemia and hyperthyroidism, although there exists the possibility of a spontaneous fluctuation of Graves' disease.

## Conclusion

We report a unique case of a patient with hyperthyroidism, iron deficiency anemia, and celiac disease. The patient's thyroid function improved and anemia normalized after a gluten-free diet, without antithyroid medication and iron supplementation. Currently it is not known whether treatment of celiac disease reduces the likelihood of developing autoimmune disorders or changes the natural history of Graves' disease. We suggest screening for celiac disease in patients with both hyperthyroidism and iron-deficiency anemia.

Treating celiac disease by withdrawing gluten may reduce morbidity and improve quality of life in patients with hyperthyroidism, iron deficiency anemia, and celiac disease.

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