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Refractory Hypothyroidism and Celiac Disease in Selective IgA Deficiency: an Endocrine–Autoimmune Overlap

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Abstract

Refractory hypothyroidism often results from impaired levothyroxine absorption [1]. Celiac disease, particularly in the presence of selective IgA deficiency, can complicate diagnosis due to false-negative serologies. We describe a 24-year-old male presenting with chronic weakness, fatigability, and weight loss. He had iron deficiency anemia, primary hypothyroidism unresponsive to escalating levothyroxine doses, selective IgA deficiency, and vitamin D deficiency. Celiac serologies were negative, but deamidated gliadin peptide IgG was positive. Duodenal biopsy confirmed celiac disease with villous atrophy. A gluten-free diet, parenteral iron, vitamin D supplementation, and optimized levothyroxine led to marked clinical improvement, weight gain, and stabilization of thyroid function at a reduced levothyroxine dose. This case highlights the importance of considering malabsorption and autoimmune overlap syndromes in patients with refractory hypothyroidism and iron deficiency anemia.

Keywords: Refractory hypothyroidism; Celiac Disease; Autoimmune Overlap; Fatigability

Introduction

Refractory hypothyroidism is characterized by persistence of hypothyroid state despite adequate or escalating doses of levothyroxine [1]. Malabsorption syndromes, particularly celiac disease, are recognized causes [2]. However, selective IgA deficiency can obscure diagnosis by yielding false negative IgA-based serologies [3,4]. We report a case of refractory hypothyroidism and iron deficiency anemia, ultimately diagnosed with celiac disease in the context of selective IgA deficiency.

Case presentation

A 24-year-old male presented with three years of generalized weakness and easy fatigability, worsening over six months, along with unintentional weight loss of 5 kg. Past history included recurrent respiratory infections in childhood, complicated by chronic suppurative otitis media. He denied gastrointestinal bleeding, abdominal pain, diarrhea, constipation, or systemic symptoms. On examination, he was pale, weighed 48 kg with BMI 18.5, and had no goiter, organomegaly, or skeletal deformities. Systemic examination was unremarkable. Investigations revealed microcytic hypochromic anemia (Hb 8.7 g/dL, MCV 67 fL, MCH 18 pg) with low ferritin (5.5 ng/mL) and serum iron (38 µg/dL). Thyroid profile confirmed primary hypothyroidism (T4 3.1 µg/dL, T3 1.0 ng/mL, TSH 26.3 µIU/mL). Despite levothyroxine initiation at 50 µg/day, escalating doses up to 200 µg/day failed to normalize thyroid function. Vitamin D was deficient (25OH vitamin D 8.3 ng/mL), while cortisol was normal (19.7 µg/dL). Selective IgA deficiency was detected (22mg/dL). IgA-based celiac serologies were negative, but deamidated gliadin peptide IgG was positive. Upper GI endoscopy with duodenal biopsy showed total villous atrophy and crypt hyperplasia (Marsh grade III). CT enterorrhaphy demonstrated jejunalization of the ileum (Figure 1). The patient received parenteral iron, vitamin D replacement, and commenced on a gluten-free diet along with titrated levothyroxine. At three-month follow-up, he had gained 4 kg, reported resolution of fatigue, and achieved stable thyroid function on a reduced levothyroxine dose of 75 µg/day.

Discussion

This case illustrates the diagnostic challenge of refractory hypothyroidism due to underlying celiac disease with selective IgA deficiency. Iron deficiency anemia and vitamin D deficiency raised suspicion of malabsorption [4,5], while persistently high levothyroxine requirements suggested impaired absorption [6]. The markedly low IgA levels invalidated standard serological

screening, necessitating IgG-based testing and histological confirmation [7]. Selective IgA deficiency is the most common primary immunodeficiency, strongly associated with celiac disease [3,8]. In such patients, negative IgA-based serologies can delay diagnosis, underscoring the value of IgG-based tests and duodenal biopsy [7,9]. Management required a multidisciplinary approach, including correction of nutritional deficiencies, gluten-free diet initiation, and reassessment of levothyroxine dosing. Clinical and biochemical improvement following dietary modification confirmed malabsorption as the major contributor to refractory hypothyroidism [10]. This case underscores the importance of considering celiac disease in hypothyroid patients with unexplained anemia and levothyroxine resistance, particularly when selective IgA deficiency is present [11].

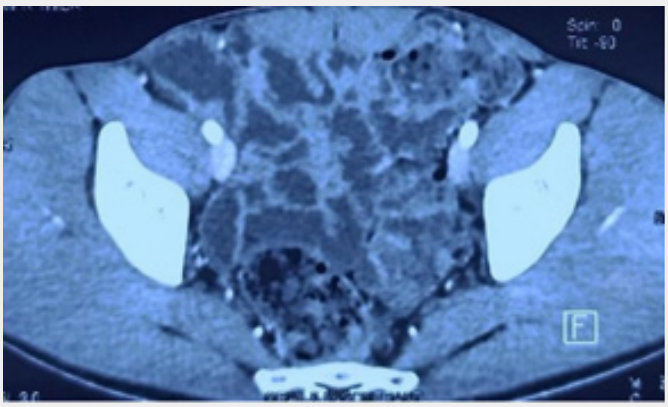

Figure 1: CT enterorrhaphy showing jejunation of the ileum, suggesting a potential link to malabsorption.

Conclusion

Refractory hypothyroidism should prompt evaluation for malabsorptive disorders such as celiac disease. Selective IgA deficiency can mask the diagnosis by rendering conventional celiac serologies negative [3]. Early recognition and dietary intervention can restore thyroid hormone absorption and improve overall outcomes [1,2,11].

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