Case Report

When Thyroxine Isn't Enough: Coeliac Disease as a Silent Contributor to Treatment-Resistant Hypothyroidism

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ABSTRACT

Background: Refractory hypothyroidism, characterized by persistently elevated thyroid-stimulating hormone (TSH) levels despite high-dose levothyroxine therapy, necessitates a thorough evaluation for underlying causes. While noncompliance is a common reason, it must be carefully excluded before considering alternative explanations such as malabsorption syndromes. Coeliac disease is a known but often under-recognized cause of levothyroxine malabsorption.

Case Presentation: We report the case of a 15-year-old girl with a 3-year history of primary hypothyroidism who presented with persistently elevated TSH levels (>30 mIU/L) despite daily administration of 250 mcg levothyroxine per day. She demonstrated full compliance with medication, proper intake technique, and no interfering drugs or supplements. Her low body weight (35 kg) and disproportionate levothyroxine requirement raised suspicion for malabsorption. Serologic testing revealed positive tissue transglutaminase IgA antibodies, confirming the diagnosis of coeliac disease.

Management and Outcome: The patient was commenced on a strict gluten-free diet. Within months, her TSH levels declined, levothyroxine dose requirements dropped to 50 mcg/day, and her weight increased to 42 kg. Her most recent TSH is 1.3 mIU/L reflecting euthyroidism.

Conclusion: This case highlights the importance of considering coeliac disease as a cause of refractory hypothyroidism when noncompliance and administration errors have been clearly excluded. Identifying and treating the underlying malabsorption with a gluten-free diet can significantly reduce hormone requirements and restore euthyroidism.

KEY WORDS: Refractory hypothyroidism; Levothyroxine malabsorption; Coeliac disease.

INTRODUCTION

Hypothyroidism is a common endocrine disorder, often well-managed with levothyroxine.[1] However, persistently elevated TSH despite adherence to treatment necessitates evaluation for factors that interfere with absorption. Coeliac disease, an immune-mediated enteropathy, can impair levothyroxine absorption and lead to apparent treatment resistance.[2] Although coeliac disease frequently presents with classic gastrointestinal symptoms, it may also be subclinical or entirely asymptomatic, making diagnosis challenging and often delayed in such patients.[3]

CASE PRESENTATION

A 15-year-old girl, previously diagnosed with primary hypothyroidism at the age of 12, presented to our tertiary care center for evaluation of persistently elevated thyroid-stimulating hormone (TSH) levels.

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She had consulted multiple physicians over the past three years and was gradually escalated to a high dose of levothyroxine — 300 mcg daily. Despite this, her TSH remained consistently above 30 mIU/L. Her most recent TSH was 32.6 mIU/L.

She reported strict adherence to her medication, taking levothyroxine on an empty stomach, without concurrent intake of calcium, iron, or multivitamins. She obtained her medication from a reliable pharmacy and had never changed brands. There was no relevant family history or other notable systemic findings. Her weight at presentation was 35 kg.

Given her low body weight and the unusually high requirement for levothyroxine, a malabsorption disorder was suspected. Coeliac serology was performed, revealing positive tissue transglutaminase IgA antibodies. Moreover, tissue transglutaminase IgG levels were normal, upper gastrointestinal endoscopy was advised but patient refused because of financial constraints. Her lab investigations are shown in Table-I.

Table-I: Lab investigations summary.

S. No.	*Test*	*Result*	*Reference Range*	*Interpretation*
1	Complete Blood Count (CBC)			
	White Blood Cell Count (WBC)	8.7 $\times 10^9$/L	4.5 – 11.0 $\times 10^9$/L	Normal
	Hemoglobin (Hb)	11.1 g/dL	11.0 – 14.0 g/dL	Low-normal
	Red Blood Cell Count (RBC)	3.6 $\times 10^{12}$/L	3.5 – 4.5 $\times 10^{12}$/L	Normal
	Hematocrit (HCT)	39 %	37 – 47 %	Normal
	Mean Corpuscular Volume (MCV)	89 fL	80 – 100 fL	Normal
	Mean Corpuscular Hemoglobin (MCH)	33 pg	27 – 31 pg	Slightly elevated
	Mean Corpuscular Hemoglobin Conc. (MCHC)	31 g/dL	33 – 35 g/dL	Low
	Neutrophils	50 %	40 – 70 %	Normal
	Lymphocytes	42 %	20 – 40 %	Mildly elevated
	Monocytes	8 %	2 – 10 %	Normal
	Eosinophils	0 %	1 – 4 %	Low
	Platelets	265 $\times 10^9$/L	150 – 450 $\times 10^9$/L	Normal
2	Celiac Antibody Panel			
	Anti-tTG IgA (ELISA)	200 RU/mL	< 20: Negative	Positive – Suggestive of celiac disease
			20–30: Borderline	
			> 30: Positive	
	Anti-tTG IgG (ELISA)	1.54 RU/mL	< 20: Negative	Negative
			20–30: Borderline	
			> 30: Positive	
3	Thyroid Function Tests			
	TSH	43.9 mIU/L	0.4 – 4.2 mIU/L	Severely Elevated – Hypothyroid
	Free T4 (FT4)	0.7 ng/dL	0.8 – 1.8 ng/dL	Low – Confirms hypothyroidism
4	Thyroid Autoimmunity			
	Anti-thyroid peroxidase (Anti-TPO)	>1300 IU/mL	< 35 IU/mL	Markedly Elevated – Hashimoto's thyroiditis

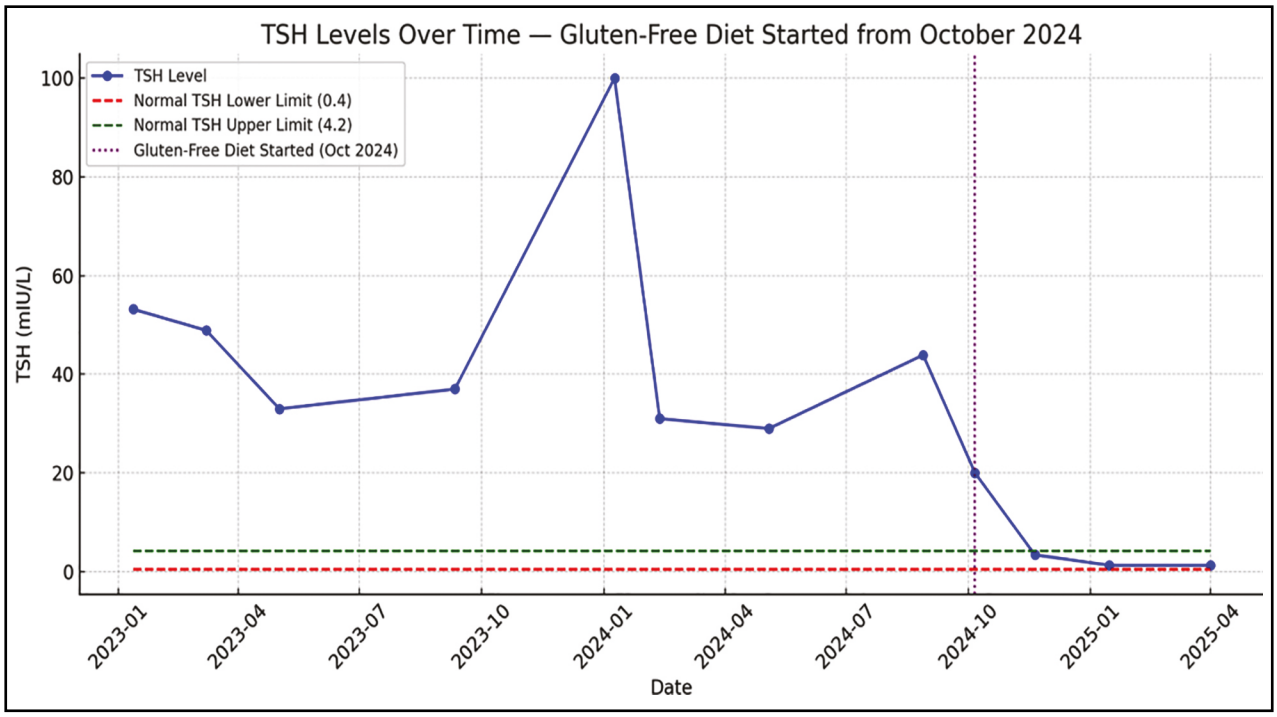

Fig.1: Showing TSH levels over time and after gluten free diet initiation.

The patient was started on a gluten-free diet. Over the following months, her TSH levels normalized, and her dose of levothyroxine was gradually tapered. At the latest follow-up, she weighed 42 kg, was clinically euthyroid, and was stable on 50 mcg/day of levothyroxine with a TSH of 1.3 mIU/L as presented in Fig.1.

DISCUSSION

Refractory hypothyroidism — defined as persistently elevated TSH despite high-dose levothyroxine — should prompt a systematic evaluation for causes beyond nonadherence and improper medication intake.[4] In patients who are compliant and take their medication correctly, as in our case, malabsorption syndromes such as coeliac disease should be considered.

Coeliac disease is an autoimmune enteropathy triggered by gluten ingestion in genetically susceptible individuals. It causes villous atrophy in the small intestine, impairing nutrient and drug absorption — including that of levothyroxine.[5] Once a gluten-free diet (GFD) is instituted, mucosal healing restores normal absorptive function, often dramatically reducing the required dose of levothyroxine. Although Coeliac disease typically presents with gastrointestinal symptoms[6] such as diarrhea, weight loss, and bloating, our patient was entirely asymptomatic, representing a silent form of the disease. This highlights the diagnostic challenge, where coeliac disease may be overlooked in the absence of classical symptoms.

Several published case reports support the link between silent coeliac disease and refractory hypothyroidism. For instance, a 68-year-old woman with persistently elevated TSH despite high-dose LT4 exhibited poor response to an LT4 absorption test. Duodenal biopsy confirmed coeliac disease, and initiation of a GFD led to normalization of thyroid function.[7] A similar case involved a 58-year-old woman with autoimmune hypothyroidism and no gastrointestinal symptoms, who was found to have cryptic coeliac sprue. Her LT4 requirements decreased significantly after starting a GFD.[8]

Additionally, a 6year-old woman with coexisting Addison's disease and newly diagnosed coeliac disease showed poor response to LT4 tablets but achieved euthyroidism after switching to an oral solution formulation and commencing a GFD.[9] In more severe presentations, such as a case of myxedema secondary to undiagnosed coeliac-related malabsorption, prompt diagnosis and dietary treatment proved life-saving.[10]

Population-level data also reinforce this association. In a prospective cohort study of hypothyroid patients requiring ≥125 µg/day of LT4, 5.6% were found to have unrecognized coeliac disease. Following GFD initiation, their average LT4 dose dropped from 154 µg/day to 111 µg/day, confirming improved absorption after mucosal recovery.[11]

Our case aligns with these findings: a patient with no GI symptoms, requiring high-dose LT4 despite

proper adherence, was found to have coeliac disease. After initiating a GFD, her levothyroxine requirement decreased markedly, consistent with resolution of the underlying malabsorption.

CONCLUSION

In cases of refractory hypothyroidism with unusually high levothyroxine requirements, clinicians should consider underlying coeliac disease even when classical gastrointestinal symptoms are absent. Early recognition and treatment with a gluten-free diet can restore normal thyroid function and prevent unnecessary dose escalation.

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