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An Uncommon Psychiatric-Dominant Presentation of Severe Hypothyroidism in a Young Adult

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ABSTRACT

Severe hypothyroidism can manifest with neuropsychiatric symptoms, but cases dominated by psychiatric features, particularly in young adults, are rare and diagnostically challenging. We present the case of a 29-year-old male medical student with a history of autoimmune comorbidities who developed progressive anxiety, cognitive slowing, and depressive symptoms in the absence of overt somatic signs. Thyroid testing revealed profound hypothyroidism secondary to Hashimoto's thyroiditis. Psychiatric symptoms improved significantly following initiation of levothyroxine, suggesting a causal connection. This case underscores the importance of screening for thyroid dysfunction in patients with new-onset psychiatric symptoms and highlights an atypical presentation of 'myxedema madness' in a young adult male.

Introduction

The History of Hypothyroidism: Knowledge of the effects of thyroid hormones on the human brain had rapidly expanded in medicine. Thyroid hormone dysfunctions, better known as hypothyroidism, had historically been associated with harmful cognitive and psychiatric manifestations [1]. Some of these effects can include cognitive impairment, dementia, delirium, psychosis and hallucinations [1]. Thyroid hormone deficiencies were known to disrupt multiple neurotransmitter systems such as serotonin, norepinephrine, and dopamine, which had been directly implicated in mood regulation [2]. TH deficiency had also been discovered to be implicated in the reduction of cerebral metabolism and perfusion, potentially intensifying pre-existing mood dysregulations in patients that might have otherwise been wholly attributed only to behavior [3]. Environmental iodine deficiency has long been accepted as the most frequent cause of hypothyroidism on a worldwide basis, but in areas where there is no such iodine depletion the most common cause of hypothyroidism is chronic autoimmune thyroiditis [4]. Historically, profound hypothyroidism had been described in the literature as "myxedema madness," a neuropsychiatric syndrome marked by hallucinations, delusions, paranoia, and mood disturbances [5]. Although contemporary reports were rare, a 2021 pooled analysis confirmed that such presentations remained clinically relevant in modern practice [6]. The well-known signs and symptoms of hypothyroidism unfortunately tended to be more subtle than those of hyperthyroidism which was problematic as it could delay diagnosis and treatment that might have restored a patient's quality of life, highlighting the necessity of urgently recognizing and rectifying this condition.

Neurogenesis and Cognitive Effects:

There has been a heavy implication through studies conducted with rat models, adult-onset hypothyroidism was significantly associated with decreased neurogenesis specifically what involved the survival and How to cite this article differentiation of pro genitor cells in the dentate gyrus [7]. These deficits were discovered to be reversible upon restoring normal thyroid hormone levels [7]. The broader implication is that thyroid hormones are powerful regulators of adult neurogenesis in both the hippocampus and subventricular zone [7]. This provides a mechanistic explanation for the "brain fog" and cognitive slowing in hypothyroid patients even in the absence of overt neurological disease. Reduced hippocampal neurogenesis likely contributes to the poor memory encoding and slowed cognitive speed that is typically associated with patients who have hypothyroidism.

Myelination, Remyelination, and Immune Pathways:

It had recently been uncovered that thyroid hormone abnormalities were responsible for permanent and irreversible changes not only to the central nervous system but also to the peripheral nervous system [8]. Thyroid hormones had been understood as significant for the regulation and differentiation of neurons in both the central and peripheral nervous systems [8]. There was evidence of an active form of TH that was essential for the differentiation of astrocytes, oligodendrocytes, and the development of microglial cells, part of the innate immune system [8]. Microglial cells had long been recognized within neurology for their importance as "scavengers" in the central nervous system, where they helped clear dead neurons, potential pathogens, and weak synaptic connections. Although the relationship between the immune system and thyroid hormone was complex and not yet fully understood, it had often been observed that hypothyroidism, unlike hyperthyroidism, appeared to be linked with a tendency toward reduced immune activity. Such changes could have influenced the cognitive and behavioral features seen in hypothyroidism as well.

Thyroid hormone (T_3) has been known to be a critical driver of myelin protein gene expression during developmental myelination when serum TH peaks in infancy and early childhood, but it had to be recognized that even past the initial developmental period, TH maintained a role in oligodendrocyte health and remyelination after injury [9-10]. In demyelinating conditions such as multiple sclerosis, TH and its receptors

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reactivated pathways encouraged oligodendrocyte precursor cells (OPCs) to differentiate into myelinating cells [10]. It was important to note that the realm of TH-remyelination pathways was a relatively new and underexplored area within medicine due to the well-known adverse effects of overexposure to TH. However, TH receptor-β agonists were in clinical and preclinical trials, raising the possibility that demyelinating diseases in the future might not be as devastating to patients as they had historically been [10]. Ultimately, without crucial adequate TH signaling, remyelination was impaired, and this consequently could have led to cognitive slowing, depression, and memory issues that were traditionally characteristic of hypothyroidism.

Case Significance and Broader Implications:

While hypothyroidism was known to be common, this case provided an excellent teaching opportunity because severe neuropsychiatric manifestations as the primary presenting feature remained rare, and even more so in young adults. This case also underscored the importance of considering thyroid dysfunction in the differential diagnosis of acute psychiatric symptoms, even in younger populations where it might not have been suspected. It additionally contributed to the broader collection of scientific information about hypothyroidism, as knowledge about adult-onset hypothyroidism had been surprisingly limited compared to developmental hypothyroidism [11]. Knowledge about adult-onset hypothyroidism had been limited because public health systems prioritized preventing irreversible intellectual disability due to congenital hypothyroidism. Hence, there had been more funding and research infrastructure in that area [11]. Adult hypothyroidism, while common, was viewed as treatable and straightforward with levothyroxine replacement, so it attracted less grant funding and fewer longitudinal studies [11]. Finally, the experiences of our patient illustrated that recognition was crucial, as timely thyroid hormone replacement could dramatically reverse psychiatric symptoms and prevent unnecessary suffering.

Case Presentation

We report the case of a 29-year-old male third-year medical student with a history of alopecia universalis, eczema, asthma, multiple severe allergic reactions, a family history of autoimmune disease (including possible vitiligo in his father), hypothyroidism and arthritis of unclear etiology, type 2 diabetes mellitus, and generalized anxiety disorder. He developed severe hypothyroidism secondary to Hashimoto's thyroiditis. The patient's documented atopic disease and alopecia universalis coupled with familial autoimmune clustering, suggests underlying immune dysregulation. The most common form of thyroid failure has an autoimmune etiology. There is also an increased frequency of other autoimmune disorders in this 2 of 10population such as type 1 diabetes, pernicious anemia and primary adrenal failure (Addison's disease), myasthenia gravis, celiac disease and rheumatoid arthritis [2]. Emerging literature suggests similar immune dysfunction as a potential contributor to neuropsychiatric vulnerability in endocrine disorders [6]. Symptoms began in August 2024 with mild anxiety that progressively worsened over several months.

During his surgical rotation (November-December 2024), his anxiety was acutely exacerbated and complicated by emergent depressive features. Cognitive slowing and "brain fog" became noticeable during this period, described by the patient as "running into a brick wall" in his mind. By January-February 2025, psychiatric symptoms reached peak severity, with attending physicians observing that he appeared "on the verge of panic" and as though he "might have a heart attack." Physical complaints were limited to cold intolerance and fatigue, and no myxedema stigmata were evident on examination. On February 22, 2025, psychiatric evaluation led to initiation of venlafaxine (Effexor) at 75 mg PO QD (once by mouth daily).

No formal DSM-5 diagnosis was documented at the time, though clinical presentation was suggestive of mixed anxiety and depressive features. Thyroid screening performed as part of routine psychiatric prescreening revealed a TSH level of 79.08 μIU/mL (reference range: 0.4-4.0 mIU/L, Table 1), indicating possible severe hypothyroidism. Repeat testing on March 14, 2025, confirmed persistent hypothyroidism, with a TSH of 92.8 μIU/mL and free T4 of 0.45 ng/dL (reference range: 0.8-1.8 ng/dL, Table 1), consistent with overt hypothyroidism. Full replacement levothyroxine therapy (175 mcg PO QD) was initiated immediately. Although the rationale was not explicitly documented, the choice of full replacement dose was likely based on the patient's young age, absence of cardiac disease, and the profound TSH elevation. Anti-thyroid peroxidase antibodies measured on April 19, 2025, were markedly elevated at 4200 IU/mL (reference range: <35 IU/mL), confirming Hashimoto's thyroiditis (Table 1). Prior to the initial appointment on February 22, 2025, a comprehensive laboratory work-up was conducted. The results were released on March 13, 2025, and became available through the patient portal associated with the patient's primary care visit. The initial evaluation included a complete blood count, comprehensive metabolic panel, lipid profile, glycohemoglobin A1c with estimated average glucose, vitamin and micronutrient levels (vitamin D, folate, vitamin B12), and thyroid and inflammatory studies (TSH, free T4, thyroid peroxidase antibody, and high-sensitivity C-reactive protein). These findings are presented in Tables 1-6. Cognitive symptoms improved within approximately six weeks of starting levothyroxine, consistent with the expected pharmacologic onset of thyroid hormone replacement [5].

Fatigue and cold intolerance rapidly abated. Mood symptoms stabilized during this period but later required venlafaxine titration to 150 mg daily PO QD on July 10, 2025, three days before his Step 2 exam for near-complete resolution. Gradual titration was necessary due to ongoing environmental stressors. Follow-up TSH on April 19, 2025, showed suppression (0.03 μIU/mL), prompting dose adjustment (Table 1). By July 2025, the patient had returned to meeting all academic responsibilities without residual cognitive impairment, though mild mood symptoms persisted. A figure has been provided below for visual interpretation of the patient's clinical course, depicting serial TSH and free T4 trends with levothyroxine and venlafaxine milestones (Figure 1).

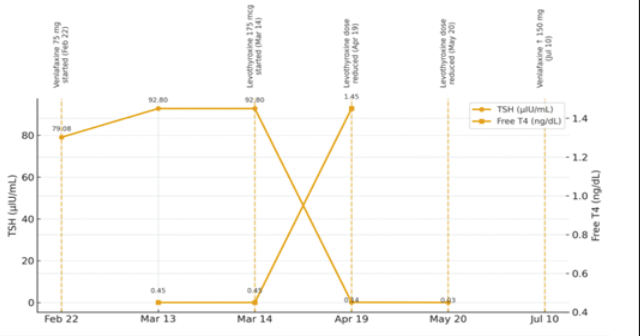

Figure 1: Serial TSH and Free T4 Trends with Levothyroxine and Venlafaxine Milestones.

Discussion

Despite profound biochemical hypothyroidism, the absence of classic signs such as myxedema underscores the importance of considering thyroid dysfunction even in subtle or atypical cases. In this patient, escalating anxiety symptoms prompted initiation of venlafaxine, though no formal DSM-5 diagnosis of generalized anxiety or major depressive disorder was documented. However, the severity of functional impairment warranted intervention. Routine pre-treatment thyroid screening revealed a markedly elevated TSH, prompting further investigation. Although frank psychosis was absent, the degree of anxiety and cognitive slowing suggests that earlier recognition and treatment may have prevented further deterioration.

A full replacement dose of levothyroxine 175 mcg PO QD (by mouth once daily) was initiated immediately upon diagnosis. In similar published cases of myxedema-related psychiatric symptoms, a median starting dose of 100 mcg PO QD is often used, particularly in older patients or those with cardiovascular risk [5]. However, this more aggressive replacement strategy proved both safe and highly effective, with rapid resolution of cognitive symptoms and marked functional recovery. Notably, while venlafaxine had started four weeks earlier, the patient did not report meaningful improvement until levothyroxine began. The sudden resolution of "mental fog" around six weeks into thyroid hormone therapy strongly suggests a hormonally mediated recovery. Later titration of venlafaxine to 150 mg PO QD in July, coinciding with academic stress from the Step 2 exam was completed to address residual mood symptoms.

The patient's atopic history and alopecia universalis raise the possibility of a shared autoimmune vulnerability contributing to neuropsychiatric manifestations [4]. Furthermore, the timeline of clinical improvement parallels the known pharmacokinetics of levothyroxine [1,2].

Limitations of this case include the absence of ancillary studies such as EEG or CSF analysis, which precludes definitive exclusion of Hashimoto's encephalopathy. These investigations were not pursued, likely due to the lack of seizures, encephalopathy, or focal neurologic signs.

Additional labs including vitamin B12 and folate were within normal limits. Cortisol testing was considered to evaluate for possible adrenal insufficiency but was not obtained due to logistical constraints. No objective neurocognitive assessments or academic scores were available to quantify cognitive recovery; however, the patient's reported return of mental clarity and observed academic functioning suggest meaningful improvement. A delayed follow-up thyroid panel, drawn approximately five weeks later than planned, reflects the real-world challenge of managing complex health needs amid academic demands.

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Table 1: Thyroid Function & Antibodies.

Test	Result	Reference Range	Notes / Interpretation	Colection Date
TSH	**79.08 uIU/mL (High)**	**0.34–4.82 uIU/mL**	**Severe hypothyroidism**	**Mar 13, 2025**
Free T4	**0.45 ng/dL (Low)**	0.59–1.61 ng/dL	Confirms hypothyroidism	Mar 14, 2025
TSH (Reflex)	**92.80 uIU/mL (High)**	0.34–4.82 uIU/mL	Repeat, very high	Mar 14, 2025
Free T4	**1.45 ng/dL**	0.59–1.61 ng/dL	Improved, normal after treatment	Apr 19, 2025
TSH (Reflex)	**0.14 uIU/mL (Low)**	0.34–4.82 uIU/mL	Suppressed; levothyroxine reduced to 150 mcg	Apr 19, 2025
Thyroid Peroxidase Antibody	**4,200 IU/mL (High)**	<60 IU/mL	Hashimoto's thyroiditis	Apr 19, 2025
TSH	**0.03 uIU/mL (Low)**	0.34–4.82 uIU/mL	Still suppressed → levothyroxine reduced to **125 mcg**	May 20, 2025

TSH:
High → Hypothyroidism (primary if Free T4 low)
Low → Overtreatment or hyperthyroidism

Free T4:
Low Hypothyroidism
High → Hyperthyroidism or over-replacement

TPO Antibody:
Positive (elevated) → Hashimoto's thyroiditis

Table 2: Lipid Panel.

Test	Result	Reference Range	Notes	Date
Total Cholesterol	**207 mg/dL (Borderline High)**	**<200 mg/dL**	**Borderline high**	**Mar 13, 2025**
Triglycerides	50 mg/dL	<150 mg/dL	Normal	Mar 13, 2025
HDL Cholesterol	**65 mg/dL (High)**	>40 mg/dL	Protective	Mar 13, 2025
LDL (calculated)	**132 mg/dL (Borderline High)**	<130 mg/dL	Borderline high	Mar 13, 2025
Cholesterol:HDL Ratio	3.2	<5.0	Favorable	Mar 13, 2025
VLDL (calculated)	10 mg/dL	5–40 mg/dL	Normal	Mar 13, 2025

Total Cholesterol:
<200 mg/dL = desirable
200-239 mg/dL = borderline
≥240 mg/dL = high

LDL (bad cholesterol):
<100 mg/dL = optimal
100-129 mg/dL = near optimal
130-159 mg/dL = borderline high
≥160 mg/dL = high

HDL (good cholesterol):
<40 mg/dL = low
260 mg/dL = protective

Triglycerides:
<150 mg/dL = normal
150-199 mg/dL = borderline high
≥200 mg/dL = high

Table 3: Diabetes/Glucose Testing.

Test	Result	Reference Range	Notes	Date
Hemoglobin A1c	**5.5%**	**3.5–5.6%**	**Upper normal; not prediabetic**	**Mar 13, 2025**
Estimated Avg. Glucose	**111 mg/dL**	~97–126 mg/dL	Matches HbA1c, normal	Mar 13, 2025
Glucose (CMP)	95 mg/dL	70–99 mg/dL	Normal fasting	Mar 13, 2025

Hemoglobin A1c:
<5.7% = normal
5.7-6.4% = prediabetes
26.5% diabetes
Estimated Average Glucose (eAG): corresponds to HbA1c value.

Fasting Glucose:
<100 mg/dL = normal
100-125 mg/dL = impaired fasting glucose
≥126 mg/dL = diabetes (if confirmed on repeat testing)

Table 4: Inflammatory Marker Testing (C-reactive Protein).

Test	Result	Reference Range	Notes	Date
hs-CRP	2.2 mg/L	<1 = low, 1–3 = average, >3 = high	Average cardiovascular risk	Mar 13, 2025

- <1.0 = low risk
- 1.0-3.0 = average risk
- 3.0 = high risk
- 10 = suggests non-cardiovascular inflammation (infection, systemic inflammation)

Table 5: Comprehensive Metabolic Panel.

Test	Result	Reference Range	Notes	Date
Sodium	139 mmol/L	136–145	Normal	Mar 13, 2025
Potassium	4.6 mmol/L	3.5–5.1	Normal	Mar 13, 2025
Chloride	104 mmol/L	98–110	Normal	Mar 13, 2025
CO_2 (Bicarb)	29 mmol/L	21–32	Normal	Mar 13, 2025
BUN	16 mg/dL	6–25	Normal	Mar 13, 2025
Creatinine	0.77 mg/dL	0.50–1.30	Normal	Mar 13, 2025
eGFR	124 mL/min/1.73m²	>60	Normal renal function	Mar 13, 2025
Calcium	8.8 mg/dL	8.2–10.2	Normal	Mar 13, 2025
Total Protein	7.7 g/dL	6.4–8.2	Normal	Mar 13, 2025
Albumin	4.2 g/dL	3.2–4.7	Normal	Mar 13, 2025
Total Bilirubin	0.4 mg/dL	<1.1	Normal	Mar 13, 2025
Alkaline Phosphatase	122 U/L	26–137	Normal	Mar 13, 2025
AST	20 U/L	0–37	Normal	Mar 13, 2025
ALT	15 U/L	0–60	Normal	Mar 13, 2025

Electrolytes (Na, K, CI, CO2): Out-of-range values may suggest dehydration, renal disease, or acid-base imbalance.
BUN, Creatinine, eGFR: Assess kidney function. eGFR <60 indicates chronic kidney disease.
Calcium: Monitored for bone metabolism, parathyroid disease, renal function.
Liver Enzymes (AST, ALT, Alkaline Phosphatase, Bilirubin, Protein, Albumin): Abnormal values may indicate liver cell injury, biliary obstruction, or impaired liver synthetic function.

Table 6: Complete Blood Cell Count.

Test	Result	Reference Range	Notes	Date
WBC	6.5 K/µL	4.0–11.0	Normal	Mar 13, 2025
RBC	5.24 M/µL	4.40–6.00	Normal	Mar 13, 2025
Hemoglobin	14.8 g/dL	13.5–18.0	Normal	Mar 13, 2025
Hematocrit	44.2%	40–52%	Normal	Mar 13, 2025
MCV	84 fL	80–100	Normal	Mar 13, 2025
MCH	28.2 pg	27–33	Normal	Mar 13, 2025
MCHC	33.5 g/dL	31–36	Normal	Mar 13, 2025
RDW	13.2%	<16.4%	Normal	Mar 13, 2025
Platelets	256 K/µL	150–400	Normal	Mar 13, 2025

WBC: High = infection/inflammation; Low = immunosuppression or bone marrow problem
RBC, Hemoglobin, Hematocrit: Low = anemia; High = polycythemia or dehydration
MCV: Low = microcytic anemia (iron deficiency, thalassemia); High = macrocytic anemia (B12 or folate deficiency)
MCH, MCHC: Indicators of hemoglobin content per red cell
RDW: Increased values suggest mixed anemia types
Platelets: Low = bleeding risk; High = clotting/inflammatory risk

Conclusions

Clinicians should maintain a high index of suspicion for hypothyroidism in patients with new-onset psychiatric symptoms, even in the absence of overt somatic findings. Prompt recognition and treatment are critical to prevent unnecessary morbidity and facilitate functional recovery. This case underscores how attributing neuropsychiatric symptoms to situational stress in young adults can obscure underlying endocrine pathology.

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