A Case and Differential Diagnosis of Catatonia in a Patient With Hypothyroidism Due to Levothyroxine Nonadherence

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The association of mood disorders, including bipolar disorder, and thyroid dysfunction is well established. Conversely, while a spectrum of psychiatric symptoms has been noted in autoimmune thyroiditis,[1] including the uncommon but well-known myxedema madness/hypothyroidism-related psychosis,[2] there is a dearth in the literature of catatonia associated with thyroid conditions[3–5] and more specifically, hypothyroidism (Table 1).[3,6–10] As such, we present a case of catatonia in the context of a patient with nonadherence to thyroxine who developed severe hypothyroidism.

Case Report

A 72-year-old woman with a medical history of hypercholesterolemia and hypothyroidism, prescribed atorvastatin and levothyroxine 100 µg/day, respectively, was brought to the emergency department by family due to failure to thrive and impaired mentation. Her family reported that, over the last 3 months, the patient had developed dysphagia, leading to poor oral intake and ~10-lb weight loss, resulting in nonadherence to levothyroxine. The patient was admitted to the hospital for mild acute kidney injury/metabolic acidosis. After the latter was treated and the patient was started on levothyroxine 50 µg/day, we were consulted due to continued "altered mental status." For a summary of the patient's evaluation, assessment, and treatment, see Table 2.[11–18]

In brief, during the aforementioned 3-month period, the patient developed symptoms of catatonia and scored 36 on the Bush-Francis Catatonia Rating Scale (BFCRS).[13] While the patient was unable to give a cogent history, she had no reported psychiatric or substance use history, with both blood alcohol and urine drug screen being negative. Lorazepam was given with immediate effect and more sustained effect within 3–5 days. There was no recurrence of catatonia on a tapering dose of lorazepam over the next 8 weeks.

Discussion

Our patient's presentation warranted an exploration of several diagnoses, including steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), myxedema coma, and catatonia due

Table 1.
Review of Cases of Catatonia Due to Hypothyroidism

Author (year)	Age and sex	Catatonic symptoms/BFCRS (if recorded)	Comorbid psychiatric history	Treatment
Woody et al[9]	33-year-old woman	Diminished speech, psychomotor retardation, lack of response to external stimuli/score = 22	Bipolar disorder	Levothyroxine 50 µg/d; lorazepam parenterally changed to oral clonazepam; olanzapine
Konda et al[10]	40-year-old woman	Mutism, posturing, negativism/score = 17	"Schizophrenia-like psychotic disorder"	Levothyroxine 100 µg/d; lorazepam; risperidone
Asnis[7]	54-year-old single woman	Immobility/stupor, mutism, staring, posturing/catalepsy, grimacing, verbigeration, rigidity, negativism, waxy flexibility, withdrawal, ambitendency/score = 18	"Misdiagnosis of schizophrenia…due to catatonia"	Levothyroxine 100 µg/d intravenously, followed by levothyroxine 88 µg/d orally; lorazepam
Shlykov et al[3]	65-year-old woman	Stupor, mutism, latency, psychomotor retardation	None listed	Levothyroxine 50 µg/d (increased to 100 µg); olanzapine
Iskandar et al[6]	22-year-old woman	Mute, with "rolled-back eyes," posturing but responsive to painful stimuli	None listed	Lorazepam; levothyroxine 100 µg once/d; bitemporal electroconvulsive therapy for 4 sessions
Nishihara et al[8]	29-year-old woman	"Catatonic excitement" (only description provided)	Schizophrenia; delusional misidentification syndrome/Capgras syndrome	Levothyroxine 25 µg/d—> increased to 75 µg/d for 2 wk; "Sequentially…risperidone, olanzapine, haloperidol, sodium valproate but catatonic symptoms remained unimproved"

Abbreviation: BFCRS = Bush-Francis Catatonia Rating Scale.

Table 2.

Summary of the Patient's Differential and Working Diagnosis[11–18]

	SREAT[11]	Myxedema coma[12]	Our patient: catatonia due to hypothyroidism
Signs and symptoms	Encephalopathy manifest by cognitive impairment and 1 or more neuropsychiatric features		Catatonia/BFCRS score[13] = 36[a]
		DSSMC[14] = 45	
		Thermoregulatory dysfunction	96.1°F
		Central nervous system effects	Obtunded
		Gastrointestinal findings	Constipation
		Precipitating event	Nonadherence to levothyroxine
		Cardiovascular dysfunction	Bradycardia, pulse = 56 bpm; blood pressure = 147/107 mm Hg; respirations: within normal limits
		Other electrocardiogram changes	None
		Pericardial/pleural effusion	Not present
		Metabolic disturbances	Decrease in GFR
Thyroid autoimmunity	Present	Overwhelming majority[15]	Present
Thyroid function tests	Euthyroid status (serum sensitive TSH, 0.3–5.0 mIU/L) or mild hypothyroidism (serum sensitive TSH, 5.1–20.0 mIU/L) that would not account for encephalopathy	TSH elevation is near universal, although may not be an accurate indicator of the severity of the hypothyroidism based on the wide range of serum TSH values reported[16]	TSH level of >90 mcU/mL T3-free and T4-free were low at 1.2 pg/mL and 0.6 ng/dL, respectively
Paraclinical evaluation	No evidence in blood, urine, or CSF analyses of an infectious, toxic, metabolic, or neoplastic process	Common findings include hyponatremia, hypoglycemia, hypoxemia, hypercarbia, decrease in GFR	UDS and BAL were negative; CBC, CMP, infectious serologies, and vitamin B_1, B_9, and B_{12} were unremarkable, except for blood urea nitrogen = 29/1.6 mg/dL; mild metabolic acidosis (pH = 7.395, pCO_2 = 31.7 mm Hg, bicarbonate = 20 mmol/L, normal pO_2 and O_2 saturation)
Presence of paraneoplastic antibodies	No serologic evidence of neuronal voltage-gated calcium channel, voltage-gated potassium channel, or other currently recognized paraneoplastic autoantibodies to indicate another diagnosis	None required, except antithyroid autoimmunity	No serologic evidence of NMDA receptor, neuronal voltage-gated calcium channel, voltage-gated potassium channel complex, or other paraneoplastic autoantibodies
Neuroimaging	No findings on neuroimaging studies indicating vascular, neoplastic, or other structural lesions to explain the encephalopathy	No findings on neuroimaging studies indicating vascular, neoplastic, or other structural lesions to explain these findings	No acute pathology; mild sequelae of chronic small vessel ischemic disease
Electroencephalogram	Unless seizure occurs, ~50% demonstrate nonspecific generalized slowing[17]	While generalized slowing may occur, findings are relevant to rule out other etiologies for coma	No evidence of ictal activity or generalized slowing
Response to treatment	Complete or near-complete return to the patient's neurological baseline status following corticosteroid treatment	Thyroid hormone supplementation is cornerstone (controversy is whether to use T4 alone, T3 alone, or some combination of the 2 hormones)[18]	HD1: levothyroxine 50 µg initiated
		If required, intensive care treatment with ventilator support; appropriate fluid management	Neither ventilator support nor intensive care treatment was required
		Correction of hypotension and dyselectrolytemia	Patient did not require treatment for hypertension; GFR returned to normal limits with administration of fluids
		Aggressive management of precipitating factors; steroid supplementation if required	Patient was restarted on levothyroxine
		Therapeutic endpoints: improved mental status, improved cardiac function, and improved pulmonary function	HD2: administered lorazepam 1 m IV, which decreased BFCRS score to 29; over the next 3 days, lorazepam titrated to 1 mg IV, 4 times/d, with BFCRS score=11; HD6: on day 5 of lorazepam treatment, BFCRS score was 0; HD9: discharged to SNF, with 8-week taper

(continued)

Table 2 (continued).

	SREAT[11]	Myxedema coma[12]	Our patient: catatonia due to hypothyroidism
Physical/psychiatric examination	Tremor, myoclonus, transient aphasia, sleep abnormalities, seizures, gait difficulties	Features of severe hypothyroidism: dry skin, sparse hair, hoarse voice, delayed tendon reflexes, macroglossia, nonpitting edema, goiter	Unremarkable, except for dry skin, sparse hair

[a]BFCRS score = 36: immobility/stupor, mutism, staring, withdrawal, catalepsy, echolalia, stereotypy, rigidity, verbigeration, negativism, gegenhalten, grasp reflex, and perseveration.

Abbreviations: BAL = blood alcohol level, BFCRS = Bush-Francis Catatonia Rating Scale, CBC = complete blood count, CMP = complete metabolic panel, CSF = cerebrospinal fluid, DSSMC = Diagnostic Scoring System for Myxedema Coma, GFR = glomerular filtration rate, HD = hospital day, IV = intravenously, NMDA = *N*-methyl-D-aspartate, pCO_2 = partial pressure of carbon dioxide, pO_2 = partial pressure of oxygen, SNF = skilled nursing facility, SREAT = steroid-responsive encephalopathy associated with autoimmune thyroiditis, TSH = thyroid-stimulating hormone, T3 = triiodothyronine, T4 = thyroxine, UDS = urine drug screen.

to hypothyroidism. See Table 2 for a review of our working and differential diagnosis for the patient.

On a recently developed scale evaluating myxedema coma,[14] our patient scored 45. On this scale, a diagnostic score ≥60 is consistent with myxedema coma, whereas a score between 45 and 59 is consistent with only overt hypothyroidism but at increased risk for myxedema coma if not treated. As per Table 2, our patient did have symptoms of myxedema coma, although when combined with her psychomotor abnormalities on the BFCRS and her relatively rapid and complete response to lorazepam, myxedema coma seemed much less likely at the time of our evaluation. As a caveat, patients may not initially present with frank coma but with milder signs of depressed mental status, only to gradually decline to a coma subsequently.[18] Lastly, while thyroid autoimmunity and neuropsychiatric symptoms are present in both patients with SREAT and our patient, the latter presented with a significant elevation of thyroid-stimulating hormone (TSH), low triiodothyronine (T3)/thyroxine (T4) levels, no seizures, and again, a relatively prompt and thorough response to lorazepam—all not consistent with SREAT. Alternatively, about 95%–98% of patients with SREAT demonstrate an improvement/complete resolution of symptoms after immunosuppressive therapy.[19]

Due to the limited evidence base, few conclusions can be garnered from our patient, although TSH levels (due to hypothyroidism) associated with catatonia have been reported to range from as little as 10.78 μIU/mL[10] to >100 μIU/mL,[3] with our patient's TSH level >90 μIU/mL. Nonetheless, it appears that the extent of thyroid dysfunction does not necessarily correlate with the degree of accompanying psychiatric manifestations.[20] Additionally, previously reported patients' catatonia responded to both lorazepam (as in our patient) and electroconvulsive therapy.[3–10]

Notably, we felt in our patient that lorazepam therapy was primarily responsible for the improvement/resolution in catatonia. That is, in hypothyroidism-induced psychiatric symptoms, including in our patient, while thyroid replacement remains the gold standard in treatment, even with proper replacement, symptoms may take several months to abate.[2]

Alternatively, while not evaluated systematically, there have been reports of using loading dose levothyroxine combined with antipsychotic medication to more rapidly treat myxedema psychosis. Traditionally, loading doses were mainly reserved in the setting of myxedema coma, as the former requires a need for a rapid response within days. Similar benefits have also been described of using loading dose levothyroxine for more rapid attentuation of manic and/or psychotic symptoms. In 1 report,[21] a 44-year-old woman was prescribed loading dose levothyroxine 300 μg daily for 1 week and 100 μg daily thereafter combined with adjunctive olanzapine. This resulted in rapid improvement of psychotic symptoms within 4 days. The described rationale was to establish a therapeutic levothyroxine level over a few days prior to continuing with maintenance dosing. Notably, olanzapine was utilized for a total of 4 weeks, from admission until after discharge. Limitations to this method include, to the best of our knowledge, that it has not been used in catatonia associated with hypothyroidism. Furthermore, this method should likely not be considered in the elderly or those with ischemic heart disease, as the increased myocardial oxygen demand that levothyroxine stimulates may trigger myocardial infarction, arrhythmias, or heart failure. Toward this end, in the case study,[21] there was no evidence of cardiac dysfunction on electrocardiogram and chest x-ray prior to or 4 days after initiating loading dose levothyroxine.

Finally, biochemical changes associated with catatonia mainly focus on γ-aminobutyric acid (GABA)ergic, glutamatergic, and dopaminergic transmission.[22] While beyond the scope of this report of the pathophysiology of how hypothyroidism can lead to catatonia, thyroid hormone has been shown to be a key factor for the induction and function of dopaminergic neurons. Thyroid hormone deficiency has been reported to lead to a decrease in the number and function of mesencephalic dopaminergic neurons,[23] a known potential precipitant for catatonia.

Intriguingly, a study[24] demonstrated reduced GABA concentrations among hypothyroid patients and an increase in GABA concentrations after 6-month treatment with levothyroxine. In conclusion, we endorse that future research should be undertaken to further elucidate the potential relationship between hypothyroidism and catatonia.

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