

Alcohol Withdrawal in Severe Hypothyroidism

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Clinical presentations of common disorders can be significantly influenced by the presence of a second active disease process. Occasionally, two disorders interact in a manner that alters expected presentations and makes detection of either difficult. Most clinicians in general medical inpatient settings readily recognize the signs and symptoms of clinical hypothyroidism as well as the syndrome of alcohol withdrawal delirium. The purpose of this report is to present and discuss an instructive case in which the autonomic signs and symptoms of alcohol withdrawal delirium were obscured and delayed in a woman with undetected severe hypothyroidism.

Case Report

Ms. A, a 57-year-old woman, presented to the Dallas Veterans Affairs Medical Center emergency department with wrist pain from a fall 1 week earlier. She had tripped over a couch in her living room. Radiographic examination identified a right distal radius fracture and a comminuted right intra-articular calcaneus fracture. Ms. A, who was not previously known to the medical center, was admitted to an orthopedic surgery ward, and preparations were made for an open reduction procedure. She was apparently in good health and was taking no regular medications except 0.15 mg/day of levothyroxine for a history of hypothyroidism. She initially reported good medication adherence. She denied any psychiatric or addiction history.

Ms. A's initial physical examination was unremarkable. At admission her heart rate was 66 bpm, her blood pressure was 139/83 mm Hg, and her temperature was 97.1°F. Her admission chemistry profile was normal except for a mildly elevated aspartate aminotransferase level (32 U/L, reference range 0–30 U/liter). A CBC was normal except for an elevated mean corpuscular volume (106.5 fl, reference range = 80–98 fl). No thyroid tests were ordered at admission.

The next morning, her fracture was reduced without

complications. Anesthesia was performed with methohexital sodium induction, nitrous oxide, and atracurium besylate. No benzodiazepines or long-acting barbiturates were given. The next 3 days, during which Ms. A underwent physical therapy, were uneventful. Throughout this time her pulse rate ranged from 68 to 75 bpm. During the fifth hospital night she told nurses that something was crawling across the ceiling and that she had dreamed a gunman was under her bed. No further symptoms appeared until the next evening. During the sixth hospital night, she experienced vivid visual hallucinations of “little people” spray-painting her room in many colors and of water rising from the floor. The nurses reported that Ms. A was anxious and mildly confused, but she showed no classic signs or symptoms of alcohol withdrawal. Her vital signs throughout the night were normal. Her pulse rate never exceeded 92 bpm, and her maximum blood pressure was 144/86 mm Hg. Her temperature was 100.1°F. An on-call resident ruled out alcohol withdrawal on the basis of the absence of elevated pulse or blood pressure and the absence of tremors or diaphoresis.

The following morning, Ms. A's surgeons requested psychiatric consultation to evaluate her for “schizophrenia.” At approximately 9:00 a.m., she was alert and oriented except for missing the date by 4 days. She reported no delusions or psychosis, but she said that the hallucinations the night before had been intense enough for her to feel that the things she saw had really happened.

In an additional review of her medical history, Ms. A confirmed that she had no history of psychiatric disturbance. She reported a history of hyperthyroidism followed by a hypothyroid state. She then admitted that she had not

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Case Reports

taken thyroid replacement therapy (levothyroxine) for a year. Although no records were available, the consultant felt that the history was consistent with primary idiopathic hypothyroidism (probably end-stage Hashimoto's thyroiditis). A laboratory test that had been belatedly requested that morning confirmed that Ms. A had profound hypothyroidism. The test showed that the level of thyroid-stimulating hormone was 107.4 μ IU/ml (reference range = 0.49–4.7), and the level of free thyroxine was 0.27 ng/dl (reference range = 0.71–1.85). The presumptive diagnosis now became delirium resulting from hypothyroidism. The consultant's recommendations were to obtain medical consultation for thyroid hormone replacement and to treat Ms. A's confusion or hallucinations with 1 to 2 mg of oral haloperidol every 6 hours as needed. A dose of 100 μ g/day of oral levothyroxine was initiated the next morning.

That night Ms. A's symptoms dramatically worsened. In addition to reporting vivid visual hallucinations, she was more confused and agitated. At one point she ran down the hall screaming that she was being chased. She received oral haloperidol every 2 hours, but the medication had minimal effect. Nursing staff initiated one-to-one observation and hourly measurement of vital signs. Ms. A's pulse was 92 bpm and increased to a maximum of 100 bpm (after running), her blood pressure was 144/86 mm Hg, and her temperature 100.1°F. She had no tremors or diaphoresis.

The next day, Ms. A's clinicians made another urgent request for a psychiatric consultation. Confronted with information obtained with permission from her family, Ms. A acknowledged consuming more than a fifth of whiskey daily (an average of approximately 250 cc/day). She had her last drink the day before her admission. The fall that caused the fracture occurred while she was inebriated. She denied any history of delirium tremens or serious withdrawal symptoms with past cessation of similar alcohol consumption. At this point, the consultant suspected that she was experiencing masked alcohol withdrawal delirium. Treatment with 25 mg of oral chlordiazepoxide every 6 hours was started, with additional doses as needed for severe hallucinations or agitation. Ms. A also received 100 mg/day of oral thiamine and 2 mg/day of oral folic acid.

Ms. A's condition improved dramatically. She slept well that night and experienced no hallucinations or agitation. No further episodes occurred. Her maximum heart rate recorded in the next 3 days was 84 bpm. Haloperidol was discontinued. The chlordiazepoxide was gradually tapered over a 1-week period. After this unexpectedly pro-

longed hospital stay, Ms. A was discharged to an alcohol treatment program.

Discussion

The lifetime prevalence of hypothyroidism is 2% in females and 0.1%–0.2% in males.¹ In persons between the ages of 45 and 64 years, alcohol use disorders have a 1-year prevalence of approximately 8% in men and 1% in women.² Although these disorders are both relatively common in general hospital practice, a MEDLINE search (for the years 1990–2002) using the keywords “hypothyroidism,” “alcohol withdrawal,” and “delirium” found no reported cases of a similar suspected interaction between the conditions. One report described hepatic encephalopathy in a 74-year-old nonalcoholic woman with hepatitis C who also had unsuspected hypothyroidism.³ In that case, the patient's mental status aberrations responded to treatment only after adequate thyroid replacement therapy was established.³

Hypothyroidism typically presents with fatigue, weakness, cold intolerance, dry skin, hoarseness, bradycardia, delayed deep tendon reflex response, constipation, menstrual disturbance in women, and weight gain.⁴ An opposite picture characterizes alcohol withdrawal delirium, with symptoms of agitation, tachycardia, tremor, diaphoresis, hyperreactive deep tendon reflexes, confusion, and visual or tactile hallucinations.⁵ In the case reported here, severe hypothyroidism appeared to blunt the autonomic symptoms of tachycardia, hypertension, diaphoresis, and tremor. Clinicians rely on these signs to recognize alcohol withdrawal. Tachycardia is one of five risk factors significantly correlated with the development of alcohol withdrawal delirium.⁶ The Revised Clinical Institute Withdrawal Assessment for Alcohol Scale⁷ also emphasizes autonomic symptoms in the objective measurement of alcohol withdrawal.

Concomitant somatic illness, such as hypothyroidism, may pose a significant risk factor for the development of alcohol withdrawal delirium.⁸ It is noteworthy that Ms. A had not previously experienced alcohol withdrawal delirium after stopping consumption of similar amounts of alcohol, raising the possibility that hypothyroidism lowered the threshold for the development of withdrawal as well as altered the presentation of withdrawal.

Triiodothyronine, acting at nuclear receptor sites, has the major effect of stimulating metabolism (oxygen and glucose consumption) in most tissues in the body. However, the brain (other than the pituitary gland) is an excep-

tion to this rule.⁹ Striking neurobehavioral and cognitive symptoms in thyroid disease do not appear to be caused by changes in brain metabolism. Blunting of alcohol withdrawal symptoms in a hypothyroid state in the absence of changes in brain metabolism suggests a role of the inhibitory CNS neurotransmitter γ -aminobutyric acid (GABA). Alcohol withdrawal seizures, attributed to subsensitivity of the GABA_A receptor channel complex as an adaptive response to prolonged alcohol exposure, and alcohol withdrawal are both treatable by GABAergic agents such as benzodiazepines.¹⁰ A pro-GABAergic effect in hypothyroidism could also account for a delayed onset of withdrawal symptoms. However, no direct evidence exists for a GABAergic effect in hypothyroidism. Up-regulation of *N*-methyl-D-aspartic acid (NMDA) receptors after prolonged alcohol exposure is believed to result in glutamatergically mediated neuronal hyperexcitability in alcohol withdrawal.¹¹ Alterations in NMDA in hypothyroidism provide another area for investigation, but the literature review found no published research specifically addressing this issue.

Although metabolism in the hypothyroid brain is normal, cerebral blood flow is reduced in proportion to diminished cardiac output.¹² Cerebral hypoperfusion is a possible mechanism for CNS dysfunction in hypothyroidism, but it is not known if this mechanism might affect the presentation of alcohol withdrawal. Another potential mechanism for severe hypothyroidism to blunt peripheral adrenergic response in alcohol withdrawal is impairment of end-organ response related to hypometabolism or hy-

perfusion. Hyperthyroid patients have no alterations in lymphocyte β -adrenergic receptor number or responsiveness.^{1,13} Unfortunately, little research has specifically focused on CNS adrenergic responsiveness or neurotransmitter changes in thyroid disease.

Finally, shortcomings in the management of this case should be noted. It is prudent to check thyroid levels on admission for patients with a history of thyroid disturbance, but this test was not done on admission in this case. Also, the patient's elevated aspartate aminotransferase level and elevated mean corpuscular volume, as well as her history of having suffered a fracture while walking across the living room, suggested the possibility of occult alcoholism. More careful screening might have detected the thyroid and alcohol-related disorders earlier in the hospital episode.

In conclusion, this case of severe hypothyroidism associated with greatly attenuated autonomic symptoms and delayed onset of alcohol withdrawal delirium should remind clinicians to reassess the differential diagnosis carefully when atypical presentations or lack of expected treatment response occurs. Given the frequency of presentation of each of the disorders, the expected comorbidity would be high. Further study might focus on CNS effects of hypothyroidism on perfusion, metabolism, and adrenergic functioning, with an investigation of how these effects might interact with GABAergic and glutaminergic mechanisms in alcohol withdrawal.

The author thanks Robert W. Greene, M.D., Ph.D., for assistance in developing the neurophysiologic review and preparing the manuscript.

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