CLINICAL VIGNETTE

Myxedema Coma in a Patient with Mild Thyroid Function Test Derangements

Diana Chang, MD and Rachael Oxman, MD

Division of Endocrinology, Diabetes and Hypertension, Department of Medicine, David Geffen School of Medicine

Case Presentation

A 73-year-old man with history of atrial fibrillation and heart failure presented to the emergency room from his skilled nursing facility with altered mental status. Of note, patient had recently been hospitalized the prior month following a ground level fall leading to a subdural hematoma that was managed non-operatively. His vital signs included BP 74/76, HR 44/min, RR 18 and temperature of 38.8°C. He was on O_2 via nasal cannula, weighed 112 kg, and was poorly responsive only arousable to painful stimuli. He had absent brachioradialis reflexes, and bilateral pretibial edema. He was persistently hypoglycemic with initial blood glucose of 37mg/dL which required multiple amps of intravenous dextrose 50%.

Other labs included: WBC 11.13, hemoglobin 11.1, platelets 163, sodium 137, potassium 4.7, chloride 105, bicarbonate 24, BUN 38, creatinine 1.16, and glucose 37. Initial thyroid labs showed TSH 10.3 (reference range 0.3-4.7 mcIU/mL), Free T4 0.6 (reference range 0.8-1.7 ng/dL), Total T3 60 (reference range 85-185 ng/dL). Random cortisol level was 22 and ACTH 4 (reference range 6-59 pg/ml). Historic labs showed TSH 2.44 from 3 months prior and elevated thyroperoxidase (TPO) antibody of 252 (reference range < 5.5 IU/ml) from 1 year prior.

Further evaluation included negative urinalysis, chest x-ray concerning for interstitial pulmonary edema and CT brain which showed unchanged subdural fluid collection along the left parietal convexity. EKG showed atrial fibrillation with heart rate of 44 bpm. COVID-19 PCR testing was negative.

The patient was admitted to the ICU. He received 2 liters of normal saline and was started on intravenous dopamine for persistent hypotension. He was passively rewarmed with a warm air blanket. He was also started on broad-spectrum antibiotics with vancomycin and ceftriaxone. He remained persistently hypoglycemic and ultimately required continuous intravenous infusion with 20% dextrose at 125 ml/hour to keep blood glucose in normal range. His mental status continued to deteriorate and he was intubated for airway protection. Endocrinology was consulted and patient was started on IV hydrocortisone 100 mg every 8 hours and loaded with IV levothyroxine 200 mcg.

Patient showed improvement within hours of the first levothyroxine dose with reduction in dextrose infusion rates and continued to improve clinically over the next few days. His hypoglycemia resolved and he was weaned off IV dextrose. Blood pressure also improved and dopamine was discontinued. Blood cultures returned positive for MRSA. Repeat thyroid testing showed improvement of free T4 up to 1.2 ng/dl (reference range 0.8-1.7 ng/dl) 1 day after starting levothyroxine, then decreased to 0.7 ng/dl. He was continued on IV levothyroxine 50 mcg daily for three days, then increased to88 mcg daily IV levothyroxine. Parenteral hydrocortisone was reduced to 50mg every 8 hours. He was extubated and transferred out of the ICU and eventually transferred to an outside hospital for further management.

Discussion

Myxedema coma is a rare, life-threatening condition characterized by manifestations of severe hypothyroidism and is associated with mortality rate, up to 50% if not promptly recognized and adequately treated.[1] Myxedema coma is not commonly seen in elderly patients with inadequately treated or untreated hypothyroidism who experience a superimposed precipitating event. Our patient had underlying Hashimoto's thyroiditis with positive thyroid peroxidase antibodies. He was previously biochemically euthyroid without thyroid replacement, but presented with decompensated hypothyroidism in setting of bacteremia.

The diagnosis of myxedema is made clinically based upon history, physical exam and exclusion of other causes of coma. Thyroid function tests are obtained to confirm diagnosis. Key hallmarks include altered mental status, defective thermoregulation, hypotension, hyponatremia, bradycardia, hypoglycemia, and hypoventilation.[2] Our patient exhibited many of these classic manifestations of myxedema coma.

Popoveniuc et al developed a diagnostic scoring system to facilitate early recognition and treatment of myxedema coma with scores above 60 suggesting likely myxedema coma.[3] Our patient had a total score of 125 with hypothermia <32 oC (20 points), heart rate 40-49 (20 points), hypotension (20 points), pulmonary edema (15 points), hypoxemia (10 points), stupor (20 points), hypoglycemia (10 points), and a precipitating event

(10 points). Furthermore, our patient's rapid improvement in response to IV levothyroxine strongly supports this diagnosis.

The classic presentation of myxedema coma is with overt and severe biochemical hypothyroidism. However, our patient had only mild derangements in his thyroid function tests despite severe clinical manifestations. Disease severity and outcomes for myxedema coma are independent of free T4 and TSH levels.[4] At least one prior case of subclinical hypothyroidism leading to myxedema coma has been reported.[5] A minority of patients will present with central hypothyroidism as cause of their myxedema coma in which case TSH levels would be low or low normal.[4] For all these reasons, myxedema coma risk cannot be determined by thyroid function abnormalities alone.

Patients with myxedema coma require intensive care. They frequently need respiratory support including mechanical ventilation, hemodynamic monitoring, careful fluid resuscitation, vasopressors as well as rewarming.[1,4] Initial treatment of myxedema coma is two-fold, consisting of both glucocorticoids and IV levothyroxine. The standard of care is to empirically administer hydrocortisone prior to any thyroid replacement and to continue steroid therapy until normal adrenal function can be confirmed to avoid precipitating adrenal crisis in patients presenting with concomitant adrenal insufficiency.[1,4,6] Thyroid replacement is initiated with a loading dose of levothyroxine 200-400 mcg IV with lower doses favored for the elderly and those with underlying cardiac disease and lower body weights.[6] Subsequent recommended daily dose of levothyroxine replacement is either 1.6 mcg/kg body weight in oral tablets or 75% of the oral levothyroxine dose given parenterally.[6] Liothyronine (T3) replacement may be used judiciously if patient does not show clinical response to initial dose of levothyroxine or as part of initial management with a loading dose of 5-20 mcg and then maintenance dose of 2.5-10 mcg every 8 hours.[6] High serum T3 has been associated with increased mortality in myxedema coma.[7]

Our patient had robust response to initial IV loading levothyroxine dose and hydrocortisone. Parenteral T3 was held due to his cardiac history and quick clinical improvement. His cortisol level was (22 nl > 18) reassuring for no adrenal insufficiency despite his low ACTH though he was noted to have a low ACTH. Pituitary corticotropin secretion may be blunted in severe hypothyroidism.[8] However, given his history of recent subdural intracranial hemorrhage, he was recommended to have pituitary MRI and cosyntropin stimulation test before discontinuing glucocorticoid therapy.

Conclusion

Our patient presented to with a clinical presentation of myxedema coma despite minor thyroid lab derangements. Myxedema coma is rare presentation, however prompt diagnosis and treatment is vital as it carries a guarded prognosis. The diagnosis is clinical and should not be overlooked in patients with mild thyroid testing abnormalities.

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