CLINICAL VIGNETTE

Myxedema Coma Following Radioactive Iodine Ablation for Graves' Disease

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Case Presentation

A 53-year-old male with history of Graves' disease presented to the emergency room with altered mental status. He was treated with two cycles of radioactive iodine (RAI) with hypothyroidism, and was non-compliant with medications and had polysubstance abuse (cocaine and alcohol). On initial interview, the patient was somnolent, only arousable by painful stimuli. Vital signs included temperature of 97.5, pulse of 60, blood pressure of 87/63, respiratory rate of 12, and pulse oximetry of >95% on room air. The physical exam of his head, ears, nose, throat and skin exam was normal. Respiratory, cardiac, and abdominal exams were normal. Patient was unable to participate in a neurological exam due to his altered mental status. Glucose was 73 mg/dL. Two liters of normal saline and naloxone did not improve his blood pressure and did not provide reversal of his symptoms. Per chart review, he was originally on methimazole and metoprolol for Graves' disease. Five years prior to presentation, he was treated with a cycle of RAI with appropriate modification of his medication regimen in accordance with thyroid function tests (TFT). Following his second round of RAI for recurrent hyperthyroidism (Figure 1), he was advised to discontinue methimazole and to start levothyroxine 100 mcg daily based upon post-RAI TFTs indicating a hypothyroid state. However, he both failed to discontinue methimazole and did not take his levothyroxine as prescribed. Subsequent TFTs seven days prior to his presentation at the emergency room demonstrated a thyroid-stimulating hormone (TSH) of 43.5 U/mL, free T4 hormone (FT4) of 0.18 ng/dL, and total T3 hormone (TT3) of 17.34 ng/dL. Blood alcohol level on presentation returned at 383 mg/dL. The patient's chest x-ray showed a left lower lobe opacity. A CT head was negative for acute intracranial abnormalities. Hydrocortisone 100 mg IV and levothyroxine 200 mcg IV were given out of concern for myxedema coma given refractory hypotension and heart rate. Parenteral Ceftriaxone and Azithromycin were started as empirical pneumonia treatment. Repeat TFTs drawn prior to levothyroxine administration demonstrated a TSH of 40.0 U/mL, FT4 of 0.26 ng/dL, and TT3 of 0.38 ng/dL. He received a second dose of levothyroxine 200 mcg IV that evening and was admitted to the medical intensive care unit for further monitoring. He received levothyroxine 50 mcg IV each day with hydrocortisone 100 mg IV every eight hours. He became more alert and responsive over the next 48 hours. The patient decided to leave against medical advice after his rapid improvement, and outpatient follow-up with endocrinology clinic was scheduled.

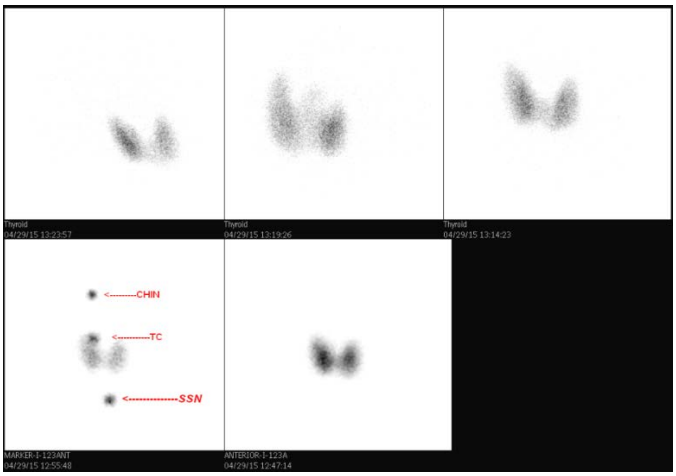

Figure 1. Thyroid radioiodine uptake scan obtained following return of hyperthyroid symptoms after first cycle of RAI demonstrating a mildly enlarged thyroid with diffusely increased thyroidal uptake of I-123 consistent with recurrent Graves' disease.

Discussion

Myxedema coma is a state of severe hypothyroidism, with major clinical manifestations including depressed mentation, hemodynamic instability, hypothermia, and lethargy. Infections, trauma, and certain medications such as narcotics, tranquilizers, sedatives, and anesthetics can precipitate the condition.[1] The majority of the clinical manifestations are due to the widespread thyroid hormone receptors in the body, particularly in the central nervous system, cardiovascular system, and respiratory system. Thyroid hormone, specifically T3 produced by 5'-monodiodination of T4 in the liver, kidney, and skeletal muscle, acts via binding to thyroid hormone nuclear receptors that induce transcription.[2] Studies of regional cerebral circulation via positron emission tomography in hypothyroidism demonstrated a generalized decrease in flow and glucose metabolism, with patients reporting increased rates of depression, anxiety, and psychomotor retardation.[3] This has been theorized to contribute to decreased ventilator drive and subsequent carbon dioxide retention in myxedema coma, oftentimes requiring mechanical ventilator support. Additional airway obstruction may be caused by body habitus and macroglossia secondary to chronic hypothyroidism.[4] Cardiovascular effects of hypothyroidism are profound; including repressed transcription of cardiac genes such as those

responsible for ß-myosin heavy chain and phospholamban in the absence of thyroid hormone, leading to decreased cardiac contractility.[5] One case report of an individual with dilated cardiomyopathy in the setting of profound hypothyroidism reported, mRNA levels of phospholamban, atrial natriuretic factor, and α-myosin heavy-chain all were severely deranged prior to thyroid hormone administration and were subsequently reversed following nine months of treatment.[6]

In the acute setting, myxedema coma typically presents with altered mental status, hypothermia, severe bradycardia, hyponatremia, hypoglycemia and a narrowed pulse pressure secondary to relative diastolic hypertension that is relatively unresponsive to fluid administration. Because of the mixed diagnostic picture, the diagnosis can be challenging. Important clues include presence of thyroidectomy scar, history of RAI treatment, and history of hypothyroidism with medication non-compliance. Phenotypic features of severe hypothyroidism on physical exam, include periorbital edema, coarse, sparse hair, macroglossia, and overall facial and pretibial myxedematous change are supportive of diagnosis.

Management requires intravenous levothyroxine with possible addition of intravenous T3. Concomitant high-dose intravenous hydrocortisone is administered to avoid precipitating adrenal crisis until coexisting adrenal insufficiency is excluded given the prevalence of additional autoimmune diseases and the increased clearance of cortisol with thyroid hormone replacement.[7,8] Other supportive measures, include passive rewarming, fluids and pressor, mechanical ventilation, monitoring for arrhythmias, and hypoglycemia and consideration of empiric antibiotics.

Conclusion

Myxedema is a medical emergency and early recognition and treatment is extremely important. The diagnosis of myxedema coma should be considered in any patients with altered level of conscious, hypothermic, hypotensive, bradycardic, and hypoglycemic patients.

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