

Received: 2020.06.11  
Accepted: 2020.08.08  
Available online: 2020.09.01  
Published: 2020.10.10

## Amiodarone-Associated Myxedema Coma

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

EF **Emily Zagorski**  
EF **Sahani Jayatilaka**  
EF **Fizza Hirani**  
E **Anthony Donato**

Department of Internal Medicine, Reading Hospital/Tower Health, Reading, PA,  
U.S.A.

**Corresponding Author:** Emily Zagorski, e-mail: [Emily.zagorski@towerhealth.org](mailto:Emily.zagorski@towerhealth.org)  
**Conflict of interest:** None declared

**Patient:** Male, 71-year-old  
**Final Diagnosis:** Myxedema coma  
**Symptoms:** Altered mental state • bradycardia  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Endocrinology and Metabolic

**Objective:** Rare disease





**Background:** Myxedema coma is an uncommon severe thyroid disorder that is fatal in 25–60% of cases. Although the differential diagnosis for altered mental status is extensive, including many more common causes such as infection, medication changes, electrolyte abnormalities, and exacerbation of chronic illnesses, profound hypothyroidism is an uncommon cause that can be overlooked.

**Case Report:** We describe the case of a 71-year-old man on long-term amiodarone treatment for atrial fibrillation who presented with altered mental status initially ascribed to uremia, hyponatremia, and pneumonia. When his mental status did not resolve, thyroid tests showed his thyroid-stimulating hormone level was 89  $\mu$ IU/mL, along with clinical criteria for myxedema coma.

**Conclusions:** We suggest that thyroid function tests should be considered in encephalopathic older adults on amiodarone.

**MeSH Keywords:** Consciousness Disorders • Hypothyroidism • Myxedema • Amiodarone • Drug-Related Side Effects and Adverse Reactions

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/926757>

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## Background

Myxedema coma is a rare cause of acute encephalopathy in older adults. It occurs most frequently in older adults, defined as above the sixth decade of life [1]. Although it is important to address common causes of confusion, including infection, exacerbation of chronic illness, and electrolyte abnormalities, it is also important to note that multiple conditions can coexist. Thyroid function should also be considered even in previously undiagnosed hypothyroidism. ✦

The aging process plays a significant role in fluctuating levels of thyroid hormones, including thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) [2]. The thyroid arm of the Framingham study showed that 5.9% of asymptomatic women and 2.3% of asymptomatic men over the age of 60 had TSH levels over 10 mIU/L [3]. In fact, a study of centenarians and supercentenarians revealed statistically higher baseline TSH levels than in matched controls in their late 60s/early 70s [4].

In addition to physiologic changes, older adults are generally on numerous medications and have more chronic diseases, which increases the risk for secondary hypothyroidism [5]. Medications reported to cause iatrogenic hypothyroidism include amiodarone, lithium, interferon, and tyrosine kinase inhibitors [6]. Here, we present a case of amiodarone-associated myxedema coma in an older adult with multiple chronic conditions and previously normal thyroid hormone levels.

## Case Report

A 71-year-old man with a past medical history of stage 5 chronic kidney disease, paroxysmal atrial fibrillation, on amiodarone 200 mg twice daily for the last year, type 2 diabetes mellitus, and heart failure with reduced ejection fraction presented with multifocal pneumonia, acute kidney injury, and acute encephalopathy. On presentation, the patient was bradycardic (heart rate: 55 beats per min) and hypothermic (35.8°C). The initial exam showed a confused and forgetful patient who was alert and oriented to person and place only, which was a change from baseline per family over the last 2 months. Significant nonpitting periorbital and lip edema without lower-extremity edema were noted. Dialysis was recommended for his acute kidney injury.

A chest X-ray showed cardiomegaly, pulmonary vascular congestion, and new, small bilateral pleural effusions. Computed tomography of the chest showed multifocal pneumonia. An electrocardiogram showed a prolonged QTc of 496 ms. Laboratory investigations included serum sodium 127 mmol/L (normal 135–145 mmol/L), blood urea nitrogen 122 mg/dL (normal

7–25 mg/dL), and creatinine 8.36 mg/dL (normal 0.6–1.3 mg/dL with patient's baseline 3.9–5.8 mg/dL).

Acute uremia causing mental status changes in the setting of stage 5 chronic kidney disease was addressed early with hemodialysis through a temporary dialysis catheter. The patient also had multifocal pneumonia, which can commonly cause acute confusion in older adults. Vancomycin, piperacillin-tazobactam, and doxycycline were empirically started. Hyponatremia was also considered as a compounding factor of the patient's altered mental status. After 24 h of addressing these factors, the patient's mental status began to worsen. Throughout the second night of his admission, the patient's mental status decompensated further, with the patient being described as increasingly lethargic and sluggish and alert to person only. He was transferred to the Intensive Care Unit and intubated as he was unable to protect his own airway.

At that point, nearly 48 h after admission, thyroid function levels were assessed. TSH on day 2 was found to be 89  $\mu$ IU/mL (normal 0.450–5.330; previous level of 3.538 1 year prior) with free T4 <0.25 ng/dL (normal 0.58–1.64), and free T3 was 1.42 pg/mL (normal 2.2–4.1). Antithyroid peroxidase was negative. Of note, thyroid function tests 2 years prior were normal.

The myxedema coma score was calculated at 120 points, with a score of 60 or above highly suggestive/diagnostic of myxedema coma [7]. The patient earned points in his myxedema coma score for hypothermia (10 points), obtunded state (15 points), anorexia/constipation before presentation (5 points), precipitating infectious event (10 points), bradycardia (20 points), pleural effusion (10 points), prolonged QTc (10 points), pulmonary edema (15 points), cardiomegaly (15 points), and hyponatremia (10 points). Hypothyroidism was recognized, and the patient was started on a dose of 200  $\mu$ g intravenous (IV) levothyroxine, 5  $\mu$ g IV liothyronine, and 50 mg IV hydrocortisone every 8 h [8].

After 3 days of treatment, the patient became arousable and was able to be extubated. Mental status returned to alert and oriented times 3 within 1 week after treatment initiation. Amiodarone was stopped by the Cardiology Department and he was discharged to subacute rehabilitation on 125  $\mu$ g daily of levothyroxine.

## Discussion

It can be quite difficult to decipher the exact etiology of altered mental status in an older adult with multiple comorbidities. In this particular case, we believe that long-term use of amiodarone induced his thyroid dysfunction in the setting of acute infection, uremia, and hyponatremia. The diagnosis of

myxedema coma should continue to be considered for encephalopathic patients, especially in older adults with pre-existing conditions on amiodarone.

Myxedema coma is the most severe sequela of hypothyroidism. Predisposing factors include female sex, history of hypothyroidism, recent surgery, infection, trauma, hypothermia, and certain medications that affect thyroid function, as was the case in our patient. The clinical presentation can be non-specific; however, symptoms may include lethargy, hypothermia, psychosis, altered mental status, periorbital swelling, lid ptosis, macroglossia, bradycardia, decreased cardiac output, pericardial effusion, prolonged QTc, hypoventilation, hypercapnia, and respiratory failure, many of which are compounded into the myxedema coma score used in diagnosis [8,9]. Given the nature of these symptoms, it is important to be vigilant in considering myxedema coma in the differential diagnosis to prompt appropriate treatment.

Amiodarone-induced myxedema coma is a rare condition that has previously been reported in the literature less than 20 times since 1971 [9–11]. Amiodarone-induced hypothyroidism is typically reported 3 months to 2 years after the initiation of amiodarone, usually at doses greater than 200 mg/day [11]. Amiodarone is known to cause both hyperthyroidism and hypothyroidism. The molecular chemistry of this medication includes an iodinated benzofuran derivative comprised of 2 iodine atoms. A 100-mg tablet contains about 37.5 mg of iodine, which is many times the daily iodine requirement [12].

The molecular impact of iodine on the thyroid is well established. Type I 5'-deiodinase is inhibited, which is responsible

for the peripheral conversion of the prohormone, T4, to the active hormone, T3. Excess iodine also inhibits the entry of T4 to the peripheral tissue. These mechanisms can lead to increased serum T4 and decreased serum T3 concentrations in euthyroid patients on long-term amiodarone therapy [13]. Subsequent inhibition of type II 5'-deiodinase activity also leads to a lower intrapituitary T3 concentration, which accounts for the increase in serum TSH levels seen with amiodarone treatment [13]. It is unclear why amiodarone use can lead to myxedema coma in some patients, but cause no thyroid irregularities in others; however, we hypothesize that this patient's advanced age and other comorbidities made him more likely to be symptomatic.

## Conclusions

In review of this case, there were many reasons why the diagnosis of myxedema coma may have been initially missed. The patient concurrently had more common causes of acute encephalopathy, including uremia due to his poor baseline kidney function, infectious pneumonia, and hyponatremia. After the patient's mental status worsened with emergent dialysis, further investigation into reversible causes of acute encephalopathy was performed. The patient also had no documented previous thyroid disorder. Even with previously normal thyroid function, amiodarone-induced myxedema coma should still be considered. In conclusion, performing thyroid function tests early in admission, in addition to physician awareness of myxedema coma in the differential diagnosis for older adults on amiodarone, can prevent potential anchoring biases in the acute encephalopathy patient.

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