Non-thyroidal illness syndrome in the setting of amiodarone use, a diagnostic challenge.

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Introduction:

- Non-thyroidal illness syndrome is the alteration in thyroid function tests (TFTs) that occurs in critically ill patients.
- These patients present with low serum concentrations of total triiodothyronine (T3), and low-normal free thyroxine (FT4), and thyroid-stimulating hormone (TSH).
- Previously, these alterations were thought to be euthyroid, and the term euthyroid-sick syndrome was used to describe it.
- However, there is evidence that these TFTs alterations may represent acquired transient central hypothyroidism.
- It is thought to be a protective reaction to prevent excessive tissue catabolism.
- Patients with severe non-thyroidal illness on chronic amiodarone therapy might represent a challenge to interpret TFTs.
- There are rare cases of Amiodarone-induced thyrotoxicosis associated with severe non-thyroidal illness, the TT3 may be normal.
- Therefore, it is a challenge to interpret thyroid function tests in a critically ill patient on amiodarone with clinical presentation suggestive of thyrotoxicosis.

Case report:

Case of 66-year-old male with history of heart failure with reduced ejection fraction at 15% with AICD, atrial fibrillation, and hypertension who presented to the emergency room due to progressive shortness of breath. Physical examination with tachycardia, positive jugular venous distention, crackles on pulmonary auscultation and tachypnea requiring eventual endotracheal intubation. Electrocardiogram showed atrial fibrillation with fast ventricular response. Afterwards, he was transferred to the intensive care unit (ICU) where Amiodarone was started due to lack of response to other rate control medications and antibiotic therapy for suspected Pneumonia. TFTs were requested prior initiation of amiodarone which showed thyroid stimulating hormone at 0.01 uIU/ml. During admission, patient developed ventilator associated pneumonia with subsequent septic shock. Thyroid function tests were repeated in 3 weeks later and revealed thyroid stimulating hormone (TSH) at 0.006 uIU/ml, free T4 at 3.07 ng/dl and total T3 at 93.52 ng/dl. Amiodarone was discontinued and methimazole + propranolol therapy was started. In the following days, clinical deterioration progressed resulting in the patient's death.

Laboratories:

Test	On admission	3 weeks later
TSH	0.01 ulU/ml	0.006 ulU/ml
FT4	-	3.07 ng/dl
TT3	-	93.52 ng/dl

Amiodarone effects on the Thyroid:

Amiodarone-induced Hypothyroidism

Amiodarone-induced Thyrotoxicosis Type 1

Amiodarone-induced Thyrotoxicosis Type 2

Discussion:

Thyrotoxicosis, as a side effect of amiodarone therapy, can be significantly detrimental, particularly in critically ill patients with cardiac disease. In contrast, Non-thyroidal illness syndrome could be considered in patients with low T3 levels which are expected to be elevated in amiodarone-induced thyrotoxicosis. The most common hormone pattern of non-thyroidal illness syndrome is low total T3 and free T3 levels, with low-normal T4 and TSH levels, but in severe illness all levels might be low. However, patients on amiodarone therapy who develop thyrotoxicosis present with evidence of increased free T4 and TT3 levels. This case illustrates the challenges of interpretation of TFTs in a critically-ill patient on amiodarone therapy.

This patient had thyrotoxicosis in the setting of critical illness. On admission, the initial suppressed TSH levels were thought to be secondary to non-thyroidal illness syndrome. Thereafter, the patient deteriorated clinically and further work up was suggestive of thyrotoxicosis except for normal T3. There are reports of rare cases of Amiodarone-induced thyrotoxicosis associated with severe non-thyroidal illness, where the TT3 may be normal. Therefore, patients with clinical presentation suggestive of thyrotoxicosis (while on amiodarone therapy), amiodarone-induced thyrotoxicosis should be high on the differential diagnosis.

Conclusion:

- Amiodarone-induced thyrotoxicosis is a deadly adverse event and should not be confused with Non-thyroidal illness syndrome.
- The ability of differentiate them is imperative because both have a very distinct management and treatment.
- In patients who develop uncontrolled arrhythmias or exacerbations of cardiac disease while on Amiodarone, Amiodarone-induced thyrotoxicosis should be high on the differential diagnosis.

References:

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