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Case Report

An uncommon side effect: amiodarone-related hypothyroidism in a patient with negative thyroid autoantibodies

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ABSTRACT

Amiodarone is an antiarrhythmic drug frequently used in cardiac dysrhythmias. One of the most important side effects of amiodarone is thyroid dysfunction. Amiodarone-induced thyrotoxicosis (AIT) and amiodarone-induced hypothyroidism (AIH) can occur depending on individuals' iodine status and previous thyroid disease. In this case, we aimed to present the hypothyroidism that developed in a patient with negative thyroid autoantibodies after amiodarone use.

Keywords: Amiodarone, levothyroxine, hypothyroidism

INTRODUCTION

Amiodarone is one of the antiarrhythmic drugs used in cardiac rhythm disorders.[1] However, there are limitations of usage due to its iodine content.[2] One of the side effects of amiodarone is dysfunction of thyroid glands.[3] Amiodarone-induced thyrotoxicosis (AIT) or amiodarone-induced hypothyroidism (AIH) may occur depending on the iodine status of individuals and previous thyroid disease history.[4]

Although AIH is more frequently seen in female patients with positive thyroid autoantibodies, it has been reported in autoantibody-negative patients in the literature. There is limited data on the prognosis of these patients in the literature. With this case report, we aimed to describe the challenges in the management of AIH in a patient with comorbidities.

CASE

A 75-year-old female patient was admitted to our internal medicine clinic with muscle weakness, and edema in the extremities and periorbital region that had increased in the last 3 months. In her medical history, she was under medication of furosemide for congestive heart failure and subcutaneous insulin for diabetes mellitus. She also had a history of one hemodialysis session a few months ago for ultrafiltration in the intensive care unit (ICU). After discharge from the ICU, 200 mg amiodarone treatment was started for supraventricular tachycardia. She had no history of alcohol or smoking.

In physical examination, she had bilateral edema in the lower extremities, on the dorsal face of the hand, and in the periorbital region. The head and neck examinations were normal, and the thyroid glands were non-palpable. In her chest examination, rales and rhonchi were present prominently on the right lung. Her heart and abdominal examinations were normal. Her blood pressure was 130/70 mmHg, and her pulse rate was 64 beats/minute. Her oxygen saturation was normal. Her electrocardiogram was in normal sinus rhythm. Her laboratory findings were as follows: creatinine: 4.7 mg/dL, BUN: 52 mg/dL PH: 7.38, HCO_3: 23.8 mEq/L, PCO_2: 38.7 mm/Hg, Hb: 8.5 g/dL platelet count:264000. TSH: 85.5 uIU/L (reference range: 0.35-4.94), triiodothyronine (T3): 0.67 pg/mL (reference range: 1.71-3.71), and T-thyroxine (T4): 0.46 (reference range: 0.58-1.64). Thyroid function tests were normal four months ago. Her thyroid autoantibodies were negative. Her thyroid ultrasound imaging (USG) showed a heterogeneous appearance with decreased echogenicity which suggests thyroiditis (**Figure 1**).

She was diagnosed with amiodarone-related hypothyroidism. After cardiology consultation amiodarone treatment was stopped, and diltiazem treatment was started with levothyroxine replacement. During follow-up, she needed oxygen therapy despite intensive diuretic treatment. Because of her critical condition, we started hemodialysis with ultrafiltration for excessive volume load (**Figure 2**).

DISCUSSION

In treating dysrhythmias such as supraventricular tachycardia, atrial fibrillation, and atrial flutter, amiodarone is usually chosen.[5] As a result of the high iodine content and long half-life of this substance, it also affects the thyroid tissues.[6]

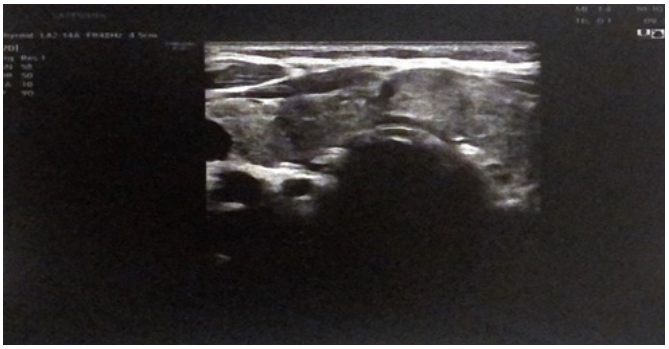

Figure 1. Thyroid ultrasound of the patient after the use of amiodarone. Thyroid gland parenchyma has a heterogeneous appearance with decreased echogenicity. Thyroiditis

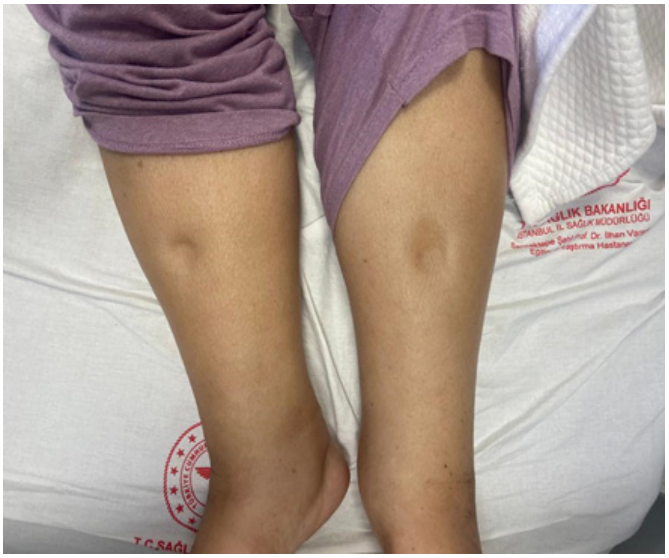

Figure 2. Rough and hard +3 edema in the lower extremities that does not respond to medical treatment

The high level of iodide released through the metabolism of amiodarone inhibits thyroid hormone release and biosynthesis (Wolff-Chaikoff effect). AIH is thought to be a result of iodine's inability to escape the Wolf-Chaikoff effect, especially in Hashimoto's disease.[7] Amiodarone discontinuation in AIH is not always necessary. It was recommended to start levothyroxine replacement therapy without discontinuing the amiodarone, especially for uncontrolled dysrhythmias.[8] Since our patient's dysrhythmia was managed with beta-blockers and her existing co-morbid diseases, we stopped amiodarone medication to control the hypothyroidism earlier.

The basal TSH level is important before starting amiodarone treatment. TSH elevation during treatment could be a sign of AIH . Increased levels of TSH in the first three months may not be useful because it may also occur in euthyroid patients. On the other hand, a significant elevation (>20 uIU/L) in the early period is usually a sign of thyroid disease.[9] In this case, before the start of amiodarone treatment, her TSH levels were within the normal range. A significant increase in TSH after only the first month of treatment provided evidence of the diagnosis. Thyroid autoantibodies increase the risk of development of AIH.[10] It was also reported that women are at higher risk than men.[11] This situation is supported by the fact that the patient in our patient is a woman. However, her thyroid autoantibodies were negative. This reflects the significance for us to pay attention to the development of AIH in the group of patients who do not have autoantibodies. Martino et al. showed in a study of 28 AIH patients, that 70% of autoantibody-positive patients developed persistent hypothyroidism, whereas 10% of autoantibody-negative patients developed persistent hypothyroidism.[12] Before starting amiodarone therapy, it is advised to check the patient's thyroid autoantibodies, TSH, T4, and T3 levels in the serum.[9] By doing so, the risk of AIH can be recognized in patients at early stages and prevented without resulting in permanent hypothyroidism. Before starting treatment, we can determine the patient's thyroid condition with USG, which can be helpful when observing signs of permanent hypothyroidism after amiodarone cessation. Our patient's thyroid USG was compatible with thyroiditis (**Figure 1**). A comparison could not be possible, hence she had not thyroid USG before starting amiodarone treatment.

CONCLUSION

The indications for starting amiodarone treatment should be clearly defined. Because hypothyroidism may disrupt the compensatory mechanisms of patients with comorbid diseases such as congestive heart failure and chronic renal failure. Thus, by closely observing these patients, these complications may be prevented.

ETHICAL DECLARATIONS

Informed Consent: Written consent was obtained from the patient.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: The author declare that they have all participated in the design, execu-tion, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Van Erven L, Schalij MJ. Amiodarone: an effective antiarrhythmic drug with unusual side effects. *Heart*. 2010;96(19):1593-1600. doi:10.1136/hrt.2008.152652
2. Eskes SA, Wiersinga WM. Amiodarone and thyroid. *Best Pract Res Clin Endocrinol Metab*. 2009;23(6):735-751. doi:10.1016/j.beem.2009.07.001
3. Amador F, Mendonça F, da Costa C, et al. Total thyroidectomy in a patient awaiting heart transplant with amiodarone-induced thyrotoxicosis: a case report. *Clin Case Rep*. 2023;11(2):e6892. doi:10.1002/ccr3.6892
4. Narayana SK, Woods DR, Boos CJ. Management of amiodarone-related thyroid problems. *Ther Adv Endocrinol Metab*. 2011;2(3):115-126. doi:10.1177/2042018811398516
5. Medić F, Bakula M, Alfirević M, Bakula M, Mucić K, Marić N. Amiodarone and thyroid dysfunction. *Acta Clin Croat*. 2022;61(2):327-341. doi:10.20471/acc.2022.61.02.20
6. Florek JB, Lucas A, Girzadas D. Amiodarone. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
7. Eng PH, Cardona GR, Fang SL, et al. Escape from the acute Wolff-Chaikoff effect is associated with a decrease in thyroid sodium/iodide symporter messenger ribonucleic acid and protein. *Endocrinology*. 1999;140(8):3404-3410.
8. Ursella S, Testa A, Mazzone M, Gentiloni Silveri N. Amiodarone-induced thyroid dysfunction in clinical practice. *Eur Rev Med Pharmacol Sci*. 2006;10(5):269-278.
9. Basaria S, Cooper DS. Amiodarone and the thyroid. *Am J Med*. 2005;118(7):706-714. doi:10.1016/j.amjmed.2004.11.028
10. Trohman RG, Sharma PS, McAninch EA, Bianco AC. Amiodarone and thyroid physiology, pathophysiology, diagnosis and management. *Trends Cardiovasc Med*. 2019;29(5):285-295. doi:10.1016/j.tcm.2018.09.005
11. Trip MD, Wiersinga W, Plomp TA. Incidence, predictability, and pathogenesis of amiodarone-induced thyrotoxicosis and hypothyroidism. *Am J Med*. 1991;91(5):507-511.
12. Martino E, Aghini-Lombardi F, Mariotti S, et al. Amiodarone iodine-induced hypothyroidism: risk factors and follow-up in 28 cases. *Clin Endocrinol*. 1987;26(2):227-237.