CASE REPORT

Amiodarone-induced myxoedema coma

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SUMMARY

A 62-year-old man was found to have bradycardia, hypothermia and respiratory failure 3 weeks after initiation of amiodarone therapy for atrial fibrillation. Thyroid-stimulating hormone was found to be 168 μ IU/mL (nl. 0.3–5 μ IU/mL) and free thyroxine (FT4) was <0.2 ng/dL (nl. 0.8–1.8 ng/dL). He received intravenous fluids, vasopressor therapy and stress dose steroids; he was intubated and admitted to the intensive care unit. He received 500 μ g of intravenous levothyroxine in the first 18 h of therapy, and 150 μ g intravenous daily thereafter. Haemodynamic improvement, along with complete recovery of mental status, occurred after 48 h. Twelve hours after the initiation of therapy, FT4 was 0.96 ng/dL. The patient was maintained on levothyroxine 175 (g PO orally daily. A thyroid ultrasound showed diffuse heterogeneity. The 24 hour excretion of iodine was 3657 (mcg (25–756 (mcg). The only two cases of amiodarone-induced myxoedema coma in the literature report patient death despite supportive therapy and thyroid hormone replacement. This case represents the most thoroughly investigated case of amiodarone-induced myxoedema coma with a history significant for subclinical thyroid disease.

BACKGROUND

Amiodarone is a class III antiarrhythmic frequently used in patients with severe congestive heart failure (CHF) because of its minimal negative inotropic action.¹ Amiodarone contains approximately 37% iodine by weight and has a mean elimination half-life of 40 $\pm$ 10 days.² The usual maintenance dose ranges from 100 to 600 mg daily; once the drug is metabolised in the liver, 3–21 mg of iodide are released into the blood each day (a quantity 50–100 times greater than the recommended daily intake).³ Amiodarone-induced thyroid dysfunction, particularly in those with pre-existing thyroid disease, occurs in 15–20% of patients. It is more common in iodine sufficient areas of the world, and occurs more frequently in patients with underlying autoimmune thyroid disease.⁴

Myxoedema coma is a rare complication of hypothyroidism, with a mortality rate as high as 50%.⁵ There are only two reported cases of myxoedema coma in the context of amiodarone therapy; both patients died days after the initiation of supportive therapy and thyroid hormone replacement.^{6,7}

In any patient on amiodarone therapy, thyroid function should be assessed prior to and during treatment. Our case highlights the need for greater awareness of the amiodarone-induced hypothyroidism, in order to prevent myxoedema coma, a life-threatening condition.

CASE PRESENTATION

A 62-year-old man with CHF (ejection fraction of 30%) presented with altered mental status and progressive unresponsiveness, hypotension, bradycardia, hypothermia, hypoglycaemia and respiratory failure 3 weeks after being started on amiodarone therapy for refractory atrial fibrillation. Medical history included coronary artery disease, ischaemic cardiomyopathy, systolic CHF, hypertension, hyperlipidaemia and atrial fibrillation. He did not smoke or drink. There was no personal or family history of any thyroid disease. His medications included amiodarone 200 mg twice daily, aspirin 325 mg daily, furosemide 40 mg twice daily, lisinopril 20 mg daily and metoprolol 50 mg twice daily. On physical examination, he was lethargic with cold, clammy skin. Temperature was 95°F (35°C), blood pressure 66/40 mm Hg and heart rate 25bpm. The patient had marked puffiness of the eyes and delayed relaxation phase of the deep tendon reflexes. There were no scars indicative of previous neck surgeries. Serum thyroid-stimulating hormone (TSH) was 168 μ IU/mL (nl. 0.3–5 μ IU/mL) and free thyroxine (FT4) was <0.2 ng/dL (nl. 0.8–1.8 ng/dL). FT4 was 0.96 ng/dL after 12 h; marked improvements in haemodynamic status and return to baseline mental status occurred after 48 h.

INVESTIGATIONS

One year prior to presentation, TSH and FT4 were 8.8 (uIU/mL (nl. 0.3–5) and 1.121 ng/dL (nl. 0.8–1.8 ng/dL), respectively. FT4 was 0.96 ng/dL, 1.01 ng/dL, and 1.14 ng/dL after 12 hours, 48 hours and 120 hours respectively. Twenty-four hour urinary excretion of iodine was 3657 μ g (nl. 25–756 mc g).

Thyroid ultrasound showed normal size, diffuse heterogeneity and slightly increased vascularity of the thyroid, consistent with an underlying autoimmune thyroiditis. Thyroid peroxidase antibody test was negative. No nodules or suspicious calcifications were present.

DIFFERENTIAL DIAGNOSIS

- Myxoedema coma/severe hypothyroidism
- Amiodarone induced
- Worsening of underlying chronic autoimmune thyroiditis

TREATMENT

In the emergency department, the patient promptly received dextrose 50%, fluid hydration and was started on vasopressor therapy and hydrocortisone 50 mg intravenously every 8 h. He was intubated, placed on mechanical ventilation, and admitted to

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intensive care unit. He received levothyroxine 100 (mcg IV intravenously, 200 (mcg intravenously IV and another 200 (mcg IV intravenously every 6 hours for the first 18 h without evidence of cardiac dysrhythmia. The patient was started on levothyroxine 150 (mcg IV intravenously daily as maintenance. He showed marked haemodynamic and clinical improvement, as well as complete recovery of mental status. He was successfully weaned from vasopressors and hydrocortisone, and was extubated after 72 h. He was transferred to a regular medical floor and was maintained on levothyroxine 175 µg daily.

Amiodarone therapy was permanently discontinued after consulting with the cardiology team. FT4 after five 5 days was 1.41 ng/dL (nl. 0.3–5 ng/dL). The patient was discharged home in stable condition and continues to follow-up at the endocrinology clinic.

DISCUSSION

Our case represents a case of amiodarone-induced myxoedema coma in a patient with a pre-existing subclinical thyroid disease. Early diagnosis and prompt initiation of supportive measures, along with adequate thyroid replacement therapy, are of paramount importance in the management of this lethal endocrine emergency. The temporal association between the initiation of amiodarone therapy and the development of severe hypothyroidism/myxoedema coma, along with the markedly elevated levels of urinary iodine, confirms excess iodine as the aetiology of severe hypothyroidism with myxoedema coma. The presence of elevated TSH prior to the initiation of amiodarone, along with the diffuse heterogeneity on ultrasound, points to the presence of an underlying autoimmune thyroid disease. These findings underscore the importance of knowing a patient's underlying thyroid status prior to the initiation of amiodarone therapy. The most likely pathogenic mechanism of amiodarone-induced hypothyroidism is the inability of thyroid gland of these patients to escape from the acute Wolff-Chaikoff effect after an iodine load, particularly when damaged by pre-existing autoimmune thyroiditis.⁸

Only two cases of amiodarone-induced myxoedema coma are reported in the literature—that of Mazonson and Williams in 1984 and that of Shaheen⁹ in 2009, with both patients dying after 6 and 2 days, respectively, despite reportedly adequate supportive measures and thyroid hormone replacement. Regrettably, neither case mentioned measurements of 24 h urinary iodide, which, when elevated, strongly supports iodine as the aetiology of amiodarone-induced myxoedema coma.

We believe our case represents the most thoroughly documented case of amiodarone-induced myxoedema coma; this is also

the first reported case in which the patient was successfully treated and survived this highly fatal but potentially treatable condition. This case provides support for the assessment of thyroid function prior to and during amiodarone.

Learning points

- In the setting of pre-existing thyroid dysfunction (even subclinical thyroid dysfunction), there is a risk of serious and rapidly progressive thyroid dysfunction following the initiation of amiodarone therapy.
- Thyroid function should be assessed prior to and during therapy with amiodarone.
- Early diagnosis, as well as prompt institution of thyroid hormone replacement and supportive measures, is the key to successful management of this lethal endocrine emergency.

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Competing interests None.

Patient consent Obtained.

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