

# Initial treatment of myxedema coma using oral levothyroxine: a case report from Tanzania

Nyasatu G Chamba<sup>1,2</sup>, Abid M Sadiq<sup>1,2</sup>, Norman J Kyala<sup>2</sup>, Joachim E Mosha<sup>1</sup>, Ibrahim A Muhina<sup>2</sup>, Fuad H Said<sup>2</sup> and Elichilia R Shao<sup>1,2</sup>

<sup>1</sup>Department of Internal Medicine, Kilimanjaro Christian Medical Centre, Moshi, Tanzania and <sup>2</sup>Department of Internal Medicine, Kilimanjaro Christian Medical University College, Moshi, Tanzania

Correspondence  
should be addressed  
to N G Chamba

**Email**  
[nyasatuchamba@yahoo.com](mailto:nyasatuchamba@yahoo.com)

## Summary

Myxedema coma is a severe complication of hypothyroidism, commonly affecting women over 60 years of age, causing slow, progressive multi-organ dysfunction, and mental deterioration. Due to improved diagnostics and treatment of hypothyroidism, myxedema coma has become uncommon. However, it is hardly reported in resource-limited settings. We present an elderly female with a history of total thyroidectomy due to multi-nodular goiter. She presented with features of heart failure, excessive weight gain, and cold sensation. Although the patient was on levothyroxine replacement therapy, her laboratory tests were suggestive of overt primary hypothyroidism. During the course of her hospitalization, she developed subcutaneous bleeding with frank hematuria. This led to an altered mental state and hypotension that were suggestive of myxedema coma. Stroke and pulmonary embolism were ruled out as potential differential diagnoses of her current state. She was treated with a high dose of oral levothyroxine followed by 150 µg of oral levothyroxine daily, which resulted in a favorable outcome despite being a fatal emergency. She was also treated with intravenous hydrocortisone and furosemide. Oral thyroid hormone replacement may be an effective option in those resource-limited settings where intravenous thyroid hormone replacement is not available. However, early diagnosis and treatment with an adequate dose of thyroid hormones are crucial to achieve a favorable outcome.

## Learning points:

- Myxedema coma is an uncommon complication of hypothyroidism with a fatal outcome.
- The diagnosis of myxedema coma is based on clinical suspicion, especially in patients with hypothyroidism and in the presence of precipitating factors. Although diagnostic and scoring criteria based on clinical, laboratory, and imaging features have been proposed, no consensus has been reached.
- This article shows an alternative treatment option for myxedema coma using oral levothyroxine, which led to a favorable outcome.

## Background

Myxedema coma is a severe complication of hypothyroidism, commonly affecting women over 60 years of age, causing slow, progressive multi-organ dysfunction, and mental deterioration (1). It has become uncommon worldwide due to improved diagnostics and treatment of hypothyroidism. The incidence of myxedema

coma in European countries is estimated to be around 0.22 per 1 000 000 people per year (2), while it is unknown in the African continent.

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scoring for myxedema coma based on clinical, laboratory, and imaging features have been proposed, no consensus has been reached.

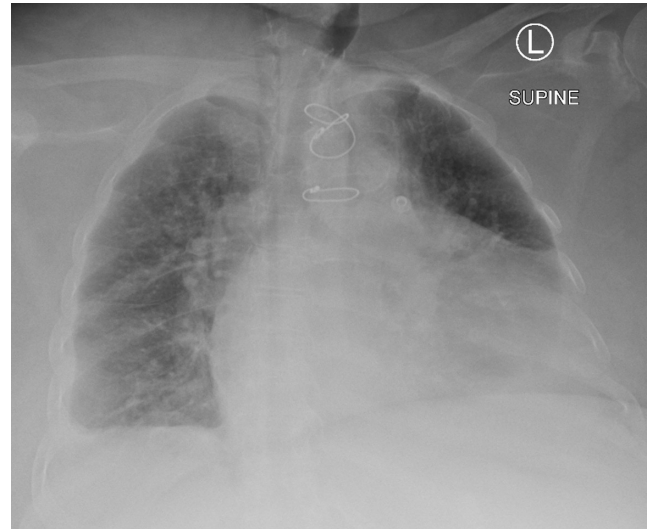
In this case, we present a 67-year-old female with a history of hypothyroidism, hypothermia, and altered mental state in the presence of heart failure. She was treated with oral levothyroxine, leading to a favorable outcome.

## Case presentation

A 67-year-old female presented with an acute onset of dyspnea at rest, a dry cough, and constipation. She also suffered from a progressive cold sensation which was associated with an excessive weight gain of 17 kg (from 98 to 115 kg) over the previous 3 months. She underwent total thyroidectomy 3 years earlier due to a multinodular goiter and was supplemented with 100 µg of oral levothyroxine daily.

On admission, she was conscious with a Glasgow Coma Score (GCS) of 15/15, morbidly obese (her BMI was 39.8 kg/m<sup>2</sup>), with generalized edema, elevated blood pressure (BP) of 181/90 mmHg, a pulse rate (PR) of 70 b.p.m., and a temperature of 35.5°C. She had an elevated jugular venous pressure of 10 cm H<sub>2</sub>O, bilateral rhonchi, and basal crepitations. Her initial thyroid-stimulating hormone (TSH), free thyroxine (fT<sub>4</sub>) and free triiodothyronine (fT<sub>3</sub>) were 18.9 µIU/mL (normal 0.27–4.20), 9.3 ng/mL (normal 52.0–127.0), and 1.3 ng/mL (normal 0.69–2.15), respectively. One year before admission, her TSH was 11.2 µIU/mL. She presented with hyponatremia of 120.7 mmol/L (normal 135.0–145.0), hypoalbuminemia of 34.2 g/L (normal 35.0–55.0), hypocalcemia of 1.7 mmol/L (normal 2.1–2.5), and a partial thromboplastin time of 50.3 s (normal 25–35). Her chest X-ray revealed cardiomegaly, right-sided pleural effusion, and bilateral infiltrates (Fig. 1). An ECG revealed flat or inverted T waves and a low voltage reading (Fig. 2). An echocardiogram revealed a dilated left ventricle with moderate mitral insufficiency and an ejection fraction of 75%.

Due to her rapid clinical deterioration, she was initially diagnosed with heart failure with a differential diagnosis of pulmonary embolism and was nursed in the intensive care unit. She was treated with low-dose lisinopril, intravenous furosemide, unfractionated heparin, oxygen, and maintained on 100 µg of oral levothyroxine. Moreover, 1000 mg of oral calcium carbonate were administered thrice daily to treat hypocalcemia.

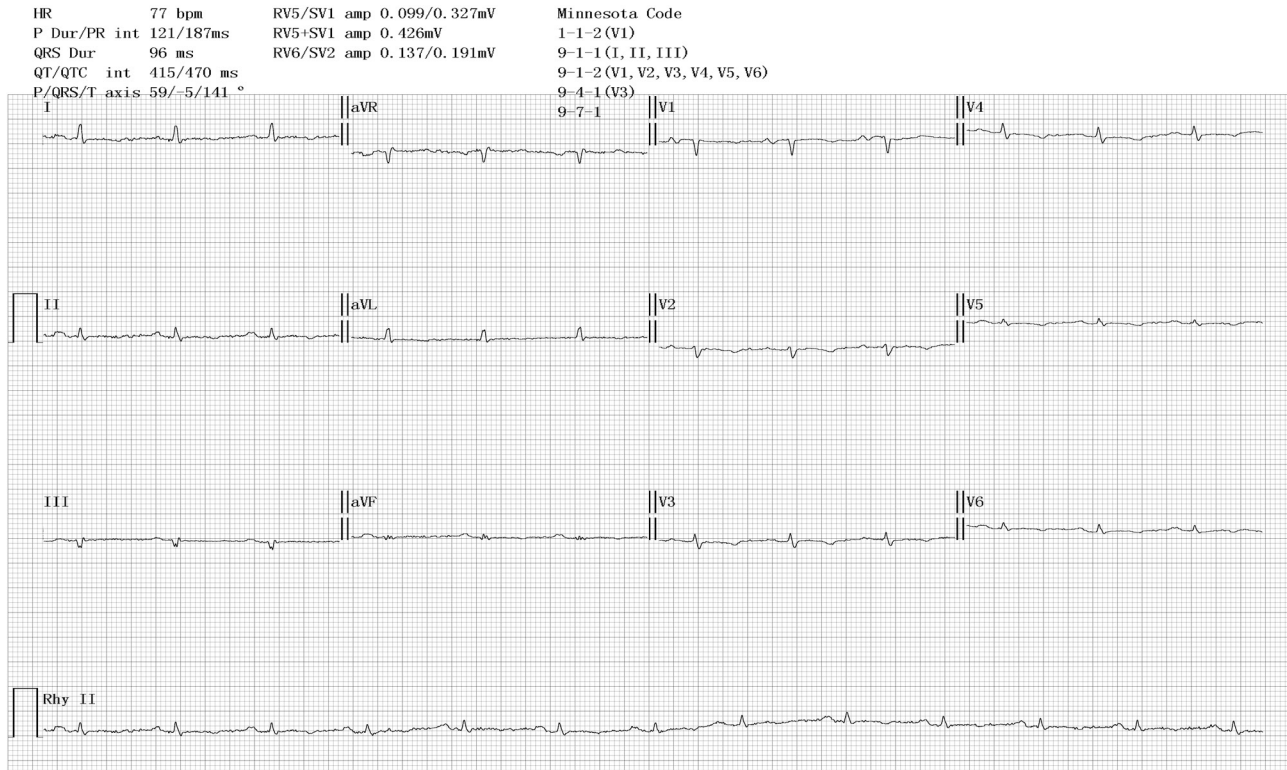


**Figure 1**

Chest X-ray in supine position showing cardiomegaly, right-sided pleural effusion, and bilateral infiltrates.

On the third day of her admission, her BP, PR, and temperature were 112/60 mmHg, 64 b.p.m., and 35.6°C, respectively. She underwent a CT pulmonary angiography, which ruled out pulmonary embolism. By the afternoon, frank hematuria and ecchymosis around the cannula sites appeared. An urgent partial thromboplastin time was ordered, which was prolonged for over 300 s. The unfractionated heparin was discontinued and protamine sulfate was administered. By the evening, she developed an altered level of consciousness with a GCS of 12/15. Her BP was 98/56 mmHg, her PR was 61 b.p.m., and the temperature was 35.4°C. A diagnosis of myxedema coma was made. Due to the altered level of consciousness, a nasogastric tube was inserted to allow the administration of oral medications. She was given oral levothyroxine 300 µg once, together with intravenous hydrocortisone 200 mg. She underwent an emergency brain CT, which ruled out a concomitant hemorrhagic stroke. She was maintained on oral levothyroxine 150 µg once daily together with a 3-day course of intravenous hydrocortisone 100 mg thrice daily.

Over the course of her hospital stay, she was kept warm with blankets, and her water and electrolyte status were monitored regularly. Her clinical presentation improved gradually with stabilization of BP, temperature, and PR. Her mental deterioration regressed, and the patient eventually became oriented. The nasogastric tube was removed and she was able to take her oral medications. Her edema was still present but had reduced significantly since admission.



**Figure 2**  
An ECG showing a low voltage reading with a sinus rhythm, flat/inverted T waves, and QT prolongation.

The serum 25-hydroxy vitamin D was 28 ng/mL (normal 20–50). Her laboratory investigations were monitored as shown in Table 1. The treatment of myxedema coma resulted in significant general improvement, and she was discharged home to continue with her medication.

On follow-up, the patient reported a weight loss of 9 kg (from 115 to 106 kg) over 3 months and of 5 more kg over 6 months (from 106 to 101 kg). Her control thyroid panel revealed a euthyroid state as shown in Table 1. Her levothyroxine was titrated to 125 µg once daily and calcium carbonate to 1000 mg twice daily. She was advised to adhere to her medication and to continue regular monitoring of her thyroid function.

## Discussion

Fifty years ago, myxedema coma had a mortality of 80%, but currently, it is up to 29% (3), mainly due to early recognition and available treatment options. In our case, the patient had a favorable outcome due to early detection, even though she presented with heart failure and bleeding. Myxedema coma is more likely to occur in the winter than in the summer season, suggesting hypothermia as a precipitating factor. Other precipitating factors described are respiratory infections, heart failure, stroke, medications such as amiodarone, and metabolic disturbances (1). Due to its proximity to the Equator, Tanzania does not have the typical four seasons (spring, summer, fall, and winter), as it

**Table 1** Laboratory investigations over the course of the patient’s admission and follow-up.

Laboratory tests	Reference range	On admission	On 4th day	On 14th day	On 24th day	At 3 months	At 6 months
TSH (µIU/mL)	0.27–4.20	18.9	24.6	15.4	20.4	1.04	0.82
ft4 (ng/mL)	52.0–127.0	9.3	44.1	56.7	10.7	63.1	127.5
ft3 (ng/mL)	0.69–2.15	1.3	0.5	0.7	2.6	1.8	1.4
Sodium (mmol/L)	135.0–145.0	120.7	125.9	137.0	134.1	139.0	143.0
Albumin (g/L)	35.0–55.0	34.2	31.2	33.4	35.6	41.0	39.5
Total Calcium (mmol/L)	2.1–2.5	1.7	1.6	1.7	1.7	2.1	2.2

ft3, free triiodothyronine; ft4, free thyroxine; TSH, thyroid-stimulating hormone.



only gets two: dry and wet. In fact, the patient presented to us during the wet season.

Low levels of  $fT_4$  and  $fT_3$  have negative inotropic and chronotropic effects on the heart, leading to reduced cardiac function and vasoconstriction. The longstanding effects of circulating catecholamines cause a  $\beta/\alpha$ -adrenergic imbalance, reduced total blood volume, and myocardial dysfunction, leading to heart failure (4).

Myxedema patients may easily bleed due to acquired Von Willebrand syndrome as well as a decrease in intrinsic factors (5), especially with heparin use. Other causes of bleeding in myxedema may be poor platelet adhesiveness, prolonged bleeding and clotting time, and elevated partial thromboplastin time (4).

The inability of the body to excrete free water is thought to be one of the pathophysiologic mechanisms of hypothyroidism-associated hyponatremia. This is due to a combination of decreased glomerular filtration rate and interstitial mucopolysaccharide accumulation with fluid retention. Because of the decreased cardiac output and stimulation of the carotid sinus, this results in decreased effective arterial blood volume and relatively high levels of antidiuretic hormone (6).

Medical therapy includes the administration of a loading dose of intravenous levothyroxine of 200–400  $\mu\text{g}$  followed by a daily maintenance dose of oral levothyroxine of 1.6  $\mu\text{g}/\text{kg}$  body weight. In addition to levothyroxine, a loading dose of intravenous liothyronine of 5–20  $\mu\text{g}$  may be given, followed by a maintenance dose of 2.5–10  $\mu\text{g}$  every 8 h until symptom relief. Older/smaller patients and patients with a history of heart disease (coronary artery disease/arrhythmia) should be treated with lower doses of both levothyroxine load and liothyronine. The daily maintenance dose of levothyroxine should be reduced to 75% when given intravenously. However, the recommendation concerning the administration of levothyroxine is strong, the one about liothyronine administration is weak, and both have low-quality evidence (7). In our case, access to intravenous exogenous thyroid hormones or any form of liothyronine was not available. In a similar resource-limited setting, oral levothyroxine has been effective in treating myxedema coma (8), as oral levothyroxine is an effective management option for myxedema coma if intravenous is unavailable (9).

Pituitary–adrenal function may be impaired in myxedema coma, therefore the administration of intravenous hydrocortisone prior to levothyroxine administration may prevent adrenal insufficiency upon restoration of normal metabolic rate with levothyroxine

(7). Apart from medical therapy, supportive therapy also plays an important role as patients should be managed in an intensive care setting for cardiorespiratory status, possible ventilatory assistance, passive re-warming, and adequate water and electrolyte resuscitation (10).

In conclusion, myxedema coma may be rare due to the currently available diagnostic tools and therapies, but it remains a life-threatening condition. In resource-limited settings, oral levothyroxine may be a suitable alternative to the intravenous formulation in the initial treatment of myxedema coma. Early diagnosis, administration of thyroid hormones, and supportive management are vital for a good prognostic outcome.

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#### Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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#### Patient consent

We obtained written informed consent from the patient for the publication of this case report and the accompanying images.

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#### Ethical approval

The need for ethics approval was waived.

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#### Author contribution statement

All authors were involved with patient management; A M S and F H S: reviewed the inherent literature; N G C, A M S, and F H S: prepared the manuscript; N J K, J E M, I A M: provided the patient information and images; N G C, A M S, N J K, F H S, and E R S: reviewed and edited the manuscript; all authors approved the final version of the manuscript.

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