

# Myxedema coma precipitated by polypharmacy of risperidone, amiodarone and diazepam – a rare case report

## Abstract

Myxedema coma (MC) is a rare, life-threatening complication of severe hypothyroidism, marked by altered sensorium, hypothermia, respiratory failure, hyponatremia, and hypotension. While commonly triggered by cold exposure and infections, studies show it can also result from medications like Amiodarone (a class III antiarrhythmic), Antipsychotics and very rarely from Benzodiazepines. Our patient, a 77-year-old Hypertensive woman, who had been on chronic Risperidone therapy, was treated with Amiodarone infusion for atrial fibrillation and later received Diazepam for suspected extrapyramidal symptoms. This combination likely pushed an already compromised thyroid function beyond its critical threshold, leading to full-blown myxedema coma. This case report highlights the need for cautious use of antipsychotics, Amiodarone and Benzodiazepines even in subjects not known to be hypothyroid, regular thyroid monitoring in them and effective treatment strategies.

**Keywords:** Myxedema coma, hypothyroidism, amiodarone, antipsychotic, benzodiazepine

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## Introduction

Risperidone is an atypical antipsychotic used to treat schizophrenia and bipolar disorder by blocking dopamine D2 and serotonin 5-HT<sub>2A</sub> receptors in the brain, reducing psychotic symptoms, mood swings, and aggression.<sup>2,7,11,14</sup> Amiodarone is a Class III antiarrhythmic medication that blocks cardiac sodium, potassium, and calcium channels, as well as beta-adrenoreceptors. It prolongs repolarization during the third phase of the cardiac action potential, stabilizing heart rhythm.<sup>1,3</sup> Benzodiazepines are a class of psychoactive drugs that enhance the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) at GABA-A receptors, producing sedative, anxiolytic, muscle-relaxant, and anticonvulsant effects. They are commonly used to treat anxiety, insomnia, seizures, and muscle spasms.<sup>16</sup> Although rare, studies indicate that each of these three medications can precipitate Myxedema Coma (MC)—a life-threatening complication of severe hypothyroidism.<sup>1,3,16</sup> MC is characterized by metabolic suppression. Profound hypothermia, hyponatremia, confusion or coma, bradycardia, and anasarca are the Common Clinical Presentations, Signs and Symptoms of the disease.<sup>1,8,15</sup> Common triggers include stress, infection, GI bleed and sepsis. Recent reports estimate a high mortality rate of 40%, with approximately 220,000 cases occurring globally each year,<sup>1</sup> predominantly in women and older adults. Given its severity and rarity, recognizing risk factors and ensuring prompt treatment are crucial for improving patient outcome. Here, we present a case of a 77-year-old woman on prolonged Risperidone use in whom the simultaneous use of Amiodarone and Benzodiazepine precipitated MC.

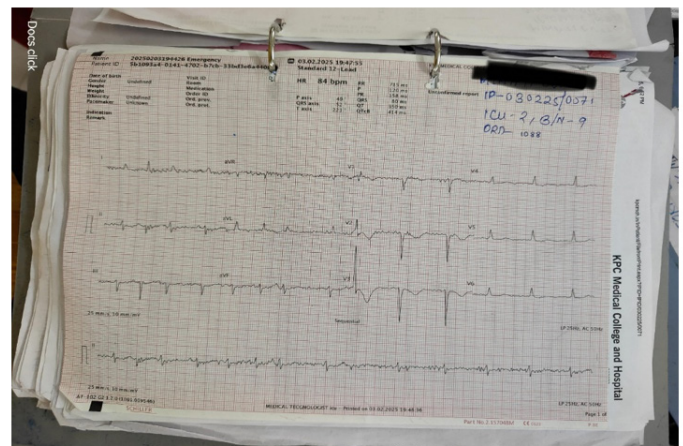
## Case presentation

A 77-year-old hypertensive female with no known thyroid dysfunction history presented to our emergency department with bilateral pitting pedal edema, and generalized weakness for the past 1 week, which had worsened over the last 2-3 days. Her caretaker reported that she had been taking Risperidone regularly for the past three years for psychotic symptoms.

On examination, her vitals were:

- I. BP: 130/80 mmHg
- II. Pulse rate: 84/min
- III. SPO<sub>2</sub>: 90% on room air
- IV. Temperature: 97.1°F
- V. CBG: 100 mg/dL

Fine basal crepitations were heard in both lungs. Emergency blood reports showed Hyponatremia (Na 114), Hypokalemia (K 2.9), Anemia (Hb 7), and Hypoalbuminemia (Albumin 2.4). ECG showed low voltage waves and atrial fibrillation (AF), for which she was started on IV Amiodarone infusion (300 mg/50 mL at 100 mL/hr) and shifted to the ICU.



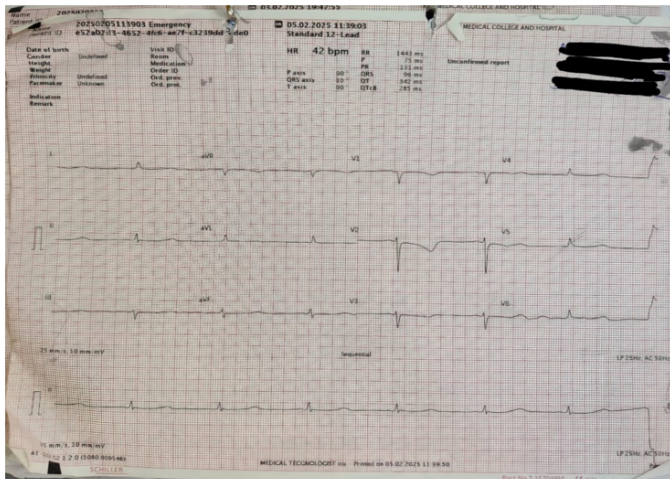
Emergency ECG showing low voltage waves and AF, prompting Amiodarone infusion

## ICU course and deterioration

In the ICU, she was managed conservatively for heart failure and dyselectrolytemia. However, she soon became progressively restless and had dystonia. Suspecting extrapyramidal symptoms Risperidone was omitted and she was given Tab Diazepam 5mg 2 such stat.

The next day, she became unresponsive with altered sensorium, vitals:

- I. Heart rate: 42/min
- II. Bp : 90/50 mmHg
- III. Progression of pedal edema to anasarca (facial swelling, a firm edematous abdomen, and 3+ pitting pedal edema)
- IV. Cold extremities
- V. Axillary temperature: 93 degree F
- VI. B/L plantar: Extensor



ICU ECG Showing low voltage waves and Bradycardia

No meningeal signs, no focal neurological deficits found.

A stat thyroid panel revealed:

- I. TSH: 29.43  $\mu$ IU/mL (normal: 0.358-3.742)
- II. Free T4: 0.68 ng/dL (normal: 0.76-1.86)

Myxedema coma score- thermoregulatory dysfunction -10 points

Stupor-10 points

Sluggish IPS – 15 points

Heart Rate (40-49 bpm) – 20 points

Hypotension – 10 points

Hyponatremia – 10 points

Total 75 (greater than 60), highly suggestive of Myxedema Coma (MC).

## Management and outcome

- I. IV Hydrocortisone 200 mg stat, followed by 100 mg TID
- II. Levothyroxine (Thyrox) 200 mcg stat via Ryle's tube, followed by 100 mcg OD
- III. Active warming with blankets

## IV. Immediate discontinuation of Amiodarone, Risperidone, and Diazepam

Her heart rate stabilized within a few hours, her temperature normalized (98°F), and within three days, she regained orientation to time, place, and person, with marked resolution of edema. She was then shifted to the general ward.

## Further workup and follow-up

- I. Endocrinology consultation: Thyroxine dose was adjusted to 125 mcg OD before breakfast.
- II. Steroid tapering was initiated.
- III. Anti-TPO antibody levels were raised- 2032 U/ml (normal <60 U/ml)
- IV. 2D Echo revealed ischemic heart disease, explaining her AF on admission.
- V. Low hemoglobin was managed with two units of PRBC transfusion.
- VI. Cardiology and nephrology consultations were sought.

She clinically recovered within seven days. However, her psychotic symptoms recurred, and she experienced 2-3 violent manic episodes. No antipsychotics or benzodiazepines were administered.

She was discharged for follow-up with psychiatry, endocrinology, and general medicine OPDs.



Our patient after complete recovery from Myxedema Coma

## Discussion

**Myxedema** coma is a rare but life-threatening complication of severe hypothyroidism that requires urgent recognition and management.<sup>1,4</sup> It is more prevalent in females, particularly those with a history of hypothyroidism, and occurs in approximately 1% of the

hypothyroid population. The condition is characterized by progressive metabolic depression and organ failure, with mortality rates ranging between 20-50% if left untreated.<sup>1,4,15</sup>

The symptoms of myxedema coma involve multiple systemic disturbances:

**Respiratory depression:** A reduced respiratory drive leads to CO<sub>2</sub> retention, causing respiratory acidosis and hypoventilation.<sup>1,5</sup>

**Fluid imbalance:** Inappropriate antidiuretic hormone (ADH) secretion results in fluid retention and myxedema.<sup>1</sup>

**Severe metabolic depression:** The markedly reduced metabolic rate leads to hypothermia, bradycardia, and decreased cardiac output, all of which contribute to cardiovascular collapse.<sup>1,5,15</sup>

Common triggers include infections, trauma, cold exposure, and sepsis. Simultaneous use of drugs like Amiodarone, and Benzodiazepines in chronic Antipsychotic use, as seen in our case, represents an extremely rare trigger for myxedema coma even in patients not known to be hypothyroid, by interfering with thyroid hormone metabolism. In ICU set up Coma can be due to various other causes including encephalitis, meningitis, hepatic coma, stroke etc. Moreover, Myxedema Coma being considered as a rare entity in Indian Subcontinent, and Sick Euthyroid Syndrome being commonly seen in ERs and ICUs, thyroid profile is not routinely done in these patients. Diagnosis is thus incredibly challenging.

**Amiodarone** is well known for its effects on thyroid gland. It contains 37% iodine, which via Wolff Chaikoff effect induces hypothyroidism. Its metabolite desethylamiodarone can induce thyroiditis and can cause both hypothyroidism and thyrotoxicosis.<sup>3</sup>

**Benzodiazepines**, while generally not considered primary triggers for myxedema coma, have sedative effects that can further suppress respiratory drive and worsen metabolic depression, exacerbating an existing hypothyroid state.<sup>16</sup>

Our patient, who had been on chronic Risperidone therapy, was treated with Amiodarone infusion for atrial fibrillation and later received Diazepam for suspected extrapyramidal symptoms. This combination likely pushed an already compromised thyroid function beyond its critical threshold, leading to full-blown myxedema coma.

Similar case reports exist, where Use of single agent, like only Amiodarone<sup>3</sup> or only Antipsychotics like Haloperidol<sup>2,11</sup> or only Benzodiazepines<sup>16</sup> have precipitated an MC attack. But our case highlights MC attack precipitated by polypharmacy in thyroid status unknown patient, making it unique and rare.

## Conclusion

This case highlights a rare but critical occurrence of medication-induced myxedema coma in an elderly patient, emphasizing the importance of recognizing iatrogenic triggers even in individuals not known to be hypothyroid. The interplay between Amiodarone, Risperidone, and Benzodiazepines likely precipitated this life-threatening endocrine emergency, underscoring the need for caution when prescribing these medications, especially in geriatric population. Successful management in this case was achieved through early recognition, interdisciplinary collaboration, and prompt initiation of appropriate therapies, including thyroid hormone replacement, corticosteroids, and supportive care.<sup>1,5,9</sup> The use of a clinical scoring tool also played a role in guiding diagnosis and treatment,<sup>13</sup> helping to minimize ICU stay and long-term complications.

In ICU set up Thyroid profile testing is generally avoided because of quite common occurrence of Sick Euthyroid Syndrome. But in

these patients the possibility of Myxedema Coma must always be kept in mind. Despite its practical insights, this report is limited by its single-case nature, making generalizability challenging. Whether any single drug or all the three drugs contributed to precipitate this MC attack, remains a mystery. There remains a possibility that the patient was already a case of undiagnosed MYXEDEMA Madness,<sup>14</sup> for which she was requiring prolonged Risperidone therapy. We must thus screen all chronic psychosis patients for hypothyroid state, and even for absolute indications, use Amiodarone and Benzodiazepines cautiously in them to avoid fatal complications.

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None.

## Additional informations

### Disclosure

**Human subjects:** Consent was obtained by all participants in this study.

### Conflicts of interest

In Compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services Info:** All authors have declared that no financial support was received from any organization for the Submitted work.

### Financial relationships

All authors have declared that they have no financial Relationships at present or within the previous three years with any organizations that might have an Interest in the submitted work.

### Other relationships

All authors have declared that there are no other Relationships or activities that could appear to have influenced the submitted work.

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