Journal of Community Hospital Internal Medicine Perspectives

Volume 14 | Issue 6 Article 22

2024

Atypical Thyroid Stimulating Hormone Levels in Myxedema Coma Complicated by Severe Sepsis

Nazmul Hasan
UCI Medical Center, nhasan1@hs.uci.edu

Daniel Yang
UCI Medical Center

Thaer Othman
UCI Medical Center

Jenny Dai-Ju
UCI Medical Center

Recommended Citation

Hasan, Nazmul; Yang, Daniel; Othman, Thaer; and Dai-Ju, Jenny (2024) "Atypical Thyroid Stimulating Hormone Levels in Myxedema Coma Complicated by Severe Sepsis," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 14: Iss. 6, Article 22.
DOI: 10.55729/2000-9666.1412
Available at: https://scholarlycommons.gbmc.org/jchimp/vol14/iss6/22

CASE REPORT

Atypical Thyroid Stimulating Hormone Levels in Myxedema Coma Complicated by Severe Sepsis

Nazmul Hasan*, Daniel Yang, Thaer Othman, Jenny Dai-Ju

UCI Medical Center, USA

Abstract

Most cases of Myxedema Coma are associated with primary hypothyroidism characterized by significantly elevated thyroid stimulating hormone (TSH) levels. However, this case presents an atypical manifestation of myxedema coma with low TSH levels despite severe hypothyroidism. The rarity of this presentation lies in the absence of central lesions typically responsible for such TSH suppression. This highlights a critical consideration: the profound impact of severe sepsis on thyroid hormone regulation and the hypothalamus-pituitary-thyroid axis.

Keywords: Myxedema, Myxedema coma, Hypothyroidism, TSH

1. Introduction

Myxedema Coma is a severe manifestation of severe hypothyroidism, which carries a mortality rate between 30 and 60%.[2] It can be precipitated by any form of acute stressor and is more commonly seen in older women, particularly with a background of poorly controlled hypothyroidism. The presentation may be broad but often may present with altered mental status, hypothermia, bradycardia, and serological derangements, including hyponatremia and hypoglycemia[1] (Fig. 1).

Because most cases are associated with primary hypothyroidism, it is often associated with low free T4 (FT4) with markedly elevated TSH. However not all cases present with this lab pattern as thyroid function biomarkers can also be affected by a component of central hypothyroidism and other clinical factors which may compromise the secretion of TSH.

Thyroid hormone imbalances can vary greatly between patients, but most have a degree of low free thyroxine. Clinicians should not wait for lab confirmation to start treatment for critical presentation. Treatment includes levothyroxine with a loading dose of 200–400 mcg IV followed by 50–100 mcg IV daily until the patient is able to take T4 orally. Because TSH levels may vary based on a multitude of factors, treatment is guided using FT4 and T3 levels. Although most clinicians are aware of treatment with thyroid hormone replacement, a critical pitfall to keep in mind is the importance of

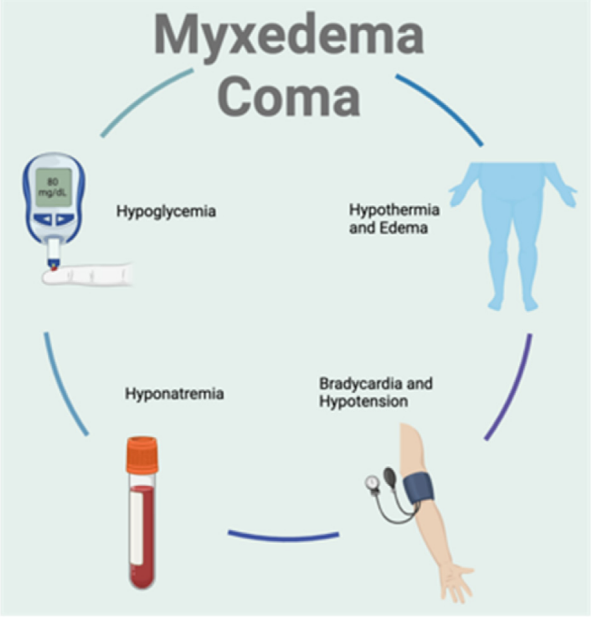

Fig. 1. Clinical features of myxedema coma.[7]

Received 10 April 2024; revised 18 August 2024; accepted 29 August 2024.
Available online 2 November 2024

* Corresponding author.
E-mail address: nazmulhasan@uci.edu (N. Hasan).

https://doi.org/10.55729/2000-9666.1412

testing and empirically treating for adrenal insufficiency.[1] This is because replacing thyroid hormone first will catabolize any residual cortisol and may hasten clinical deterioration.

2. Case presentation

A 60-year-old female with unknown past medical history was found down at her home covered in feces. On presentation, she was hypothermic to 89 °F, had a blood pressure of 90/70, and had a pulse of 62 with an EKG showing sinus bradycardia. Physical exam findings included hair loss, thick tongue, 1+ non-pitting edema bilaterally, warm and dry skin extremities, and delayed relaxation of brachial reflexes. Labs were notable for Sodium of 123 mmol/L and blood glucose of 80 mg/dL. She was found to have an acute kidney injury with creatinine 3.1 mg/dL, which improved after fluid resuscitation. CPK levels were normal. Complete blood counts revealed mild normocytic anemia with Hemoglobin of 10 g/dL. Thyroid function testing revealed only a mildly elevated TSH of 13 μIU/mL with free T4 <0.025 pmol/L. Anti-TPO antibodies were elevated at 157 IU/mL. MRI of the Sella was negative for sellar enlargement or pituitary lesions. Thyroid ultrasound showed atrophic heterogeneous bilateral thyroid lobes. Assessment for hypopituitarism did not show any significant deficiencies with Cortisol 45 μg/dL, ACTH 11 pg/mL prior to any steroid administration, LH 0.5 IU/L, FSH 8.5 IU/L, IGF-33 ng/mL, Free Testosterone 1.7 pg/mL, and Total Testosterone 10 ng/dL. During her hospital course, she was found to have septic shock with pneumoperitoneum on abdominal imaging (Fig. 2).

She was taken for emergent exploratory laparotomy and was found to have a perforated sigmoid colon requiring sigmoid colectomy. Upon initial evaluation, she was empirically administered Dexamethasone 4 mg until adrenal insufficiency was ruled out. This preemptive measure was undertaken because introducing thyroid hormone replacement in patients with undiagnosed adrenal insufficiency may precipitate an adrenal crisis. Dexamethasone was chosen over other steroids due to its potency as a glucocorticoid, and its minimal mineralocorticoid effects decreased the risk of fluid retention, which can be a concern with other steroids that have higher mineralocorticoid activity. Dexamethasone at the 4 mg dose provided an immediate and effective response with a long duration of action, allowing for sustained coverage while further workup was underway.

Once adrenal insufficiency was excluded, treatment with intravenous levothyroxine 100 mcg was initiated. A lower dose was chosen due to the patient's age and cardiac risk. Subsequently, as the patient's condition stabilized and she was able to swallow and absorb medications taken orally, she was transitioned to oral Synthroid. The oral dose of Synthroid is higher than the IV dose as oral formulations have lower bioavailability; in this case, 150 mcg was used with the improvement of her thyroid function tests to TSH of 2.7 μIU/mL and free T4 of 1.56 pmol/L at discharge.

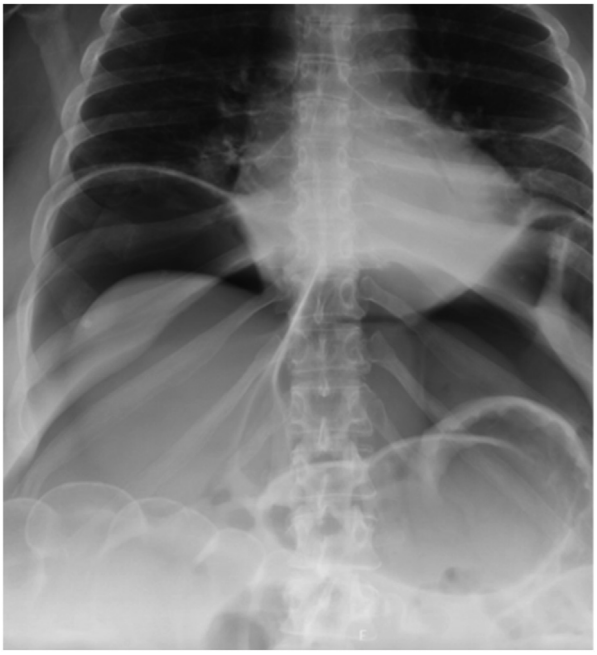

Fig. 2. Large volume pneumoperitoneum on upright KUB.

3. Discussion

The vast majority of Myxedema Coma cases are associated with primary hypothyroidism. Primary hypothyroidism occurs from insults to the thyroid gland itself, resulting in the inability to produce thyroid hormone. This can happen in a multitude of different ways, the most common of which include iatrogenic from surgery or radiation exposure, certain medications, and thyroiditis from autoimmune conditions such as Hashimoto's thyroiditis, viral infections, and postpartum inflammation. Greater than 95% of cases of myxedema are associated with primary hypothyroidism,[2] where there are low thyroxine levels with a physiologic response from the hypothalamus and pituitary to increase the production of thyroid hormone by producing TSH. In cases of myxedema coma secondary to primary hypothyroidism, the TSH levels are markedly elevated, often greater than 100 μIU/mL, with a case series in Spain reporting a typical range between 28

and 153 μIU/mL.[3] When the TSH is not as markedly elevated as we would expect or inappropriately normal, the interplay of a multitude of different factors must be considered, the first of which is central hypothyroidism.

In central hypothyroidism, TSH secretion may be impaired, leading to lower-than-expected TSH levels with a range typically between 0.43 and 9.85 μIU/mL.[3] Central hypothyroidism occurs due to dysfunction at the level of the pituitary gland or hypothalamus. Common causes include pituitary tumors, brain surgery or direct brain radiation, head trauma, and infiltrative diseases such as sarcoidosis and hemochromatosis. Our patient underwent MRI pituitary imaging, which did not reveal any mass lesions or empty sella. In addition, a hormonal assessment of her pituitary function with Adrenocorticotropic Hormone (ACTH), Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), Insulin-like Growth Factor (IGF) did not show any significant deficiency, which made hypopituitarism less likely in this case. Aside from direct central lesions, another variable that can lead to central hypothyroidism is medications. The interplay of medications and thyroid function is complex and can cause both direct injury to the gland and indirect alteration to the regulatory pathways. The two more commonly thought of medications that have direct toxic effects on the thyroid are amiodarone and lithium. Other agents affect thyroid balance by interfering with the hypothalamus–pituitary axis and decreasing TSH secretion. These include glucocorticoids, dopamine agonists, interferon alpha, and metformin 4. Ultimately, a thorough medication review was done for our patient. However, it did not yield any medications that are known to cause thyroid dysfunction.

Our patient was found to have anti thyroid peroxidase (TPO) antibodies and atrophic bilateral thyroid lobes on ultrasound which suggests a component of primary hypothyroidism. In this case we would expect to see a much more profoundly elevated TSH level however her TSH was only 13 μIU/mL. This brings us to an important consideration which is the effect of acute illness on the balance of thyroid hormones (Table 1).

Concurrent illnesses, especially severe ones, can affect the thyroid function tests, including TSH levels. Our body's response to critical illness involves complex hormonal changes which affect the hypothalamus-pituitary-thyroid axis. The mechanism behind this involves inflammation associated stressors in the bodily and associated cytokines released during illness. They decrease TSH by affecting these regular feedback loops and interfering with the peripheral metabolism of thyroid hormones (Fig. 3).

The levels of thyroxine may also be compromised due to this later effect, in addition to the fact that such cytokines can also alter circulating thyroid hormone-binding proteins. Previous studies involving patients with infections including COVID-19 revealed that the main cytokines associated with this are TNF alpha, Interferon-gamma, IL-1, and IL-6.[5] The degree of inadequate TSH secretion, in particular, is oftentimes proportional to the severity of the illness and typically improves after recovery

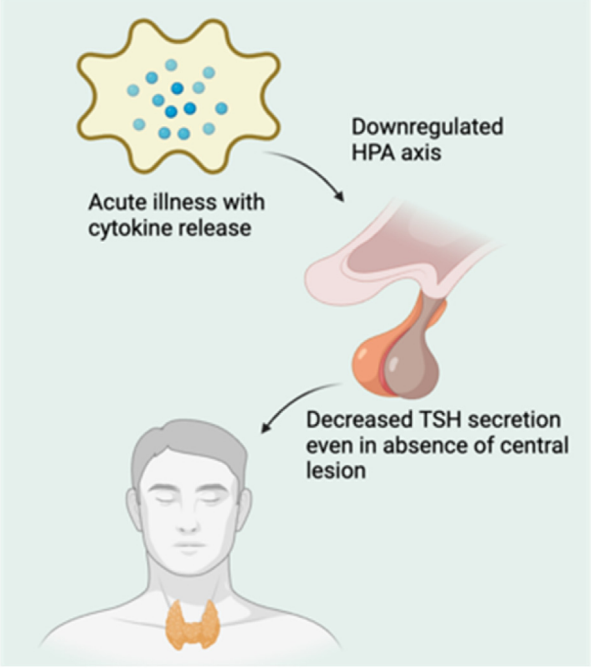

Fig. 3. Downregulated TSH secretion.[8]

Table 1. Differential diagnosis considerations for atypical TSH levels in myxedema coma.

Condition	Characteristic Features	Diagnostic Differentiation
Primary Hypothyroidism	Elevated TSH, low free T4	Confirmed with elevated anti-TPO antibodies
Central Hypothyroidism	Low/normal TSH, low free T4	Excluded by absence of pituitary lesions on MRI
Non-thyroidal Illness Syndrome	Variable TSH, low free T4, often in critical illness	Considered due to acute illness but less likely without recovery of thyroid function
Sepsis-Induced Hypothyroidism	Low TSH due to cytokine effect	Correlated with septic presentation and resolved with sepsis management

from the acute illness. Ultimately, our patient was found to have severe sepsis from bowel perforation, and this presentation was likely a critical driver of why her TSH levels may not have risen as expected despite underlying primary hypothyroidism. In addition to this aforementioned TSH suppression in critically ill patients, there is also a slower rise in TSH in the elderly, which may further confound thyroid testing results.[6] Overall, because of these factors, the assessment of myxedema coma should not rely solely on TSH.

4. Conclusion

Although most cases of Myxedema Coma occur in a background of primary hypothyroidism with an associated rise in TSH, this hormone may not manifest profound elevations due to a variety of factors. Critical illness, namely severe sepsis, stimulates elevations in many inflammatory cytokines, which disrupt the body's physiologic response to release TSH and can manifest with suppressed levels of TSH, even in myxedema coma patients without any other pituitary or central lesions. Despite the variability in TSH in critically ill patients, the entire clinical presentation should be considered to make the diagnosis of myxedema coma. Although severely low free thyroxine may be used to guide diagnosis and therapy, prompt treatment should be initiated even before serological markers result when clinical suspicion is high in critical patients.

Ethics information

None.

Funding

No funding was provided for this study.

Conflict of interest

There are no conflicts of interest to declare.

Abbreviations

TSH	Thyroid Stimulating Hormone
FT4	Free Thyroxine
T3	Triiodothyronine
ACTH	Adrenocorticotropic Hormone
LH	Luteinizing Hormone
FSH	Follicle-Stimulating Hormone
IGF	Insulin-like Growth Factor
CPK	Creatine Phosphokinase
EKG	Electrocardiogram
TPO	Thyroid Peroxidase
MRI	Magnetic Resonance Imaging
KUB	Kidneys, Ureters, and Bladder (X-ray)
TNF	Tumor Necrosis Factor
IL	Interleukin

References

1. Wall CR. Myxedema coma: diagnosis and treatment. *Am Fam Physician*. 2000;62(11):2485–2490. https://pubmed.ncbi.nlm.nih.gov/11130234/.
2. Zhu Y, Qiu W, Deng M, Zhu X. Myxedema coma: a case report of pediatric emergency care. *Medicine (Baltim)*. 2017;96(21):e6952. https://doi.org/10.1097/MD.0000000000006952.
3. Rodriguez I, Fluiters E, Pérez-Méndez LF, Luna R, Páramo C, García-Mayor RV. Factors associated with mortality of patients with myxoedema coma: a prospective study in 11 cases treated in a single institution. *J Endocrinol*. 2004;180(2):347–350. https://doi.org/10.1677/joe.0.1800347.
4. Razvi S, Bhana S, Mrabeti S. Challenges in interpreting thyroid stimulating hormone results in the diagnosis of thyroid dysfunction. *J Thyroid Res*. 2019;2019:4106816. https://doi.org/10.1155/2019/4106816, 8.
5. Croce L, Gangemi D, Ancona G, et al. The cytokine storm and thyroid hormone changes in COVID-19. *J Endocrinol Invest*. 2021;44(5):891–904. https://doi.org/10.1007/s40618-021-01506-7.
6. Elshimy G, Chippa V, Correa R. Myxedema. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2023, August 14. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK545193/.
7. Hasan N. *Clinical features of myxedema coma. Created with BioRender.com*. 2024.
8. Hasan N. *Downregulated TSH secretion. Created with BioRender.com*. 2024.