International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Myxedema Coma in Patient with COVID-19 in Hospital of Second Level of Care; A Case Report

Miguel A. Serna Reyes[1], Estanislao Antonio Calixto[2], Erick M. Ramirez Rayón[3], Paulina Janet Martínez Juárez[4], Yessica Daniela Rios Miranda[5]

[1, 3, 4, 5]Hospital General de Acapulco, Guerrero, Internal Medicine Department

[2]Hospital de Alta Especialidad de Veracruz, SESVER, Internal Medicine Department

Abstract: ***Background: Myxedema coma is the severe manifestation of severe hypothyroidism, it occurs in the context of chronically poorly controlled hypothyroidism, it is generally triggered by situations of physical stress, infections being found first, with respiratory infections being an important cause. During the current COVID 19 pandemic, the incidence of respiratory infections has been increasing. Case presentation: A 53 - year - old female patient with a history of thyroidectomy 28 years earlier, comes for care after presenting Sars - Cov2 infection with clinical and biochemical data of severe hypothyroidism and in turn myxedema coma, despite the start of replacement of steroids and with thyroid hormone replacement, the patient had an unfavorable evolution associated with underlying COVID, respiratory distress syndrome associated with it, and subsequent death. Conclusions: Myxedema coma is an entity triggered by infectious processes, among them is Sars - Cov2 in the context of poorly treated severe hypothyroidism, its detection and timely treatment must be done early and based on a high diagnostic suspicion based on the clinical and laboratory findings presented in this article.***

Keywords: Myxedema, Hypothyroidism, COVID-19, Sars - CoV - 2.

1. Background

Myxedema coma is an endocrinological emergency, it is a consequence of severe hypothyroidism, which in turn is the result of severe and prolonged depletion of thyroid hormones; is triggered by a situation of physical stress such as diseases or non - thyroid factors that cause extremely serious generalized systemic involvement, the diagnosis requires a high level of clinical suspicion. The typical picture is lethargy that progresses to stupor and finally to coma; and myxedema coma does not necessarily occur with a coma in the patient, so it would be more correct to call it "myxedema state" (1)

It is a rare condition, whose decrease in cases is related to the early detection of hypothyroidism and its effective treatment, it has an estimated incidence of 0.22 people/million/year. (1) The mortality rate historically reached 60 to 80%, but it is currently estimated at around 20 - 25% due to advances in intensive care and a better understanding of the underlying pathophysiological processes. (2) SARS - CoV - 2 infection is associated with significant pulmonary and cardiac morbidity, but there is limited knowledge of the endocrine manifestations of Sars - Cov2 disease. (3)

2. Clinical Case

A 53 - year - old female patient, from Guerrero, Mexico, with a housewife occupation, with the following data of importance: History of thyroidectomy 28 years ago due to an apparent unspecified tumor, Hypothyroidism treated with levothyroxine at an unspecified dose, the degree of adherence to treatment was unknown.

Her current condition began 17 days prior to admission, after extraction of the lower right molar, beginning with bleeding after the procedure for approximately 48 hours, which is why she is taken to a private doctor who prescribes unspecified medical treatment, presenting partial improvement of the symptomatology ceding the hemorrhage. A few days later, she began with generalized colic - type abdominal distension and pain, and later diarrheal stools were added, and she was taken again to a private doctor, performing laboratory tests, referring to coagulation and blood count alterations, which is why she was transferred to a private clinic where she was treated. for 3 days receiving unspecified treatment; During a stay in a private unit, a deterioration in alert status, respiratory distress with desaturation was documented. Therefore, advanced management of the airway was initiated, being transferred 15 days after the onset of symptoms to this unit for care. Subsequently, given the patient's general conditions, it was decided to enter the intensive care unit, which was also authorized as a covidary (Figure 1).

3. Clinical Findings

We found a patient with an endomorphic constitution, in the semi - Fowler position; under sedation with Midazolam and Propofol, RASS - 5, cold skin 34°C, pupils with isocoria 3 mm, with bilateral proptosis, bilateral photomotor reflex present, absent corneal, cough and gag reflexes, oral cavity with incomplete teeth, macroglossia with orotracheal cannula 21 cm from the dental arch, wide neck, with a scar in the suprasternal region, short chest, presence of a right subclavian central venous catheter, respiratory movements synchronous to the ventilator, with the following parameters: inspired fraction of oxygen 90%, PEEP 8, Breathing frequency 24, tidal volume 380, fine crackling rales are heard in both lung bases, pleuropulmonary syndrome was not integrated, cardiac examination was supported by norepinephrine - type vasoactive amines, with blood pressure 80/40 mmHg, with hypophonic heart sounds and

dynamic hiccups with a heart rate of 35 BPM, no murmurs or added noises were auscultated. Globose abdomen at the expense of panniculus adiposus, with hypoactive peristalsis, soft, depressible, intact limbs, with edema + no pitting in all four limbs, capillary refill 5 seconds.

Laboratory tests upon admission: A (-), Hb: 5.72 g/dL, HCT: 16.6%, MCV: 99.3 fL, HCM: 34.2 pg, PQL: 154 K/mcL, Leukocytes 2.7 K/uL, Neutrophils: 76%, Lymphocytes 21%, Monocytes: 1%, Bands: 1%, Blasts: 0%, Glucose: 103 mg/dL, Urea Nitrogen: 12 mg/dL, Urea: 25.6 mg/dL, Creatinine: 1.26 mg/ dL, eGFR: 49 mL/min/1.73m2, Uric Acid: 5.2 mg/dL, Sodium: 120 mEq/L, Potassium: 3.8 mEq/L, Chloride: 84 mEq/L, Serum Calcium: 7.2 mg/dL, Cholesterol: 229 mg/dL, BT: 0.8 mg/dL, BD: 0.2 mg/dL, BI: 0.6 mg/dL, Alkaline Phosphatase: 79 U/L, AST: 66 mg/dL, ALT: 27 mg/dL, Proteins: 5.1 g/100ml, Albumin: 5.1 g/100ml, Globulins: 2.4 g/100ml, Lactic dehydrogenase 288 u/L. Blood gas: 7.4, PCO2: 31.1 mmHg, pO2: 57.3 mmHg, SO2%: 91.4, BEecf: - 1.1mmol/L, HCO3: 22.8mmol/L.

Given the suspected diagnosis and having a Popoveniuc index of 130, treatment with levothyroxine was started with prior administration of corticosteroids, as well as electrolyte replacement.

The day after the patient was admitted, the result of the Thyroid profile: TSH: 37.68, TOTAL T - 4: 1.66, free T - 4: 0.07, t - 3 uptake: 35.3, free t - 3: 1.09, free thyroxine index: 0.59, protein iodine: 0.84. Confirming the diagnostic suspicion, given the patient's conditions, she presents greater hemodynamic instability with subsequent death. The day after death, a PCR result for SARS COV 2 is obtained, resulting positive.

4. Discussion

In the present clinical case, it shows that to start management, a high index of suspicion is initially required, leaving diagnostic confirmation as well as complementary studies in the background.

The patient presented a serious systemic condition as a risk factor for the presentation of myxedema coma. Among the most common triggers of myxedema coma we will find all those systemic conditions, and even local ones, such as infections, mainly of the respiratory tract, although to a lesser degree they have also been described urinary and soft tissue infections, heart failure, acute myocardial infarction, cerebrovascular event, including the use of antiarrhythmic drugs and tyrosine kinase inhibitors. (1)

Thyroid dysfunction is a common condition in patients with COVID-19 infection. Meanwhile, SARS - CoV - 2 could be considered responsible for the appearance of subacute thyroiditis, among other thyroid disorders. (4)

The cardinal signs and symptoms of myxedema coma which were present in the current clinical case are hypothermia and decreased sensorium, being less specific bradycardia, hypotension, hyponatremia and hypoventilation, directly proportional to the degree of severity of hypothyroidism will be the affected systems. (2)

Respiratory compromise secondary to infection by the Sars - Cov2 virus in its severe clinical presentation, like myxedema coma, will share clinical characteristics such as silent hypoxemia and respiratory acidosis. Within the respiratory muscle compromise typical of Sars - Cov2 infection, it will be aggravated by hypothyroid myopathy, obesity and total or partial obstruction of the airway due to edema of the nasopharynx and larynx; there is an exacerbation of hypoventilation, predisposing to pneumonia and vice versa, creating a vicious circle that is difficult to control. Due to the high level of respiratory compromise, both due to the clinical presentation in its severe form of Sars - Cov2 infection, as well as in myxedema coma, and despite the start of thyroid hormone replacement, there is a report of a prolonged requirement for ventilatory mechanical support. (2)

Although due to the relevance and emphasis of our exposed clinical case, the respiratory system is initially listed, the neurological manifestations are no less important, having a leading role in the clinical presentation of myxedema coma. Typical clinical features include: lethargy, obtundation, drowsiness, mental retardation, memory deficits (including amnesia), cognitive dysfunction, depression, and psychosis (myxedema dementia). Also peripheral sensory and motor neuropathy, as well as cerebellar signs, motor symptoms such as jerky movements in the hands and feet; ataxia and adiadochokinesia can be found in up to 25% of focal or generalized seizures possibly related to hyponatremia, hypoxia and hypoglycemia. The underlying mechanism of these neurological alterations would be due, in large part, to a decrease in the flow and metabolism of glucose in the brain. As an agent added to the decreased state of consciousness, it is important to mention hypoxemia, even described and documented in the patient. (1, 5)

The patient presented clinical cardiovascular manifestations resulting from altered inotropism and chronotropism, including this decrease in cardiac output with presentation of pump failure. Relating the cardiovascular alterations present both in myxedema coma and in cases of severe Sars - Cov2 infection, it has been described that the transmembrane serine protease 2 (TMPRSS2) cleaves the S protein of the virus, causing its internalization through ACE2, induced by the S2 subunit; If there is damage to ACE2, its regulatory function with angiotensin II is lost, promoting a proinflammatory state, mainly affecting the lung. In addition to endothelial dysfunction, there is activation of the innate immune system that causes cytokine storms, causing damage to the microvascular system, hypoxemia, and activation of the coagulation system with inhibition of fibrinolysis. All these alterations lead to disseminated intravascular coagulation. . (6)

The EKG findings in the clinical case coincide with some of those typically found, such as bradycardia, different degrees of block, low voltage, flat or inverted T waves and prolongation of the Q - T interval that can result in polymorphic ventricular tachycardia (torsades de pointes). In the presence of hypothermia, J or Osborn waves are also observed (extra deflection at the end of the QRS that is better evidenced in the inferior and lateral leads) (2)

On clinical examination, an obvious and important feature is characteristically non - pitting edema of the extremities, which is due to the accumulation of mucopolysaccharides and water at the level of interstitial tissue. Said edema at the facial level will be mostly located at the peri - orbital level, giving the "bloated face" (7)

The temperature records in our patient ranged around 34°C, values between 26º and 32º are classically described; due to the decrease in thermogenesis due to abolished metabolism, which will be aggravating these temperatures if they exist at the same time, hypoglycemia or severe infectious processes, even masking hypothermia, causing vascular collapse and with a higher risk of mortality. (8)

Patients with myxedema coma may have primary adrenal insufficiency (AI), sometimes associated with primary autoimmune hypothyroidism (Schmidt's syndrome); or secondary AI, most often associated with central hypothyroidism, which may go unnoticed. The administration of levothyroxine accelerates the hepatic metabolism of cortisol and for this reason, prior to the administration of thyroid hormone, the start of systemic glucocorticoids should be ensured to avoid the risk of triggering an acute adrenal crisis, which is why it was started immediately. after clinical suspicion with subsequent initiation of levothyroxine. (7)

Among the biochemical and hematological alterations that the patient suffered are hydroelectrolytic alterations, hyponatremia being the main one, and this is due to the decrease in renal excretion of free water caused by less availability of water to the distal nephron and excess of Antidiuretic hormone. This syndrome of inappropriate secretion of antidiuretic hormone would be aggravated by the concomitant presence of adrenal insufficiency. Severe hyponatremia (105 - 120 mEq/l) contributes to coma and increases the mortality rate in critically ill patients by 60 times more than in patients with normonatremia. (2)

Both at the stomach and intestinal level, alterations are observed in the context of myxedema coma, due to a hormonal decrease in T3 and T3, which will lead to a decrease in vasoactive intestinal polypeptide, which in turn decreases intestinal motility and changes in food absorption. Within the clinical picture of both myxedema coma and COVID19 they share nausea, vomiting, diarrhea. (1)

Early diagnosis is essential, if there is a delay in treatment, the prognosis worsens. To make the diagnosis of myxedema coma, we suspect such a condition based on the history such as thyroidectomy and the aforementioned clinical manifestations. . (9)

The definitive diagnosis cannot be made based on laboratory studies, nor can treatment be delayed while waiting for them. In turn, it will be necessary to differentiate manifest simple disease and myxedema coma. In the hormonal profile of the primary disease, it is characterized by a decrease in free or total T4 and T3, with a marked increase in thyrotropin (TSH). It is necessary to emphasize that the diagnosis is based on clinical symptoms and that one should not wait for results in the thyroid profile to start treatment, as previously mentioned. (9)

In 2014, an assessment system was proposed in order to more easily diagnose the clinical picture, made up of 6 parameters: dysfunction of the thermoregulatory system, altered state of consciousness, dysfunction of the gastrointestinal system, presence of a precipitating event, cardiovascular dysfunction and metabolic disturbances. A score is assigned to each parameter, according to the sum of all the scores and the final result is determined based on the score (Table 1).

- Greater than 60 is highly suggestive/diagnostic of myxedema coma.
- Between 29 - 59 is suggestive of risk of myxedema coma.
- Less than 25 makes the diagnosis of myxedema coma unlikely. (10)

Once our diagnostic suspicion was established and supported by the Popoveniuc score, we proceeded to start treatment immediately with glucocorticoids, because severe hypothyroidism induces a lower adrenal response to stress and they should be administered before thyroid replacement, since otherwise, a adrenal crisis. (11)

Hydrocortisone is administered in stress doses, 50 - 100 mg intravenously every 6 - 8 hours, for 7 to 10 days or until the patient's hemodynamic stabilization. After the use of glucocorticoids, enteral thyroid hormone replacement was started before the lack of availability of this drug for parenteral use, levothyroxine should be administered intravenously at a loading dose of 200 to 400 mcg of levothyroxine, with lower doses for smaller, older patients and those with a history of coronary disease or arrhythmia. Subsequently, daily replacement doses of 1.6 mcg/kg body weight, reduced to 75%, can be administered provided that it is administered intravenously. Oral therapy can be started when the patient improves clinically. (11)

Because of the possibility that the conversion of thyroxine to triiodothyronine may be decreased in patients with myxedema coma, intravenous liothyronine may be given in addition to levothyroxine. High doses should be avoided because of the association of elevated serum triiodothyronine during treatment with mortality. A loading dose of 5 to 20 mcg may be given, followed by a maintenance dose of 2.5 to 10 mcg every 8 hours, with lower doses chosen for smaller and older patients and those with a history of coronary artery disease or arrhythmia. Therapy may continue until the patient is clearly recovering. (12)

5. Conclusion

The effectiveness of the treatment is related to the improvement in mental status, heart function and lung function. Measurement of thyroid hormones every 24 - 48 hours is reasonable to ensure a favorable trajectory in biochemical parameters. Although the optimal levels of serum TSH and thyroid hormones are not well defined in this circumstance, the failure of TSH to lower or improve thyroid hormone levels may be considered as an indication

to increase levothyroxine therapy and/or add levothyroxine therapy. liothyronine, while high serum triiodothyronine could be considered an indication to decrease hormonal therapy, unfortunately given the severity of the pathology that triggered the myxedema coma, the patient died even before obtaining the thyroid hormone profile, therefore it was impossible to reassess the same. (2)

Given the additional conditions that the patient had, management of them was granted as the start of broad - spectrum empirical antibiotics due to the high incidence of infections. Also mechanical ventilation to reduce CO2 retention and respiratory acidosis. Hypothermia is managed with passive methods (blankets), avoiding active methods (thermal blankets, hot baths) because they can cause vasodilation and vascular collapse. Treatment of arterial hypotension can be managed with volume replacement or vas oppressive amines, preferably with hemodynamic monitoring. Electrolytes and dextrose will be administered to correct hyponatremia and hypoglycemia. Management of hyponatremia can be started with hypertonic saline solution, in order to increase the sodium concentration by around 2 mEq/L in the initial course, followed by bolus furosemide to promote water diuresis. After reaching a sodium level greater than 120 mEq/L, water restriction is sufficient to normalize natraemia. Another therapeutic option may be the administration of an antidiuretic hormone antagonist such as tolvaptan or conivaptan. . (13)

The prognosis is related to the severity of the triggering condition as well as comorbid factors combined with those of thyroid dysfunction. (14)

References

[1] Rubén Pérez - Nieto O, Carolina Álvarez - Cruz J, Hiram López - Castro J, Flores - Ramírez R, González - Toribio R, Ramsés Ortega - Navarro H, et al. Coma mixedematoso. Medicina Interna de Mexico.2020; 36 (6).
[2] Rizzo LF, Mana DL, Bruno OD, Wartofsky L. Coma mixedematoso. Medicina (Buenos Aires).2017; 77 (4).
[3] Matta S, Chopra KK, Arora VK. Morbidity and mortality trends of Covid 19 in top 10 countries. The Indian journal of tuberculosis.2020; 67 (4s): S167 - s72.
[4] Chen W, Tian Y, Li Z, Zhu J, Wei T, Lei J. Potential interaction between SARS - CoV - 2 and thyroid: a review. Endocrinology.2021; 162 (3): bqab004.
[5] Campos - Barrera E, Alvarez - Cisneros T, Davalos - Fuentes M. Subacute thyroiditis associated with COVID-19. Case reports in endocrinology.2020; 2020.
[6] Del Prado SRSN, Steinman RA, Munir KM, Lamos EM. Supraglottic myxedema: two cases and a review of the literature. AACE Clinical Case Reports.2017; 3 (2): e101 - e5.
[7] Bernal Ruiz A, Ruiz A, Romero A, Fraile H, Gutierrez J, Rodriguez C, et al. Generalized myxedema in an adult leading to myxedema coma. ACTAS DERMOSIFILIOGRAFICAS.2000; 91 (3): 95 - 7.
[8] Peinado Acevedo JS, Rodríguez Arrieta LA, Builes Barrera CA, Román González A. Convulsiones, derrame pericárdico y rabdomiólisis en debut de coma mixedematoso.2021.
[9] Curí LL. Coma mixedematoso. Revista Cubana de Endocrinología.2012; 23 (3).
[10] Calderón ICG, Mejia PAL, Ortiz MAS, González NA, Acero SH. Urgencias endocrinológicas: coma mixedematoso. Revista Repertorio de Medicina y Cirugía.2021.
[11] Luster M, Duntas LH, Wartofsky L. The Thyroid and Its Diseases: Springer; 2019.
[12] Ueda K, Kiyota A, Tsuchida M, Okazaki M, Ozaki N. Successful treatment of myxedema coma with a combination of levothyroxine and liothyronine. Endocrine journal.2019: EJ18 - 0469.
[13] Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, et al. Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. thyroid.2014; 24 (12): 1670 - 751.
[14] Wartofsky L, Klubo - Gwiezdzinska J. Myxedema coma. the Thyroid and Its Diseases.2019: 281 - 92.

Table 1: Diagnostic scale for myxedema coma (Popoveniuc scale)

Dysfunction of the thermoregulatory system (ºC)	
>35	*0*
32 - 25	*10*
<32	*20*
Consciousness state	
Awake	0
Drowsiness/lethargy	10
Clouded	15
Stupor	20
Coma/seizures	30
Gastrointestinal findings	
Anorexia/abdominal pain/constipation	5
Decreased intestinal motility	15
Paralytic ileus	20
Precipitating events	
Absent	0
Present	10
cardiovascular dysfunction	
absent bradicardia	0
50 - 59	10
40 - 49	20
<40	30
*Other electrocardiographic changes**	10
Pericarditis - pleural effusion	10
Pulmonary edema	15
Cardiomegaly	15
Hipotention	20
metabolic alterations	
hiponatremia	10
hypoglycemia	10
hipoxemia	10
hipercapnia	10
GFR decrease	10

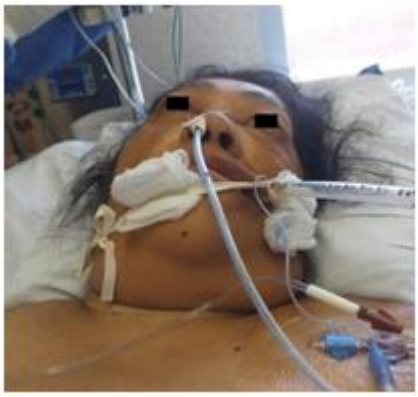

Figure 1: Facie characteristic of hypothyroidism in the patient.

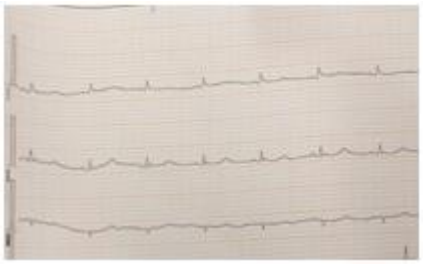

Figure 2: Electrocardiogram. Sinus bradycardia was prominent (long D2 image is shown)

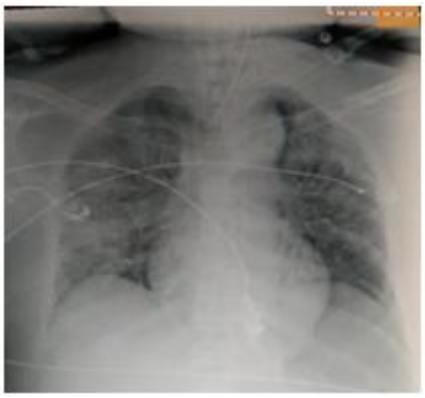

Figure 3: Chest x - ray with areas of bilateral radiopacity

Abbreviations: GFR: glomerular filtration rate
**QT interval prolongation, low - voltage complexes, bundle branch blocks, nonspecific ST changes, heart blocks. Adapted from Popoveniuc et al., Endocrine Practice 2014; 20: 808–17*

Author Profile

Miguel A. Serna Reyes, Hospital General de Acapulco, Guerrero. Internal Medicine Departm. E - mail: drmasr20[at]gmail.com, ID: 0000 - 0002 - 7735 - 7740.

Estanislao Antonio Calixto, Hospital de Alta Especialidad de Veracruz, SESVER. Internal Medicine Department. E - mail: dr. antonio.018[at]gmail.com, ID: 0000 - 0002 - 4186 - 6818.

Erick M. Ramirez Rayón, Hospital General de Acapulco, Guerrero. Internal Medicine Department. E - mail: erick_ok1[at]hotmail.com

Paulina J. Martínez Juárez, Hospital General de Acapulco, Guerrero. Internal Medicine Departm. E - mail: paulinajanet. martinez[at]upaep. edu. mx

Yessica Daniela Rios Miranda, Hospital General de Acapulco, Guerrero. Internal Medicine Departm. E - mail: drariosm_18[at]hotmail. com