Thyroid storm and COVID-19 with a need for plasmapheresis

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DOI: https://doi.org/10.36104/amc.2023.2707

Abstract

Thyroid storm is a life-threatening exacerbation of thyrotoxicosis. It is characterized by tachycardia, hyperthermia, an altered state of consciousness and dysfunction of other organs. It is a clinical emergency; without early recognition and treatment it may be fatal. Since the pandemic began, SARS-CoV-2 infection has triggered endocrine emergencies like diabetic ketoacidosis and thyrotoxicosis. We present the case of a patient with COVID-19 and thyroid storm, who, to our knowledge, is the first patient to have this combination of illnesses, and who required treatment with plasmapheresis. (**Acta Med Colomb 2022; 48. DOI: https://doi.org/10.36104/amc.2023.2707).**

Keywords: *thyroid storm, COVID-19, intensive care, SARS-CoV-2 infection, plasmapheresis*.

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Received: 26/VIII/2022 Accepted: 26/X/2022

Introduction

Within the spectrum of thyroid endocrine emergencies, hyperthyroidism is the result of excess circulating thyroid hormone, with thyroid storm being the maximal expression of this condition and having high mortality (1). The gap between hyperthyroidism and thyroid storm many times is hard to determine; however, in 1993, Burch and Wartofsky devised a risk score to identify thyroid storm, with ≥ 25 as the cut-off for diagnosis (2). SARS-CoV-2 viral infections may have pulmonary and extrapulmonary signs and symptoms. Recent evidence suggests that the virus often affects thyroid function, with various manifestations including hypothyroidism, thyrotoxicosis, and subacute thyroiditis (3). COVID-19 is thought to potentially exacerbate these disease states and even trigger autoimmune diseases like Graves' disease. However, there are few reports of patients with thyroid storm and SARS-CoV-2 infection in the intensive care unit (ICU) (4). We present the first case of thyroid storm and COVID-19 in Colombia, and this is one of the few reports worldwide of this combination of serious and potentially fatal diseases, for which plasma exchange therapy was required.

Clinical case

This was a 55-year-old patient with a 14-day history of weakness, fatigue and a dry cough, with COVID-19 infection confirmed by a positive PCR. His clinical condition worsened with more severe symptoms and a quantified fever. On admission to the emergency room he markedly worsened, with hypoxemic respiratory failure requiring invasive mechanical ventilatory support. His medical history was positive for type 2 diabetes mellitus being treated for one year with a basal insulin regimen. He was admitted to the ICU on ventilatory support with sedation, analgesia and deep neuromuscular relaxation, with acid-base balanced arterial gases and a severe oxygenation disorder (PaO_2/FiO_2: 76 mmHg), and no vasopressor support. He was pronated for 22 hours, with which his oxygenation increased significantly (PaO_2/FiO_2: 199 mmHg), with no need for further pronation cycles. During his ICU stay, he had high blood pressure along with tachycardia and documented febrile episodes, despite negative cultures. An ultrasensitive thyroid stimulating hormone (TSH) test was ordered, which was suppressed, with elevated free T4 (FT4). Therefore, the Burch and Wartofsky scale was applied, with a score of 45, diagnosing thyroid storm; treatment was begun with methimazole and metoprolol. Despite treatment, he continued to have high blood pressure, fever and tachycardia, so the methimazole dose was increased. Progressive reduction of sedation and analgesia was begun to evaluate the possibility of withdrawing invasive support, but the patient had episodes of psychomotor agitation, which limited the possibility of advancing with extubation. On the seventh day, he had a documented episode of atrial fibrillation with rapid ventricular response; the beta blocker and antithyroid medication dose was increased to the maximum level (60 mg/day of methimazole). He continued to have an unsatisfactory response, with persistent atrial fibrillation and arterial hypertension, and plasma exchange therapy was decided on. After the first session, the heart rate was controlled, with a sinus rhythm and adequate blood pressure control, improving the neurological symptoms. A

new spontaneous breathing test was done, and extubation was accomplished with no complications. Given his good clinical progress, he was transferred to the regular floor and then discharged home. The most important laboratory tests are summarized in Table 1.

Discussion

Thyroid storm is difficult to diagnose; there are still no universally accepted criteria. The Burch and Wartofsky scale is the most widely used globally; however, it can overdiagnose this serious disease. In 2012, the Japanese association that studies thyroid disease published new diagnostic criteria for thyroid storm in which the laboratory findings together with central nervous system abnormalities and other organ dysfunctions are essential for diagnosis (5). In the case we have presented, the patient met the clinical criteria for thyroid storm according to Burch and Wartofsky, with a severe classification due to the cardiovascular and neurological complications, and a poor response to the usual medical treatment (antithyroid medication, beta blockers, corticosteroids), requiring plasma exchange as a last-resort treatment. This is a very rare case with no known reports in the medical literature of thyroid storm being associated with SARS-CoV-2 infection and the need for plasmapheresis.

Table 1. *Laboratory studies.*

Study	Report	Reference
Glycemia	207 mg/dL	74 – 106 mg/dL
BUN	30 mg/dL	9 – 20 mg/dL
Creatinine	0.58 mg/dL	0.66 – 1.55 mg/dL
Aspartate aminotransferase	44 IU/L	17 – 59 IU/L
Alanine aminotransferase	41 IU/L	0 – 50 IU/L
Total bilirubin	2.8 mg/dL	0.2 – 1.3 mg/dL
Direct bilirubin	1.29 mg/dL	Adults: 0.0 – 0.3 mg/dL
Alkaline phosphatase	119 IU/L	38 – 126 IU/L
Leukocytes	15.9 x 10 ^3/mm^3	5 – 10
Hemoglobin	14.3 g/dL	14 – 18
Hematocrit	47.8%	46 – 50
Lymphocytes #	0.66	1,500 – 4,000
Platelets	162 x 10 ^3/mm^3	150 – 400
Troponin I	26 ng/L	Cut-off point (99th percentile): 19 ng/L
Ferritin	996 ng/mL	Males: 17.9 - 464 ng/mL
TSH	0.015 uIU/mL	0.34 – 5.6
Free T4	6.84 ng/dL	0.78 – 2.19
Free T3	6.89 pg/mL	2.30 – 4.20
Antimicrosomal antibodies	More than 1,000 units	Negative: 0 to 100 units Positive: more than 100 units.
Antithyroglobulin antibodies	1.37 units	Negative: less than 0.6 units Positive: more than 1.0 unit
Anti-thyroid peroxidase Ab	More than 1,000	Negative: 0 to 100 units Positive: more than 100 units
1. Plasma exchange session		
Free T4	5.88 ng/dL	0.78 – 2.19
2. Plasma exchange session		
Free T4	3.34 ng/dL	0.78 – 2.19

BUN : blood urea nitrogen, TSH: ultrasensitive thyroid stimulating hormone, Ab: antibody.

The clear mechanism to explain why thyrotoxicosis progresses to thyroid storm is still unknown. However, there is always an additional disease which triggers or exacerbates the endocrine disorder. Known causes of thyroid storm include infections, surgeries, trauma and the use of certain medications, all of which lead to increased sensitivity to catecholamines and triggering of all the complications of a thyroid storm (1). In our case, the SARS-CoV-2 infection may have precipitated the progression of an uncomplicated thyrotoxicosis to a thyroid storm. A retrospective study in 2020 showed that patients with COVID-19 have a high risk of thyrotoxicosis, as they have more immune system activation triggered by the virus (3). It was recently shown that patients with COVID-19 have markedly elevated proinflammatory cytokines, and elevated IL-8 and IL-6 are especially associated with TSH suppression and FT4 and FT3 elevation (6).

In addition to the pathophysiological aspects, this case report highlights some specific clinical aspects related to the relevance and management of thyroid storm in patients with COVID-19. Early recognition of thyroid storm helped instate appropriate treatment, which reduced mortality. In our patient, treatment was begun with thyroid hormone synthesis inhibition, countering the peripheral and systemic effects with beta blockers. However, due to its resistance to treatment and the severity of the clinical case, plasmapheresis was selected for treatment.

Thyroid apheresis was first described in 1970 in three cases of thyroid storm (7). It is based on eliminating free thyroid hormones, junction proteins and type 5 deiodinase as well as cytokines and antibodies. It is the fastest and most clinically effective method (8), as shown in our clinical case. The combined effect of all the instated treatments, as well as the elimination of proinflammatory cytokines present in COVID-19 patients, may have led to the satisfactory outcome in our patient.

In conclusion, we can say that the link between SARS-CoV-2 infection and thyrotoxicosis is not limited to mild cases like those reported in the literature. Correct identification and early treatment of this type of patient definitely have a significant effect on the clinical outcome.

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