

Letter to Editor

Myxedema coma in COVID-19

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Abstract

SARS-CoV-2 infection is associated with thyroid disorders. It has been reported that myxedema coma (MC) can be complicated with COVID-19. COVID-19-related thyroid disorders consist of a broad spectrum of thyroid dysfunction, from thyrotoxicosis to decompensated hypothyroidism. It is possible that both primary and central thyroid disorders are induced by COVID-19 due to systemic inflammatory and immune responses. We experienced two cases in which patients with COVID-19 developed MC with central hypothyroidism. It is likely that MC affected the severity of COVID-19. It is necessary to consider the existence of MC during SARS-CoV-2 infection. We propose the potential mechanisms.

To the Editor,

The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently a global pandemic. COVID-19 can rapidly progress to acute respiratory distress syndrome and cytokine storm, resulting in multiple organ failure due to systemic inflammation [1].

Myxedema coma (MC) is associated with a high mortality rate and an extremely rare ultimate stage of severe hypothyroidism caused by infection, cardiac disease, cerebrovascular disease, or trauma [2]. It is characterized by hypothyroidism, hypothermia, consciousness disturbance, hypoventilation, circulatory insufficiency, and dilutional hyponatremia [3]. Furthermore, it has been reported that SARS-CoV-2 infection is associated with MC [4]. However, the mechanisms underlying this observation remain unclear. We herein report two cases in which patients with severe COVID-19 were simultaneously diagnosed with MC based on their symptoms and hypothyroidism.

We sequentially experienced two Japanese men (age: 73 years [Case 1] and 72 years [Case 2]) with COVID-19 infection who were managed in the intensive care unit of our hospital in September and October 2020, respectively. At that time, the patients were treated for severe COVID-19 with artificial ventilation, continuous hemodiafiltration, and the intravenous administration of glucocorticoids due to hypoventilation and circulatory insufficiency.

Intensivists were concerned about their hypothermia

More Information

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(body temperature: 30.9°C [Case 1] and 32.2°C [Case 2]) and consciousness disturbance (Glasgow Coma Scale: 3 [E1VTM1] in both cases). Although neither had been diagnosed with hypothyroidism previously, we considered the possibility of myxedema coma due to hypothyroidism and decided to measure their thyroid function. Both patients showed central hypothyroidism (Case 1: TSH 1.86 μU/ml, free T3 0.94 pg/ml, free T4 0.49 ng/dl; Case 2: TSH 0.144 μU/ml, free T3 0.55 pg/ml, free T4 0.45 ng/dl). We therefore diagnosed the patients with MC and initiated treatment, consisting of the administration of thyroid hormone and the correction of associated physiologic disturbances.

In cases with sluggish circulation and severe hypometabolism, the absorption of therapeutic agents from the gut can be unpredictable. Therefore, we started the intravenous administration levothyroxine (200 mg, daily). Their body temperature increased within 24 h in response to levothyroxine (body temperature: 36.6°C [Case 1] and 37.2°C [Case 2]). However, case 1 died five days later without

recovering from consciousness disturbance, hypoventilation, or circulatory insufficiency. In case 2, the patient's circulatory insufficiency progressively worsened and the patient died after one month.

We propose two hypotheses regarding MC and the severity of COVID-19. First, central hypothyroidism may result from the rapid manifestation of cytokine storm due to COVID-19. Impairment of the pituitary-thyroid axis under conditions of cytokine storm has been proposed [5]. Second, the patients may have suffered decompensation of preexisting undiagnosed hypothyroidism precipitated by COVID-19. Because thyroid hormones regulate the immune system [6], hypothyroidism may be a risk factor for the exacerbation of COVID-19. In addition, the destruction of thyroid tissue and apoptosis have been demonstrated in patients infected with SARS-CoV-1 [7]. Furthermore, COVID-19 has been proposed to affect hypopituitarism due to hypophysitis or hypothalamus damage [8]. However, whether their hypothyroidism is central or primary has been unclear, due to the administration of glucocorticoids. Furthermore, we were unable to evaluate the anti-thyroid autoimmune antibody status in the present patients. Recently, Dixit, et al. reported a case of SARS-CoV-2 infection with MC. In their case, the thyroid peroxidase antibody level was elevated with primary hypothyroidism, suggesting that MC resulted from preexisting hypothyroidism. These observations raise the possibility that MC during SARS-CoV-2 infection could occur from both primary and central hypothyroidism.

In conclusion, the severity of COVID-19 and hypothyroidism are related to each other, and appropriate monitoring and treatment of hypothyroidism are important for preventing the aggravation of COVID-19. In particular, patients with MC may develop hypothermia, despite the presence of COVID-19. In patients with COVID-19, increased suspicion of myxedema coma is required in order to diagnose the condition at a stage that is early enough to start appropriate treatment

with levothyroxine. Future studies to elucidate the precise mechanism underlying COVID-19-related thyroid dysfunction will be interesting.

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