THE NEW ARMENIAN MEDICAL JOURNAL
Vol.16 (2022), No 1, p. 13-16
DOI: https://doi.org/10.56936/18290825-2022.16.1-13

MYXEDEMA COMA ASSOCIATED WITH COVID-19 INFECTION: CASE REPORT

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Receive 15.08.2021; accepted for printing 18.01.2022

Abstract

The coronavirus disease 2019 pandemic continues to exert a significant impact on global health care systems, causing devastating mortality and morbidity. As time passes and our understanding of this novel respiratory virus deepens, it is increasingly clear that its effects extend beyond that of the respiratory system. The link with endocrine disorders was noticed quite early when it was found that patients with diabetes and uncontrolled hyperglycemia were at an increased risk of severe disease as well as mortality from COVID-19. However, the other endocrine manifestations of COVID-19 probably were more subtle and information about them emerged more gradually over a period of time. Thyroid diseases are common endocrine disorders, and accordingly, a lot of attention has gone into the study of how COVID-19 affects the thyroid. Although the majority of mild to moderate COVID-19 patients remain euthyroid, a significant proportion of those with severe disease manifest with abnormalities in thyroid function. These manifestations include low thyroid stimulating hormone and low T3 levels, whereas low T4 levels were observed less commonly. Apart from this, several reports of subacute thyroiditis following COVID-19 have also been published. Similarly, Graves' disease has been reported to occur in patients who had recovered from COVID-19. We present a case of a 55-year-old woman who presented to the emergency department and her physical examinations and laboratory results were significant for myxedema coma and the patient was given levothyroxine with improvement of symptoms and mild change in thyroid hormone levels during hospitalization.

Keywords: *hypothyroidism, myxedema coma, COVID-19*

Introduction

Myxedema coma is defined as severe hypothyroidism leading to decreased mental status, hypothermia, and other symptoms related to slowing of function in multiple organs. It is a medical emergency with a high mortality rate [*Ross DS et al.,2022*]. If the condition is not promptly diagnosed and treated, the mortality rate can be more than 50%. Even with immediate recognition and timely medical intervention, mortality rates are as high as 25%[*Eledrisi MS et al., 2020*]. Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. It usually is a primary process in which the thyroid gland is unable to produce sufficient amounts of thyroid hormone. Hypothyroidism is four times more common in women than in men; 80 percent of cases of myxedema coma occur in females. Myxedema coma occurs almost exclusively in persons 60

Cite This Article as:
Maghakyan S.A., Aghajanova E.M., Hovhannisyan A.H., Asoyan V.A., Barseghyan E.S. (2022); Myxedema coma associated with Covid-19 infection: case report; NAMJ v.16 (2022) No.1, p. 13-16;
DOI: https://doi.org/10.56936/18290825-2022.16.1-13

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years and older. More than 90 percent of cases occur during the winter months [*Wall CR, 2000*]. It can occur as a culmination of severe, longstanding hypothyroidism or be precipitated by acute stressors such as infection, myocardial infarction, cold exposure, and surgery in patients with poorly controlled hypothyroidism [*Elkattawy S et al., 2021*].

Patients with hypothyroidism may exhibit a number of physiologic alterations to compensate for the lack of thyroid hormone. If these homeostatic mechanisms are overwhelmed by factors such as infection, the patient may decompensate into myxedema coma [*Wiersinga WM, 2018*]. A diagnosis of myxedema coma should be suspected in a patient with coma or altered mental status who is also hypothermic, hyponatremic, and/or hypercapnia. Physical findings in myxedema coma may include the classic myxedematous face, which is characterized by generalized puffiness, macroglossia, ptosis, periorbital edema, and coarse, sparse hair. However, most patients do not present with myxedema or coma and so the important feature is altered mental status. A medical emergency, myxedema coma requires immediate attention. If the diagnosis is suspected, immediate management is necessary before confirming the diagnosis due to the high associated mortality rate. Patients with myxedema coma should be treated in an intensive care unit with continuous cardiac monitoring. Initial steps in therapy include airway management, thyroid hormone replacement, glucocorticoid therapy, and supportive measures [*Eledrisi M et al., 2020*]. While there is concern regarding the precipitation of arrhythmias or myocardial infarction by administering large doses of intravenous levothyroxine, this concern must be balanced against T_4's potentially life-saving and usually nondetrimental effect. The lower initial dose should be administered to patients who are frail or have other comorbidities, particularly cardiovascular disease [*Wall C, 2000]*. Patients with hypothermia should be covered with regular blankets, the use of warming blankets should be avoided because the resulting peripheral dilatation may lead to hypotension and cardiovascular collapse [*Eledrisi M et al., 2020*].

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

COVID-19 is the pandemic of the new millennium. COVID-19 patients with comorbidities including hypothyroidism could develop a life-threatening situation. The thyroid gland and the virus infection with its associated inflammatory-immune responses are known to be engaged in complex interplay. Severe acute respiratory syndrome coronavirus-2 infection invades cells via the angiotensin-converting enzyme 2 receptor. The angiotensin-converting enzyme 2 receptor is highly expressed in thyroid tissue, which may result in direct thyroid damage by severe acute respiratory syndrome coronavirus-2 [*Dixit NM et al., 2020*]. Thyroid abnormalities are associated with a higher risk of disease severity, mortality, intensive care unit (ICU) admission, and hospitalization among COVID-19 patients. This association was significantly influenced by an increase in age [*Damara FA et al.,2021*]. It has been reported that myxedema coma can be complicated with COVID-19. 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 [*Takashi Y, Kawanami D,2021*].

CASE PRESENTATION

A 55-year-old female with positive severe acute respiratory syndrome coronavirus 2 polymerase chain reaction test was brought to Emergency department due to progressive dyspnea associated with general weakness which had lasted for 7 days. She had an ischemic heart disease and a thyroidectomy for hyperthyroidism 5 years ago, however, she did not go through regular medication control. Her vital signs showed Ps=58*bpm*, BP=80/50*mmHg*, T=36.1^0*C*, SpO_2 88% (O_2-), 95% (O_2+) on arrival. On examination, the patient was not alert or oriented to person, place, or time, and she didn't respond to painful stimuli. Her consciousness was clouded. Physical examination was remarkable for macroglossia, myxedematous face and questionable intellectual disability. The patient's general condition was extremely severe, and she was ad-

mitted to COVID intensive care unit department. Laboratory findings were remarkable for white blood cell count 10000*/uL* (normal 4000-9000*/uL*), C-reactive protein 77.76*mg/L* (normal < 5 *mg/L*), lactate dehydrogenase 936 *U/L* (normal135-220), D-dimer 4.174*ug FEU/ml* (normal 0-0.5), sodium 130 *mmol/L* (normal 134-148 *mmol/L*) and potassium 3.2 *mmol/L* (normal 3.6-5.0 *mmol/L*), calcium 1.1*mmol/L* (normal 2.1-2.6*mmol/L*), TSH 43.27*uIU/mL* (normal 0.3-4.5), FT4 3.9 *pg/mL* (normal 8.9-17.2). Other blood tests, including creatinine, troponin-I and albumin levels were within normal range. Her electrocardiogram reported sinus bradycardia with a heart rate of about 56. Her echocardiogram showed dilatation of the left atrium and the right ventriculi, diffuse hypokinesis of the left ventriculi, ejection fraction -30 %. Chest X-ray showed bilateral pneumonia with a lesion up to 15-20%. Brain computed tomography scan was without pathology.

According to the above test results and absence of fever despite infectious disease together with the decreased mental status and general edema, myxedema coma was highly suspected.

The patient was given oral levothyroxine 25 *mcg* at the first day, after this she responded to painful stimuli. Then she followed by 50 *mcg* daily for 7 days. After 7 days she was awake, alert and started to respond to the questions, FT4 was 4.48 *pg/mL* (normal 8.9-17.2) and the daily levothyroxine dose was increased to 75 *mcg*. Besides thyroxine therapy, the patient received oxygen therapy, dexamethasone, calcium gluconate, infusion therapy, anticoagulation therapy, antiplatelet therapy, antibiotics. The patient improved on treatment. She was discharged on the 14th day on oral 75 *mcg* of levothyroxine daily, calcium 1000 *mg* daily, vitamin D 5000*IU* daily and outpatient follow up with endocrinologist.

Discussion

The term myxedema coma is a misnomer as neither coma nor myxedema is required for diagnosis. There are no clear diagnostic criteria for the condition, however, patients typically present with altered mental status, confusion, and lethargy [*Rodriguez I et al., 2004*]. As a result of the lack of objective criteria for diagnosis of myxedema coma, response to treatment should be evaluated based on clinical judgment. An appropriate response to treatment would be evidenced by improvement in mental status and stabilization of vital signs. However, TSH levels are reflective of the thyroid status for the prior 6-8 weeks, therefore these levels may not be representative of response to thyroid treatment. For this reason, clinical improvement and T4 status may be superior in assessing response to therapy.

Our patient had a long-term history of untreated hypothyroidism, which was deteriorated by Covid-19 infection. So Covid-19 as infectious disease was stressor for culmination of longstanding, untreated hypothyroidism. The patient's general severe condition was associated with hypothyroidism. She was treated with levothyroxine and improved clinically. There were small improvements in the patient's T4 and TSH status throughout the hospital stay. As per endocrinology, triiodothyronine would be indicated only if the patient's status deteriorated or failed to improve on a maximum daily dose of T4. Our patient vitals and mental status improved on 75*mcg* levothyroxine daily.

Conclusion

Although myxedema coma is now a rare occurrence given the widespread availability of TSH assay and frequent monitoring by primary care physicians, it is a life-threatening event and emergency treatment is warranted. As one of the causes of myxedema coma is infectious disease in patients with hypothyroidism, it is so important to maintain TSH control during Covid-19 pandemic. Old females or patients that are having medical history of thyroidectomy, come together with "cold", "slow", and "weak" conditions need to be taken note. Although there is high mortality rate of myxedema coma, the patient had been diagnosed in time, cured and finally discharged after thyroxine, glucocorticoid and intensive care are provided. As long as myxedema coma is suspected, treatments should be administered without any delay [*Han KW et al., 2017*].

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THE NEW ARMENIAN MEDICAL JOURNAL
Vol.16 (2022). No 1

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THE NEW ARMENIAN MEDICAL JOURNAL

Vol.16 (2022). No 1

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Our journal is registered in the databases of Scopus, EBSCO and Thomson Reuters (in the registration process)

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THOMSON REUTERS

Copy editor: Tatevik R. Movsisyan

Printed in "VARM" LLC
Director: Ruzanna Arakelyan
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