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Kathleen E.H. Douangchak

A.T. Still University School of Osteopathic Medicine in Arizona, sa202082@atsu.edu

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COVID-19 Infection with Severe Hypothermia in a Fully Vaccinated Patient

ABSTRACT

Hypothermia is an uncommon presentation of COVID-19 infection, typically observed in patients with severe disease prior to the availability of vaccines. However, the occurrence of hypothermia in vaccinated patients with COVID-19 disease has not yet been documented. This case reports a rare presentation of severe hypothermia in a 41-year-old female with COVID-19 disease, who suffered from several comorbidities, including heart failure with preserved ejection fraction, chronic pericardial effusion, nephrotic syndrome, CKD 4, hypertension, type 2 diabetes, thyroid cancer status post-thyroidectomy with resultant postsurgical hypothyroidism, glaucoma, and anemia of chronic disease. Upon presentation, the patient was encephalopathic with hypothermia of 27.2°C (81 °F) per rectal thermometer and bradycardia of 35 beats per minute. The patient underwent active rewarming, which included warm fluids, heated high flow nasal cannula 5L/min FiO2 28%, and Bair hugger with the goal of rewarming the patient at no greater than 2°C per hour. The patient recovered her temperature overnight, but remained encephalopathic. Despite adherence to the established therapeutic measures for severe hypothermia, the patient clinically declined and expired. This case underscores the potential for hypothermia to manifest in patients with COVID-19 who have received two vaccine doses. The implications of this finding will be discussed, highlighting the need for further research and awareness regarding hypothermia as a possible presentation of COVID-19 in vaccinated individuals.

INTRODUCTION:

Severe hypothermia is defined as a temperature less than 28°C and its clinical features can include apnea, coma, decreased or no activity on electroencephalography, nonreactive pupils, oliguria, pulmonary edema, and ventricular dysrhythmias.¹ These possible symptoms exist on a spectrum with those seen with mild to moderate hypothermia, so each patient may present differently. Treatment of a severely hypothermic patient requires active rewarming. Active rewarming consists of providing an external heat source to the patient's skin, which can be done with convection via forced-air warming systems (e.g., Bair Hugger), via arteriovenous anastomoses, and via airway rewarming with humidified oxygen.¹ In addition to rewarming, hypothermic patients should receive bedside glucose and thiamine and antibiotics and/or steroids if appropriate.¹

Hypothermia is commonly seen in patients exposed to cold temperatures, but can also be seen in patients with dermal, endocrine, and neurological disease with additional causes including drug-induced, iatrogenic, and sepsis.¹ Notably, hypothermia has also been present in cases of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection with the first documented case study showing hypothermia as an initial presenting symptom.² Subsequently, a retrospective study of 57 patients found hypothermia in hospitalized patients with COVID-19 to be associated with "longer intubation periods, longer ICU stays and increased risk of mortality."³

A retrospective review of 331 patients showed a significant association between hypothermia and death.⁴ These retrospective reviews took place prior to the availability of SARS-CoV-2 vaccines and thus the patients in the studies were not vaccinated.

The Centers for Disease Control and Prevention (CDC) state that a patient is fully vaccinated against SARS-CoV-2 within two weeks of receiving two doses of the Pfizer-BioNTech (BNT162b2) vaccine, two doses of the Moderna (mRNA- 1273) vaccine, or one dose of Johnson and Johnson's Janssen vaccine (JNJ- 78436735).⁵ Prior to this publication, there was no preexisting documentation detailing cases of hypothermia in patients with COVID-19 infection who had received full COVID-19 vaccination.

CASE DESCRIPTION

This is a case of a 49-year-old female with a history of heart failure with preserved ejection fraction, chronic pericardial effusion, nephrotic syndrome, CKD 4, hypertension, type 2 diabetes, thyroid cancer status post thyroidectomy with resultant postsurgical hypothyroidism, glaucoma, and anemia of chronic disease. She had received two doses of the Moderna COVID-19 vaccine less than one year prior and had not received additional doses. Seventeen days prior to the ICU admission detailed by this case, she was diagnosed with COVID-19 and hospitalized for five days for management of ascites and COVID-19. Her family reports that she had slowly been declining since discharge. She presented this admission via ambulance for altered mental status and was found to be profoundly hypothermic with bradycardia.

The patient's vital signs were significant for hypothermia of 27.2 °C (81 °F) per rectal thermometer and bradycardia of 35 beats per minute. Physical exam was significant for acute distress in that the patient was obtunded with GCS 11; the patient was not alert or oriented, but responsive to painful stimuli for which she had movement of all extremities. The patient's right pupil was about 4 mm and her left pupil was pinpoint, which according to the medical record was a chronic constriction due to an unknown cause. Respiratory examination was notable for crackles upon auscultation; patient was protecting her airway. Her skin was very cold to the touch with clammy extremities. Anasarca with 4+ pitting edema of the lower extremities to the abdomen bilaterally.

Pathological Tests and Other Investigations:

Chemistry panel was significant for mild respiratory acidosis. The patient was hyperglycemic without evidence of high anion gap metabolic acidosis with a hemoglobin A1c of 9.2%. Renal studies showed that the patient's creatinine remained at baseline of 2.1mg/dL. Complete blood count was significant for pancytopenia with elevated LDH and normal reticulocyte count. CK, troponin, CRP, lactate, and triglyceride evaluations were negative. Infectious disease workup was significant for a positive COVID-19 PCR test. HIV, influenza, Streptococcus, and Legionella were negative. Blood cultures and MRSA swab showed no growth. Ammonia was within normal limits. Thyroid stimulating hormone (TSH) was elevated at 43.2 mcIU/mL with low T4 and T3 levels of 0.68 ng/dL and 0.97 pg/dL respectively. Autoimmune studies were negative, including tests for ANA, Anticardiolipin IgG and IgM, and B2 Glycoprotein IgG/IgM. Urine toxicology was negative. Additional labs were notable for Vitamin D deficiency

and thiamine deficiency. The patient's phosphatidylethanol levels were negative for alcohol use. Vitamins B6, B9, and B12 were within normal limits.

Electrocardiogram showed a junctional bradycardia. CT head without contrast showed no acute intracranial findings. Chest X-ray showed decreased mild to moderate right and trace left pleural effusions and improved aeration of the lungs with decreased mild to moderate hazy pulmonary infiltrates. Echocardiogram noted a LVEF of 70% and a small/moderate circumferential pericardial effusion without hemodynamic compromise. The effusion appeared chronic dating back to at least 2020 by previous echocardiograms.

On hospital day 2, that patient began to exhibit intermittent seizing. The patient was intubated for airway protection. Subsequent MRI of the brain without contrast was notable for numerous foci of restricted diffusion involving multiple vascular territories with associated FLAIR signal hyperintensity which was most suggestive of recent embolic phenomenon, including bland and septic etiologies. Electroencephalogram showed a delta wave pattern consistent with severe generalized slowing; there was no active epileptiform activity.

To address the patient's right pleural effusion, a thoracentesis was performed during which 1.5 liters of transudative pleural fluid was removed. Vascular bilateral carotid duplex showed mild scattered heterogeneous plaque formation within the bilateral carotid arterial tree with no evidence for hemodynamically significant stenosis.

Treatment plan:

The patient was admitted to the ICU for controlled warming measures and additional management of her many medical problems. To address the severe hypothermia, the patient received active rewarming with warm fluids, heated high flow nasal cannula 5L/min FiO₂ 28%, and Bair hugger with the goal of rewarming the patient at no greater than 2°C per hour. A low threshold for intubation was maintained in the event that any hemodynamic issues or worsening mental status were to occur while rewarming.

Additionally, the patient received IV levothyroxine to address her known hypothyroidism and suspicion of myxedema coma. She additionally received IV hydrocortisone prior to concomitant adrenal insufficiency being ruled out. Blood cultures and MRSA swab were performed and she was started on broad-spectrum antibiotics until an infectious etiology could be ruled out. Nephrology and endocrinology were consulted. Electrolytes were monitored closely. Strict inputs/outputs due to the patient's volume overloaded state. With resolution of the hypothermia, the healthcare team expected clinical improvement of the accompanying encephalopathy and bradycardia.

The patient was able to spontaneously recover body temperature overnight. Blood pressure and heart rate normalized. However, the patient remained obtunded. The patient began to demonstrate an irregular flexion of both upper extremities, right lateral gaze with horizontal nystagmus, and was no longer responding with intention as well as audible gurgling that was concerning for aspiration. The patient was intubated to protect the airway.

The patient was found on MRI without contrast of the brain to have a bihemispheric stroke. No definite etiology of embolic phenomenon was identified. The patient was compassionately extubated and placed on comfort care. No further workup was performed. The patient continued to decline clinically and expired. An autopsy was not performed.

DISCUSSION

This case documents the importance of treating severe hypothermia in patients with COVID-19 infection. This case shows that a patient with several comorbidities is at risk for severe COVID-19 even when vaccinated and that hypothermia may be a presenting symptom, even late in the course of COVID-19 infection. This case supports the existing literature that hypothermia in COVID-19 is associated with increased mortality.⁴

Upon admission to the ICU, warming protocols were initiated and followed the standard of care as described above. The patient's temperature was recovered overnight and the bradycardia resolved. Despite this, the patient clinically declined after a subsequent bihemispheric stroke. One limitation of this case study is the inability to definitively establish the causal relationship between hypothermia, COVID-19, and the subsequent stroke. Because her COVID-19 positive test and symptoms had started more than two weeks prior to the stroke, there is a low likelihood that it contributed to a hypercoagulable state. However, given the existing literature about higher risk of mortality, we believe it to be associated with the patient's clinically declining state and hypothermia.

Nevertheless, without additional investigations or an autopsy, it remains challenging to establish a clear cause-and-effect relationship. The patient's family's decision to forego an autopsy in this case limited the ability to gain a more comprehensive understanding of the specific factors contributing to the patient's clinical decline and subsequent death. While the COVID-19 PCR test remained positive this admission, other etiologies of hypothermia were considered and ruled out, including sepsis, hypoadrenalism, autoimmune, and other viral infection. The patient was initially treated for a presumed myxedema coma, however, the T4 levels were not profoundly low enough and the endocrine team ruled out hypothyroidism as the etiology of hypothermia. Though the patient's thiamine levels were low, the phosphatidylethanol level ruled out alcohol use as the cause of the hypothermia and encephalopathy.

CONCLUSION

In conclusion, COVID-19 patients who had previously received a two-dose series of the Moderna vaccine can present with severe hypothermia. Hypothermia in COVID-19 has been shown to increase mortality, which can also be seen in patients who have received the two-dose Moderna COVID-19 vaccine series. This case underscores the importance of recognizing and promptly treating severe hypothermia in COVID-19 patients, even in those who have received full vaccination. Further research and investigations are needed to better understand the underlying mechanisms and associations between hypothermia, COVID-19, and related complications.

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