


CK-MB Elevation in Mild Hypothermia: What We Did and We Should Have Done

Journal of Investigative Medicine High
Impact Case Reports
Volume 9: 1–3
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Medical Research
DOI: 10.1177/2324709621995335
journals.sagepub.com/home/hic


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Abstract

An 88-year-old male patient with a past medical history of hypertension and gastroesophageal disease presented with nausea, vomiting, and hypothermia. He was admitted for further testing, which revealed elevated creatine kinase and its MB isoenzyme (CK-MB) and troponin with no significant electrocardiogram changes. He denied cardiac symptoms or any previous cardiac history. The patient was treated with fluids and antibiotics in which improvement in his symptoms was noted. In this article, we share this rare case of hypothermia associated with elevation of CK-MB.

Keywords

hypothermia, CK-MB elevation, creatine kinase, MB isoenzyme

Introduction

Creatine kinase (CK) and its MB isoenzyme (CK-MB) were the most used serologic tests for the diagnosis of myocardial infarction (MI) prior to the widespread adoption of troponin. Their use has markedly diminished over time. An elevated CK-MB is relatively specific for myocardial injury, particularly in patients with ischemic symptoms, when skeletal muscle damage is not present. Elevations return to baseline within 36 to 48 hours, in contrast to elevations in troponin, which can persist for as long as 10 to 14 days.¹ This means that CK-MB, unlike troponins, cannot be used for the late diagnosis of an acute MI but can be used to suggest infarct extension if levels rise again after declining. It also can be caused by non-cardiac causes such as hypothermia as reported in this case.²

Case Presentation

An 88-year-old male patient with prior history significant for hypertension and gastroesophageal disease presented with sudden-onset nausea, vomiting, and dizziness. He presented during the summer season. One day prior to admission, he reports eating a burger and fries for dinner and subsequently woke up with these symptoms 5 hours later. On arrival at the emergency department, he was found to be hypothermic to 92.8 °F (33.8 °C), blood pressure of 153/71 mm Hg, heart rate of 57 beats per minute, respiratory rate of 12 breaths per minute, and saturating at 98% on room air. Temperature

throughout his stay was taken orally. The ambient temperature in the room was approximately 74 °F in the hospital. Significant laboratory results were lactic acid of 1.0, white blood cell 11 700/μL (4500-11 000), CK 304 U/L (55-170), CK-MB 10.4 ng/mL (0-2.37), troponin 0.031 ng/mL (0-0.034), and brain natriuretic peptide 2440 pg/mL (0-450). His urine was positive for small blood but was negative for any protein or infection. On physical examination, he was alert and oriented to time, place, and person with shivering noticed. Throughout his stay, his creatinine and glomerular filtration rate were consistently at 1.1 mg/dL and 59.6 mL/min. Computed tomography (CT) scan of his abdomen and pelvis showed mild mesenteric adenitis with benign cholelithiasis, nephrolithiasis, and diverticulosis. Chest X-ray showed no acute cardiopulmonary processes. The patient was feeling well until waking up with the symptoms, and he denied recent sick contacts and travel history.

Although the patient had a markedly elevated CK-MB, he denied any chest pain, palpitations, dyspnea, extremity swelling, or orthopnea throughout his admission. He also

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Received November 20, 2020. Revised January 17, 2021. Accepted January 24, 2021.

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denied prior cardiac history. A transthoracic echocardiogram showed mild to moderate global cardiomyopathy with ejection fraction of 40% to 45%. Troponins peaked at 0.056 ng/mL (0-0.034) during admission before down trending. CK gradually decreased to 221 U/L (55-170), while CK-MB was not trended. Cardiac monitoring with serial electrocardiogram and telemetry were with normal sinus rhythm with no arrhythmias. He was also evaluated for hypothyroidism, but both thyroid-stimulating hormone and free T4 were within normal limits at 2.87 uIU/mL (0.465-4.68) and 1.18 ng/dL (0.78-2.19), respectively.

He was treated with intravenous fluids and antibiotics. There was concern he may be suffering from food poisoning, but the patient and his daughter reported that they both have been eating similarly for past few days. Heating blankets were applied, and his temperature was restored to normothermic levels after 24 hours. Leukocytosis and presenting symptoms resolved. Blood cultures had no growth by the third day. The patient was subsequently discharged home after resolution of his symptoms and to follow-up with his primary care.

Discussion

While CK-MB elevation has been shown to occur in specifically severe hypothermia, we believe that our case shows CK-MB elevation in mild hypothermia. CK-MB elevation has various causes ranging from trauma, nonischemic cardiac injury to recreational drug abuse.³ While hypothermia has been noted to increase CK-MB levels, the mechanism remains poorly understood.⁴ A 1978 study provided 6 different cases of CK-MB elevation but without any evidence of MI.⁵ In addition, experiments utilizing canine subjects revealed that hypothermia can cause cardiac muscular injury and increase CK-MB enzyme levels without necessarily inducing any infarction.⁵

In our patient, we essentially ruled out any concern for tissue hypoperfusion or cardiac damage. In addition, his blood pressure was stable throughout his hospital stay. As previously stated, CK-MB is utilized in diagnosing cardiac muscular damage during MI. Although our patient's troponin did mildly rise during his stay, all other cardiac workup has been unequivocal. An echocardiogram revealed global dysfunction with an ejection fraction of 40% to 45%, while repeated electrocardiograms and telemetry have been negative for any cardiac arrhythmias or acute changes. Myocardial necrosis in congestive heart failure has been shown to cause increases in CK-MB and troponin. However, our patient did not exhibit any symptoms of acute congestive heart failure exacerbation, and we believe that the echocardiogram results were not new findings. Most important of all, the patient himself denied any chest pain, chest discomfort, or increased oxygen demand throughout his stay. Another relevant finding in our workup was the CT abdomen/pelvis that indicated mild mesenteric adenitis with

benign cholelithiasis, nephrolithiasis, and diverticulosis. Our literature review only indicated one instance where diverticular sigmoiditis could falsely lead to increased CK-MB.⁶ However, the CT scan showed that our patient only had diverticulosis but no signs of diverticulitis.

Rhabdomyolysis has been shown to be triggered by therapeutic hypothermia protocol as shown in the case of a 23-year-old male student who was resuscitated after suffering from football-induced cardiac arrest.⁷ Although our patient did have an elevated CK (257) with mild blood on urine analysis at admission, he did not meet criteria for rhabdomyolysis. His renal function had also remained stable throughout his stay. Similarly, there was a case of hypothermic myxedema coma being incorrectly diagnosed as MI due to elevated CK-MB.⁸ However, our patient never had a history of hypothyroidism and also did not exhibit any symptoms related to myxedema coma. In addition, our workup revealed that his thyroid-stimulating hormone was 2.87 and his free T4 was 1.18.

Based on literature, hypothermia can be commonly classified into 3 different categories, mild (core temperature of 90 °F to 95 °F), moderate (core temperature of 82 °F to 90 °F), and severe (core temperature below 82 °F).⁹ Our patient's core temperature falls into the mild category. There are also further classifying stages based on symptomatic presentation. Our patient did not have any alteration of consciousness or shivering. Based on the staging scheme derived from the International Commission for Mountain Emergency Medicine (or also known as the "Swiss system"), our patient can be labelled under the HT1 stage.¹⁰

Despite our extensive efforts, there are still a few limitations to our case. First, we did not order a lactate dehydrogenase or a procalcitonin, both of which make it difficult for us to rule out other etiologies. While we did treat this patient with fluids and antibiotics, we did not believe he was clinically unstable enough to concern us for sepsis workup as his clinical condition improved quite rapidly. Unfortunately, we do not have any previous laboratory results to compare previous leukocyte counts. We also did not test him for COVID-19 during his hospitalization. Our reasoning for not ordering a COVID-19 swab was the limited supply of COVID-19 diagnostic tests at the time, and the lack of any COVID-19-like signs on chest X-ray at admission. Four days after discharge, the patient did eventually follow-up with his primary care provider and was found to have tested negative for COVID-19. In addition, food poisoning, especially with salmonella, has been shown to cause elevated CK levels.¹¹ Could this patient have been food poisoned? Although it is a possibility, we feel that it is unlikely given his daughter also had similar exposures but was asymptomatic. We also failed to obtain a urine drug screen to rule out recreational drug abuse. Despite the lack of drug testing, we believe that patient has lower likelihood of drug abuse based on patient's own insistence confirmed by his own daughter and further confirmation from records of follow-up primary care provider visit notes.

Conclusion

We have reported a unique case of a patient with CK-MB elevation associated with mild hypothermia. We have provided a rigorous means of ruling out other potential causes of elevated CK-MB including cardiac, endocrine, gastrointestinal, and renal etiologies and also further highlighted additional diagnosis protocols we have missed. Although our case does have limitations, specifically in terms of ruling out other etiologies, we still believe that hypothermia, whether intentional or unintentional, should always be considered as a differential diagnosis for elevated CK-MB. Our intent is that this case can be a guide for future cases of elevated CK-MB.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Informed consent for patient information to be published in this article was obtained verbally directly from the patient.

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