Title: Hypothermia Induced CK-MB elevation.

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Key Clinical Message

We have reported a unique case of a patient with CK-MB elevation induced by hypothermia. We believe hypothermia, whether intentional or unintentional, should be always considered as a differential diagnosis for elevated CK-MB.

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 CK-MB and Troponin with no significant electrocardiogram changes. He denied cardiac symptoms or any previous cardiac history. This was diagnosed as a case of sepsis due to gastroenteritis. Patient was treated with fluids and antibiotics in which improvement in his symptoms was noted. We share this rare case of hypothermia induced elevation of CK-MB.

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. One day prior to admission he reports eating a burger and fries for dinner and subsequently woke up with these

symptoms 5 hours later. Upon arrival at ED, he was found to be hypothermic to 92.8 F with other vital signs being stable. Significant laboratories were WBC 11.7 K/uL (4.5-11.0), CK 304 U/L (55-170), CK-MB 10.4 ng/mL (0-2.37), Troponin 0.031 ng/mL (0-0.034), and BNP 2440 pg/mL (0-450). His urine was positive for small blood. Computed tomography of his abdomen and pelvis showed mild mesenteric adenitis with benign cholelithiasis, nephrolithiasis and diverticulosis. Chest x-ray showed no acute cardiopulmonary processes. Patient was feeling well until waking up with the symptoms, 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 denied prior cardiac history. A transthoracic echocardiogram showed mild to moderate global cardiomyopathy with ejection fraction of 40-45%. Troponins peaked at 0.056 ng/mL (0-0.034) during admission before down trending. CK gradually decreased to 221 U/L (55-170). Cardiac monitoring with serial EKG's and telemetry revealed no arrhythmias. He was also evaluated for hypothyroidism, but both TSH 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 for sepsis due to gastroenteritis with intravenous fluids and antibiotics. 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 3rd day. Patient was subsequently discharged home after resolution of his symptoms and to follow up with his primary care.

Discussion

CK-MB elevation in hypothermia has been seen before, but there is very minimal literature regarding this matter. CK-MB elevation has various causes ranging from trauma, non-ischemic 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 six different cases of CK-MB elevation but without any evidence of myocardial infarction.[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 cardiac damage. As previously stated, CK-MB is utilized in diagnosing cardiac muscular damage during myocardial infarctions. 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 EKGs and telemetry have been negative for any cardiac arrhythmias. Myocardial necrosis in congestive heart failure has been shown to cause increases in CK-MB and troponin. However, our patient did not exhibit any physical symptoms of congestive heart failure. Most important of all, the patient himself denied any chest pain, chest discomfort or increased oxygen demand throughout his stay. Although we did not obtain a urine drug screen, there was very little concern for drug abuse. 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 creatine kinase (257) with mild blood on UA 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 his TSH was 2.87 and his free T4 was 1.18.

Conclusion

We have reported a unique case of a patient with CK-MB elevation induced by hypothermia. We have also provided a rigorous means of ruling out other potential causes of elevated CK-MB including cardiac, endocrine, gastro-intestinal and renal etiologies. We believe hypothermia, whether intentional or unintentional, should be always considered as a differential diagnosis for elevated CK-MB.

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