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# Elevated Troponin I Levels in Diabetic Ketoacidosis Without Obstructive Coronary Artery Disease

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Elevated troponin levels have been observed in a wide spectrum of patients who do not have ischemic heart disease, including nonacute coronary syndrome and cardiovascular and noncardiovascular conditions. The cases of two patients with diabetic ketoacidosis who had elevated troponin levels in the absence of coronary artery disease are presented. This clinical scenario can pose a diagnostic dilemma for the physician. The objective of the present report is to highlight the mechanism of troponin elevation in patients with diabetic ketoacidosis, in addition to the clinical and prognostic significance of this finding.



**Freeform/Key Words:** cardiac biomarker, diabetic ketoacidosis, elevated troponin I

In addition to acute myocardial infarction, numerous other clinical conditions, including pulmonary embolism, sepsis, and myopericarditis, can lead to elevated cardiac troponin I levels. These clinical conditions usually cause myocardial necrosis owing to a supply–demand mismatch or direct myocardial toxicity. Diabetic ketoacidosis (DKA) is another condition that can lead to myocardial necrosis in the absence of coronary artery disease (CAD) and has been the subject of previous case reports [1, 2], case series [3], and retrospective reviews [4, 5]. The present case report contributes to the reported data regarding this finding, which has prognostic implications.

## 1. Case Report

### *A. Case 1*

A 53-year-old man with a 15 pack-year smoking history, prediabetes (based on a hemoglobin A1c value of 6.4), and a family history of diabetes presented with two episodes of right-sided chest pain (Table 1). The pain was nonexertional, nonradiating, and sharp, and it was associated with shortness of breath. Additionally, the patient reported polyuria, polydipsia, and a 3-lb weight loss within 1 week. His vital signs on admission were normal. He did not have jugular venous distension. The chest examination did not reveal crackles or wheezes. The cardiovascular examination findings were also normal, and he did not have lower extremity edema. The basic metabolic panel findings showed bicarbonate of 14 mEq/L, anion gap of 23, and glucose level of 655 mg/dL. The venous pH was 7.21, and lactate was mildly elevated at 2.6 mmol/L. The complete blood count revealed mild leukocytosis. His hemoglobin A1c, tested ~18 months earlier, had been 6.4; however, the value at the present admission was 12.1. The urinalysis revealed glycosuria and ketonuria. His troponin level on admission

Abbreviations: CAD, coronary artery disease; DKA, diabetic ketoacidosis.

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**Table 1. Patient Characteristics and Laboratory Values**

| Parameter (Normal Range) | Case 1 | Case 2 |
|---|---|---|
| Age, y | 53 | 57 |
| Sex | Male | Male |
| Venous pH (7.33–7.43) | 7.21 | 7.136 |
| Bicarbonate (23–31 mEq/L) | 14 | 13 |
| Anion gap (5–17) | 23 | 29 |
| Glucose level (65–110 mg/dL) | 655 | 879 |
| Lactate (0.9–2.47 mmol/L) | 2.6 | 5.4 |
| Peak troponin level (0.0–0.034 ng/mL) | 4.46 | 0.443 |

was 4.46 ng/mL. The urine toxicology screen results were negative. The CT angiogram was negative for a pulmonary embolus. The ECG revealed deep T-wave inversions from V2 to V4. A coronary angiogram was performed, but no angiographic evidence of occlusive coronary artery disease was seen. The echocardiogram showed an ejection fraction of 55% to 65%, with no regional wall motion abnormalities. With treatment and resolution of the DKA, his troponin level decreased to 0.783 ng/mL. Although the patient experienced myocardial necrosis from the metabolic derangement, he was discharged with instructions to take aspirin and a high-intensity statin.

*B. Case 2*

A 57-year-old man with a medical history of hypertension and type 2 diabetes presented with abdominal pain, nausea, and vomiting after his insulin had been stolen from him 2 days before admission (Table 1). He also reported generalized weakness and polydipsia. He denied any chest pain and stated that he had good exercise tolerance. On admission, the patient's heart rate was 118 bpm, and his blood pressure was 86/36 mm Hg. Other than tachycardia, the cardiopulmonary examination findings were normal. His abdomen was soft but mildly tender to palpation. The basic metabolic panel results showed potassium of 6.9 mEq/L, bicarbonate of 13 mEq/L, anion gap of 29, blood glucose of 879 mg/dL, blood urea nitrogen of 45 mg/dL, and creatinine of 2.5 mg/dL. The venous pH was 7.136, and lactate was elevated at 5.4 mmol/L. The white blood cell count was elevated at 18.3 K/μL. The hemoglobin A1c value at this admission was 8.9. CT of the abdomen without contrast was negative for an acute intra-abdominal process. ECG revealed right bundle branch block and sinus tachycardia. The patient's troponin level was 0.099 ng/mL on admission but increased to 0.443 ng/mL. An echocardiogram was obtained, which showed an ejection fraction of 55% to 65% and no regional wall motion abnormalities. The cardiology service did not pursue a coronary angiogram, because they believed that demand ischemia and the acidotic state might have been the reason for the elevated troponin. The patient was, nonetheless, discharged with instructions to take aspirin 81 mg and atorvastatin 40 mg daily.

## 2. Discussion

Infection, omission of insulin doses, and intercurrent illness are the most common precipitants of DKA. Acute myocardial infarction is a well-recognized, albeit uncommon, precipitant, accounting for 1% to 4% of the cases [4, 6]. On the other hand, diabetes is a major risk factor for obstructive CAD and can lead to acute coronary syndrome. However, myocardial necrosis secondary to DKA in the absence of CAD can occur and has been previously reported [1–5].

Several mechanisms have been proposed to explain the troponinemia in DKA in the absence of CAD. DKA is characterized by a state of insulin deficiency. This results in high levels of ketones and free fatty acids, which in turn, inhibit glucose uptake by myocardial cells, depriving them of their fuel source [6]. Increased uptake of free fatty acids, which are

toxic to myocardial cells, could be contributory [6]. Another hypothesis to explain the elevated troponin levels is the acidotic state [1, 5]. In a retrospective study by Eubanks *et al.* [5], an admission serum pH <7.1 was associated with elevated troponin levels. The proposed mechanism is that acidemia leads to an increase in intracellular calcium. This results in proteolysis and myocardial stunning, ultimately leading to elevated troponin levels [5]. Finally, DKA results in elevated levels of counterregulatory hormones that increase the myocardial oxygen demand, thereby unmasking underlying CAD [4, 5].

According to the third universal definition, acute myocardial infarction is defined by the detection of an increase and/or decrease in cardiac biomarker values, accompanied by ischemic symptoms or ischemic electrocardiographic changes, identification of an intracoronary thrombus by angiography or autopsy, or imaging evidence of a new loss of viable myocardium or a new-regional wall motion abnormality [7]. Cardiac ischemia can be silent in patients with diabetes. In a study by Hernández *et al.* [8], true silent ischemia was detected in 21.9% of patients with diabetes. The metabolic derangements that accompany DKA can result in electrocardiographic changes that could be confused with those due to cardiac ischemia. Hyperkalemia can result in a pseudoinfarction pattern, with ST elevation and peaked T waves [1, 2]. Hyperkalemia can also result in intraventricular conduction defects, including left bundle branch block [6]. Hypokalemia can result in ST-segment depression and T-wave inversion [6]. As a result, confidently excluding obstructive CAD as the cause of troponin elevation, without angiographic confirmation, can pose diagnostic challenges.

The prognostic significance of this finding has not been the focus of many clinical studies. The study by Al-Mallah *et al.* [4], which evaluated the short- and long-term outcomes of patients with DKA and elevated troponin levels, found that 27% of the patients with DKA had elevated troponin levels on admission. No differences were found between the two groups in the severity of DKA, as estimated by the anion gap. 23.1% of the patients with elevated troponin compared with 8.6% without died during the index hospitalization. The 2-year major adverse cardiac event rate, driven primarily by mortality, was greater for the patients with elevated troponin compared with the patients with normal troponin levels (hazard ratio, 2.3; $P = 0.02$), even after adjusting for confounding variables. The study by Eubanks *et al.* [5] found similar results, except that the prevalence of elevated troponin was 10%, and the greater major adverse cardiac event rate, during an average follow-up period of 40 months, was primarily driven by the higher number of myocardial infarction.

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