Case in Point

Pseudomyocardial Infarction in Diabetic Ketoacidosis: A Clinical and Diagnostic Dilemma

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These researchers present a 59-year-old man with diabetic ketoacidosis (DKA) and disturbances in both electrocardiogram and cardiac troponin tests. However, the patient proved to have a noncritical occlusion of his coronary arteries. The problems facing the clinician who suspects cardiac injury in a patient who presents with DKA are reviewed.

Diabetes mellitus (DM) is a risk factor for the development of atherosclerotic coronary artery disease (CAD). Even though DM and CAD commonly occur together, acute cardiac events (CEs) are not often associated. In fact, acute myocardial infarction (MI) is associated with about 1% of diabetic ketoacidosis (DKA) episodes.[1] Nevertheless, prompt identification of a concurrent CE is essential to ensure correct diagnosis and appropriate and timely treatment.

A recent task force for the redefinition of MI suggests that an acute MI is present when the detection of a rise in the cardiac biomarker troponin is accompanied by electrocardiographic (EKG) changes of new ischemia.[2] The clinician attempting to apply the recommended diagnostic standards for acute MI faces a challenge when dealing with the adult patient with diabetes admitted with DKA, because both EKG changes mimicking ischemia or infarction and elevated troponins have been described as a consequence of this diabetic emergency.

CASE REPORT

A 59-year-old man reported nausea and intermittent vomiting over a 3-day period. He did not report abdominal pain, fever, chills, or diarrhea. His past medical history included insulin-dependent DM for 19 years as well as hypertension and depression. His DM was treated with regular insulin adjusted on a sliding scale. He acknowledged that the nausea had begun after he had exhausted his insulin prescription. Despite the nausea, he managed to take his oral maintenance medications, which included lisinopril 2.5 mg once daily, metoprolol tartrate 50 mg once daily, and mirtazapine 30 mg at bedtime. He did not use over-the-counter medications, vitamins, herbal remedies, or illicit drugs. He also did not consume alcohol. He smoked 1 pack of cigarettes each day and had a cumulative 30-pack-year history of tobacco use. His family history was unremarkable for heart disease.

The patient was well nourished. His blood pressure was 120/48 mm Hg in both arms. He was afebrile. His heart rate was 124 beats per minute in a regular rhythm, and his respiratory rate was 36 breaths per minute. He was alert and communicative despite his tachypnea. His oral mucous membranes were dry. The cardiopulmonary examination was normal. His abdomen was soft and nontender with active bowel sounds. There was no cyanosis, clubbing, or edema of his extremities.

The initial laboratory analysis measured the serum glucose level as 1,964 mg/dL (reference range [RR], 75-110 mg/dL). The serum sodium level was 113 mEq/L (RR,

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135-145 mEq/L) with a serum potassium level of 7.3 mEq/L (RR, 3.6-5.0 mEq/L), a serum bicarbonate level of 5 mEq/L (RR, 21-31 mEq/L), and a serum chloride level of 81 mEq/L (RR, 101-111 mEq/L). The calculated anion gap was 27 mEq/L. An arterial blood gas analysis with the patient breathing room air measured the pH at 6.96, the partial pressure of carbon dioxide as 12 mm Hg, and the partial pressure of oxygen at 131 mm Hg. Ketones were present in the serum and urine. Serum creatinine was slightly elevated to 1.5 mg/dL (RR, 0.7-1.3 mg/dL), and the blood urea nitrogen level was 31 mg/dL (RR, 9-21 mg/dL). The white blood cell count was 28.6 x 103/mcL (4.8-10.5 x 103/mcL). The urinalysis was unremarkable except for ketonuria. Blood cultures were obtained and returned with no growth. Posterior-anterior and lateral chest radiographs were unremarkable.

Two EKGs were performed during the first 12 hours. These tracings suggested nonspecific ST and T wave changes. The electrical activity could not be more accurately analyzed due to the artifact and wandering baseline introduced by the patient's labored breathing. Cardiac isoenzymes were obtained on admission to the emergency department and at 4-hour intervals until 3 samples had been sent for analysis.

The patient received treatment directed at his DKA with intravenous (IV) fluid administration and an IV insulin infusion. The initial troponin (cardiac troponin I [cTnI]) was 20.1 ng/mL, followed by 14.1 ng/mL and 8.0 ng/mL (RR, 0.000-0.034 ng/mL).

A left heart cardiac catheterization was performed because of concern for acute myocardial ischemia. This study demonstrated that left ventricular function was preserved with an estimated ejection fraction of 55%. There was a 25% proximal nonobstructive lesion in the left anterior descending coronary artery, a 50% nonobstructive lesion in the nondominant left circumflex coronary artery, and a 50% nonobstructive lesion in the dominant right coronary artery.

The patient's condition improved over the next 24 hours with the return to normal of his arterial pH and electrolytes. He was able to tolerate both liquids and solids and returned to his outpatient insulin prescription. An echocardiogram prior to discharge was normal.

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DISCUSSION

About 2% to 8% of all hospital admissions for patients with diabetes are for the treatment of DKA.[3] Myocardial infarction has been recognized in association with this diabetic emergency in about 1% of DKA cases.[1] Acute MI and congestive heart failure are responsible for 28% of the deaths in DKA.[4] It is, therefore, imperative that the clinicians consider MI in the adult patient with diabetes who presents with DKA.

To be successful in recognizing MI in the context of DKA, a clinician must be aware that the severe metabolic abnormalities and stress of the illness can affect the cardiac electrophysiology and rhythm as well as the cardiac biomarkers.[5] These parameters have increased significance in recognizing an actual MI in DKA, because myocardial injury can be clinically silent in patients with DM.[5]

An EKG is typically included in the initial baseline data of most adult patients with DKA who are admitted to the special care units to determine the effects of volume depletion and electrolyte abnormalities on the cardiovascular system. Usually this tracing is normal. However, it is often the first test to suggest myocardial ischemia in the patient admitted with DKA. It has long been known that hyperkalemia can have a significant effect on myocardial conduction and repolarization that may be reflected on the EKG. In some cases, the changes induced by hyperkalemia mimic MI with ST-segment elevation. This occurrence is well described in the medical literature as a pseudoinfarction pattern.[6] Since the serum potassium is > 6.0 mmol/L in 20% to 30% of patients with DKA, ample opportunity exists for the clinician to encounter this EKG change.[7-11] However, hyperkalemia may not be the only explanation for the pseudoinfarction pattern seen in patients with DKA, since the phenomenon has also been witnessed in patients with DKA without elevated serum potassium levels.[12] In this situation, ST-segment changes have been attributed to other mechanisms, such as anoxia, severe acidosis, and coronary artery spasm.[8]

The recognition of an abnormal cardiac rhythm or electrical forces on the initial EKG will likely prompt the clinician to check the patient's cardiac biomarkers, especially cTnI. In the correct context, an elevated troponin is part of the defining criteria for acute MI.[2] In most reports of the pseudoinfarction pattern occurring in DKA, the cardiac biomarkers have remained

within the accepted range of normal, helping the clinician attribute the aberrant conduction to the severe metabolic abnormalities associated with the diabetic emergency rather than to myocardial injury. Likewise, serial EKGs done during successful treatment of the ketoacidosis and hyperkalemia typically show rapid resolution toward normal. The EKG often returns to baseline within 12 hours.

The new methods of measuring cTnI, however, have a high-sensitivity and allow for the detection of very minor damages of the heart muscle.[13] As the use of cTnI measurement has expanded in clinical practice, it has been realized that noncoronary diseases may also injure myocytes and result in elevation of this biomarker.[14] Within the last decade, there have been reports of increased cTnI in patients with DKA.[15-19] Diabetic ketoacidosis must now be included in the list of conditions other than acute MI that may cause an elevated cTnI.[16] The mechanism of myocardial necrosis secondary to metabolic derangements is still unclear and is likely multifactorial. Those patients with a noncoronary elevation of cTnI in the context of DKA are believed to experience a nonspecific myonecrosis without permanent changes in their cardiac function as determined by echocardiography. There is observational evidence suggesting that the myocardial injury is due to the severe acidosis inherent in DKA.[15] In one study, the serum cTnI levels correlated inversely with the blood pH on admission.[15]

Few reports in the medical literature described patients with DKA who had both elevated myocardial biomarkers and initial EKG changes compatible with myocardial ischemia.[10,17] However, the occurrence of elevated cTnI levels in patients with DKA is likely more frequent than previously recognized. In a 2-year retrospective study, 26 of 96 patients with DKA who had cTnI measured had elevated levels.[18] In a prospective study of adult patients with diabetes at another center, 4 of 40 patients presenting with DKA had an increase in cTnI.[19] In both series, the patients with positive troponins had no identifiable macrovascular coronary disease or myocardial dysfunction. Whether the cTnI elevation observed in some cases of DKA was due to demand ischemia, enzyme leak due to tachycardia, myocardial cell injury from acidosis or electrolyte imbalance, or microvascular diseases is not known.

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The clinical relevance of the presence of cTnI in ketoacidosis has not been examined in a large scale study over a prolonged period of time. However, when patients with DKA who have positive cTnI were followed over a 2-year period, the presence of an elevated cTnI on admission seemed to identify a subset of patients with diabetes that is at high risk for future CEs and mortality.[18]

CONCLUSION

Although acute MI is known to occur with DKA, it may be difficult to recognize. There are limitations of both the EKG and cTnI measurement in the setting of DKA as aides in the decision-making process. The clinician should perform serial EKGs and cardiac enzyme tests during the first 12 hours of treatment. The EKG is expected to resolve from its pseudoinfarction pattern during this interval. Pretest probability that an elevated serum cTnI in the setting of DKA reflects active CAD may be aided by the observation that the degree of elevation of the serum cTnI seems to have an inverse relationship to the admission pH.[15] Finding an elevated cTnI in a patient with DKA with only mild acidosis would suggest an alternate explanation. In essence, this sensitive biomarker is less helpful in ruling in a MI in this setting, yet remains a useful tool in ruling out an acute coronary syndrome. Invasive action to investigate the coronary arteries when both the EKG and cTnI are abnormal in a patient with diabetes with DKA should be tempered by the observation that both may quickly return to normal with effective treatment of the diabetic emergency.[15,20] ●

Author disclosures

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REFERENCES

1. Chen HF, Wang CY, Lee HY, et al. Short-term case fatality rate and associated factors among inpatients with diabetic ketoacidosis and hyperglycemic hyperosmolar state: A hospital-based analysis over a 15-year period. *Intern Med.* 2010;49(8):729-737.
2. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF /AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Eur Heart J.* 2007;28(20):2525-2538.
3. Delaney MF, Zisman A, Kettyle WM. Diabetic ketoacidosis and hyperosmolar nonketotic syndrome. *Endocrinol Metab Clin North Am.* 2000;29(4):683-705, V.
4. Krentz AJ, Natrass M. Acute metabolic complications of diabetes mellitus: Diabetic ketoacidosis, hyperosmolar non-ketotic syndrome and lactic acidosis. In: Pickup J, Williams G, eds. *Textbook of Diabetes.* 3rd ed. Oxford, UK: Blackwell Sciences, LTD; 2003.
5. Moulik PK, Nethaji C, Khaleeli AA. Misleading electrocardiographic results in a patient with hyperkalaemia and diabetic ketoacidosis. *BMJ.* 2002;325:1346-1347.
6. Tatli E, Altun A, Yilmaztepe M. ST segment elevation following sinoventricular rhythm in a patient with diabetic ketoacidosis. *Cardiol J.* 2007;14(5):497-499.
7. Chiasson JL, Aris-Jilwan N, Bélanger R, et al. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ.* 2003;168(7):859-866.
8. Ziakas A, Basagiannis C, Stiliadis I. Pseudoinfarction pattern in a patient with hyperkalemia, diabetic ketoacidosis and normal coronary vessels: A case report. *J Med Case Rep.* 2010;4:115.
9. Bellazzini MA, Meyer T. Pseudo-myocardial infarction in diabetic ketoacidosis with hyperkalemia. *J Emerg Med.* 2010;39(4):e139-e141.
10. Egred M, Morrison WL. Images in cardiology: Diabetic keto-acidosis and hyperkalaemia induced pseudo-myocardial infarction. *Heart.* 2005;91(9):1180.
11. Sims DB, Sperling LS. Images in cardiovascular medicine. ST-segment elevation resulting from hyperkalemia. *Circulation.* 2005;111(19):e295-e296.
12. Aksakal E, Duman H, Ulus T, Bayram E. Acute inferior pseudoinfarction pattern in a patient with normokalemia and diabetic ketoacidosis. *Am J Emerg Med.* 2009;27(2):251.e3-251.e5.
13. Agewall S, Giannitsis E, Jernberg T, Katus H. Troponin elevation in coronary vs. non-coronary disease. *Eur Heart J.* 2011;32(4):404-411.
14. Jeremias A, Gibson CM. Narrative review: Alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded. *Ann Intern Med.* 2005;142(9):786-791.
15. Atabek ME, Pirgon O, Oran B, Erkul I, Kurtoglu S. Increased cardiac troponin I concentration in diabetic ketoacidosis. *J Pediatr Endocrinol Metab.* 2004;17(8):1077-1082.
16. Mahajan N, Mehta Y, Rose M, Shani J, Lichstein E. Elevated troponin level is not synonymous with myocardial infarction. *Int J Cardiol.* 2006;111(3):442-449.
17. Moller N, Foss AC, Gravholt CH, Mortensen UM, Poulsen SH, Mogensen CE. Myocardial injury with biomarker elevation in diabetic ketoacidosis. *J Diabetes Complications.* 2005;19(6):361-363.
18. Al-Mallah M, Zuberi O, Arida M, Kim HE. Positive troponin in diabetic ketoacidosis without evident acute coronary syndrome predicts adverse cardiac events. *Clin Cardiol.* 2008;31(2):67-71.
19. Geddes J, Deans KA, Cormack A, et al. Cardiac troponin I concentrations in people presenting with diabetic ketoacidosis. *Ann Clin Biochem.* 2007;44(pt 4):391-393.
20. Fuller PJ, Colman PG, Harper RW, Stockigt JR. Transient anterior electrocardiographic changes simulating acute anterior myocardial infarction in diabetic ketoacidosis. *Diabetes Care.* 1982;5(2):118-121.