Multiple admissions to the coronary care unit due to falsely elevated cardiac troponin

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ABSTRACT

The measurement of cardiac troponin, released from injured cardiomyocytes, is of paramount importance in the diagnosis of acute myocardial infarction. Elevated troponin can be encountered, however, in patients with cardiomyopathy, significant cardiac arrhythmias, vasculitis, right-sided heart strain, critical systemic illnesses, stroke, drug toxicity (such as Adriamycin), poisons (such as snake venoms), renal failure, seizure, and rhabdomyolysis. If the clinical picture is not consistent with any of these causes, a false-positive result should be considered. We herein describe a 94-year-old man with a prior history of coronary artery disease who presented with altered mental status and was found to have a persistently high troponin level resulting in three admissions to the coronary care unit for various noncardiac complaints. Because of discordance between clinical and laboratory data, immunological interference due to heterophile antibodies in the locally used assay (AccuTnI+3, Beckman Coulter) was suspected. The same serum sample tested on a different assay (Elecsys Troponin I Assay, Roche) resulted in an undetectable cardiac troponin I level, thus confirming the diagnosis.

KEYWORDS Cardiac troponin; myocardial infarction; troponin immunoassay

Measurement of cardiac troponin (cTn) is useful in the diagnosis of acute myocardial infarction. At times, elevation of cTn may not be secondary to cardiac injury, and other causes of cTn elevation should be considered. We herein describe a 94-year-old man who presented with altered mental status and had three different admissions to the coronary care unit for false-positive cTn.

CASE PRESENTATION

A 94-year-old white man was known to have coronary artery disease and had coronary artery bypass grafting at age 88. A permanent pacemaker had been implanted for symptomatic bradycardia. He presented to the hospital with altered mental status and change in behavior. He denied any chest pain or dyspnea. On exam, he was frail. His blood pressure was 130/78 mm Hg; heart rate, 76 beats per minute; respiratory rate, 16 breaths per minute; and pulse oximetry, 95% on room air. His temperature was 98.6°F. Precordial exam

disclosed no abnormalities. His chest was clear to auscultation bilaterally. His abdomen was mildly tender on palpation. No neurological abnormalities were noted. Laboratory work revealed a normal hemoglobin of 13 g/dL, a white blood cell count of $9.0 \times 10^3/\mu\text{L}$, a platelet count of $141 \times 10^3/\mu\text{L}$, and creatinine of 0.7 mg/dL. Importantly, serial cTnI was markedly elevated at 30.8 ng/mL, 29.6 ng/mL, and then 29.9 ng/mL (AccuTnI+3, Beckman Coulter, reference <0.03 ng/mL). Electrocardiogram revealed ventricular paced rhythm unchanged from previous visits. The patient was admitted to the coronary care unit and started on subcutaneous enoxaparin. A transthoracic echocardiogram showed normal left ventricular wall thickness and internal dimensions with no wall motion abnormalities. A urinary tract infection was diagnosed and the patient had an uneventful recovery with antibiotics. Review of records revealed three different admissions to the coronary care unit over the previous 3 years for various noncardiac complaints and similar troponin elevations (all without a rise and fall).

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Received November 13, 2017; Revised December 27, 2017; Accepted December 28, 2017.

Figure 1. (a) A schematic illustration of an immunometric assay for cardiac troponin. (b) Falsely elevated result caused by interference from heterophilic antibodies.

Because of persistent elevations in cTn with a clinical presentation that did not support any specific diagnosis, the possibility of spuriously elevated Tn was considered. Other tests included creatine kinase-MB, 6 IU/L (reference 5–25); myoglobin, 80 ng/mL (reference range 28–72); low-density lipoprotein, 252 U/L (reference 100–190); alkaline phosphatase, 59 IU/L (reference range 31–126); and normal protein electrophoresis. Testing was negative for the presence of rheumatoid factor or human anti-mouse antibodies. The patient's blood sample was tested with different immunoassays (Elecsys Troponin I and T Assay, Roche), which revealed undetectable cTnI and cTnT levels. The diagnosis of spurious elevation of troponin was confirmed.

DISCUSSION

Cardiac troponin is a member of a complex group of proteins that modulate the calcium-mediated interaction between actin and myosin within the cardiac myocytes.¹ In acute myocardial infarction, cTn levels rise within 3 to 4 hours after the occurrence of clinical symptoms, reaching a peak at 12 to 16 hours, and can remain elevated for up to 9 to 14 days after myocardial infarction.^{1–3} Different clinical syndrome settings can cause troponin elevation without direct cardiac ischemia. These include but are not limited to right and/or left heart failure, significant cardiac arrhythmias, cardiac surgery, vasculitis, severe sepsis, critical illnesses, ischemic and hemorrhagic stroke, drug toxicity, poisons, end-stage renal disease, seizure, and rhabdomyolysis.^{4–6} However, most of these clinical conditions do not exhibit the classic rise and fall pattern typically seen with ischemic cardiac injuries.^{7,8}

Various assays are available for detection of cardiac troponin in the clinical setting with poor correlation between assays.⁹ The principle behind these tests is usually a two-site immuno-enzymatic (sandwich) assay. The presence of heterophile antibodies in the serum can interfere with the assay and produce false-positive tests.^{10,11} Heterophile antibodies can be present in patients who have been routinely exposed to animals or have received immunotherapy. Other endogenous substances such as rheumatoid factor, excess fibrin, and endogenous alkaline phosphatase can also produce false-positive results.^{12–14}

Our laboratory uses the AccuTnI+3 assay, which uses monoclonal antibodies specifically directed against human cardiac troponin I. The AccuTnI+ assay uses mouse monoclonal

antihuman cTnI alkaline phosphatase conjugate and uses a surfactant, bovine serum albumin matrix, and protein (bovine, goat, mouse) as reagents. By using the Elecsys Troponin assay, which utilizes two monoclonal antibodies specifically directed against human cardiac troponin, we identified normal levels of cTn. The Elecsys Troponin assay utilizes biotinylated monoclonal antitroponin antibody (mouse), with streptavidin-coated microparticles and phosphate buffers as reagents. We believe that the falsely elevated cTnI result on AccuTnI+3 assay was due to the presence of a human antianimal antibody (goat or bovine) causing immunologic interference (*Figure 1*). The prevalence of false-positive troponin elevations was found to be as high as 3.1% in a cohort study.¹⁵ A systematic approach is needed to diagnose false-positive elevations and avoid unnecessary testing.

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