SciMedCentral

JSM Atherosclerosis

Case Report

Increase in Troponin I Levels due to Heterophilic Antibody Interference: Is Influenza Responsible for this False Troponin Elevation?

Heyi Li[1], Udit Joshi[1], Fady Iskander[2], Tareq Alyousef[2], and Vamsi Kodumuri[2]*

[1]*Internal Medicine, John H. Stroger Jr. Hospital of Cook County, USA*
[2]*Department of Cardiology, John H. Stroger Jr. Hospital of Cook County, USA*

***Corresponding author**
Vamsi Kodumuri, Department of Cardiology, John H. Stroger Jr. Hospital of Cook County, 1901 W Harrison St Rm 3620, Chicago, IL, 60608, USA, Tel: (312)8643427; Email: vkodumuri@cookcountyhhs.org

Submitted: 24 April 2018

Accepted: 01 May 2018

Published: 02 May 2018

ISSN: 2573-1270

OPEN ACCESS

Keywords
- Heterophile antibodies
- Troponin I
- Immunoassay interference
- Influenza A

Abstract

A 63-year-old woman was admitted for influenza A infection and elevated cardiac troponin I without dynamic changes on the ECG. She had recently undergone coronary angiography which had shown normal coronary vessels. Her troponin I levels were persistently elevated while simultaneous CK-MB levels were normal. Troponin I levels tested using a different assay remained significantly lower. Subsequent testing confirmed the presence of heterophile antibodies interfering with the troponin I assay leading to a false positive result. Further research is needed to elucidate the role of influenza in producing heterophile antibodies.

ABBREVIATIONS

HA: Heterophilic Antibodies; ECG: Electrocardiography; POC: Point-of-Care; TTE: Transthoracic Echocardiogram; CCU: Coronary Care Unit; NSTEMI: Non ST Elevation Myocardial Infarction

INTRODUCTION

Heterophile antibodies (HAs) are a category of weak antibodies against poorly defined antigens. HAs usually arise after infection or contact with animal tissues or animal serum products [1]. Such interfering antibodies can potentially cause erroneous results in any assays employing antibodies. The prevalence of false positive troponin elevations in routine populations has been found in studies to be as high as 3.1% [2]. We report a 63-year-old female who was admitted for an influenza A infection whose serum troponin I concentration was persistently elevated due to interference from heterophilic antibodies, which lead to inevitable prolonged hospitalization. The association of the presence of HAs and the influenza infection remains unclear.

CASE PRESENTATION

A 63-year-old female with a history of hypertension and end-stage renal disease on hemodialysis presented to the emergency room for a two-week history of mildly productive cough. She did not have any chest pain, shortness of breath, orthopnea, paroxysmal nocturnal dyspnea or leg swelling. Her blood pressure was elevated to 188/86 mmHg. She was febrile to 100.8 F. Physical exam was also remarkable for 4/6 holosystolic murmur heard all over the precordium. Her ECG (Electrocardiography) showed sinus tachycardia with a heart rate of 100/ minute and ST-T wave changes. Her first set of serum Point-of-Care (POC) troponin I concentration was 0.395 ng/ml measured by FASTPATH assay (reference range 0.000-0.028 ng/ml), and 24.163 ng/ml measured by DxI 800 Immunoassay System (Beckman Coulter, reference range 0.000-0.039 ng/ml). She stated that she recently had a coronary angiogram, which showed normal coronaries without any significant epicardial stenosis. She was loaded with aspirin and clopidogrel in the Emergency room and was admitted to the CCU (Coronary Care Unit) for further monitoring and management.

In the CCU, she was started on heparin drip as a part of the management of Non ST-elevation Myocardial Infarction (NSTEMI) given very high troponin levels. ECGs and troponin were repeated every 6 hours. The sequential ECGs didn't show any dynamic ST-T changes. Repeated troponins were persistently elevated in the range of 23-24 ng/ml for four days (measured using DxI 800 Immunoassay System). In the meantime, CK-MB was normal (2.2 ng /ml, reference 0.60-6.30ng/ml). A TTE (transthoracic echocardiogram) revealed normal ejection fraction with normal wall motion, mild to moderate mitral valve stenosis, severely dilated left atrium, elevated estimated pulmonary artery systolic pressure (80-85 mmHg), dilated

right ventricle, right atrium and severe tricuspid regurgitation. She was found to be positive for influenza A and was started on Oseltamivir. Blood pressure normalized after her home anti-hypertensive medications were resumed.

Considering her atypical symptoms, persistently elevated non-trending troponin, the absence of dynamic ECG changes, normal wall motion on TTE and recent normal coronary angiogram, the concern of falsely elevated Tn levels was raised. POC troponin-using FASTPATH was sent again which was still low (0.251 ng/ml, reference range 0.000-0.028 ng/ml) while the troponin measured on the same sample with Coulter method was elevated (23ng/ml, reference range 0.000-0.039 ng/ml). These findings suggested that one of those troponin assays was giving false results. Rheumatoid factor and heterophile antibody test were sent given their previously reported potential in causing a false elevation of troponin [3,4]. The levels returned as negative. The patient opted not to have more ischemic evaluation during the index admission.

Her serum and plasma samples were sent to Beckman Coulter for investigative testing. Testing of the neat sample confirmed the elevated troponin levels. Interference testing using heterophileHBR1) and alkaline phosphatase (AP Mutein) blockers were performed. Result recovery was significantly reduced using the heterophile blocker but the recovery was not reduced using alkaline phosphatase blocker. This was consistent with heterophile antibody interfering causing false troponin elevation.

After a five-day CCU stay, the patient was decided to be clinically stable and was discharged home with outpatient follow-up.

DISCUSSION

Heterophilic antibodies have been reported as an important source of interference in laboratory medicine. They are previously reported as a potential cause of falsely elevated troponins [1] which sometimes causes unnecessary admissions and multitude of investigations. HAs mimic troponin and bind the Fc portion of the antibodies impregnated on ELISA [5]. These antibodies were reported to arise from infections, blood transfusion [6], vaccinations [7], exposure to pets, ingesting animal proteins, rheumatoid factor [8] and other unknown causes. Despite the high prevelance of HAs (reported to be as high as 40% [9]), it is usually hard to identify the stimulating factor causing HA production. In our case, the patient had persistently high troponin I levels which were confirmed to be caused by interference from HAs. However, there is no literature on the association of influenza infection and the presence of HAs. The role of influenza A infection in this case remains unclear.

The interference caused by HAs should be suspected when the elevated troponin does not correlate with the clinical course and other investigations. A number of strategies exist to counteract interference from heterophile antibodies. Repetition of the test with a different assay is an easy way to identify the possibility of interference. Patient samples are sometimes diluted to reduce the effect of HAs but this is no longer recommended since it inevitably lowers the concentration of troponin at the same time. Removal of interfering antibodies using heterophilic antibodies blocking reagent can help to rule out the inference caused by HAs as in our patient.

It is very important for the physicians to be cognizant of this phenomenon, which is not uncommon, and subjects patients to multiple investigations and unnecessary hospital stay. Any troponin elevation should be interpreted based on the overall clinical picture.

ACKNOWLEDGEMENTS

Dr. Tony Wicheanvonago, phD, John. H. Stroger Jr. Hospital of Cook County.

REFERENCES

1. Ammann P, Pfisterer M, Fehr T, Rickli H. Raised cardiac troponins: causes extend beyond acute coronary syndromes. BMJ. 2004; 328: 1028.
2. Fleming SM, O'Byrne L, Finn J, Grimes H, Daly KM. False-positive cardiac troponin I in a routine clinical population. Am J Cardiol. 2002; 89: 1212-1215.
3. Krahn J, Parry DM, Leroux M, Dalton J. High percentage of false positive cardiac troponin I results in patients with rheumatoid factor. Clin Biochem. 1999; 32: 477-480.
4. Lippi G, Aloe R, Meschi T, Borghi L, Cervellin G. Interference from heterophilic antibodies in troponin testing. Case report and systematic review of the literature. Clin Chim Acta. 2013; 426: 79-84.
5. Zaidi A, Cowell R. False positive cardiac troponin elevation due to heterophile antibodies: more common than we recognise? BMJ Case Rep. 2010; 2010.
6. Hawkins BR, Saueracker GC, Dawkins RL, Davey MG, O'Connor KJ. Population study of heterophile antibodies. Vox Sang. 1980; 39: 339-342.
7. Palache AM, Brands R, Scharrenburg GV. Immunogenicity and reactogenicity of influenza subunit vaccines produced in MDCK cells or fertilized chicken eggs. J Infect Dis. 1997; 176: 20-23.
8. Marks V. False-positive immunoassay results: a multicenter survey of erroneous immunoassay results from assays of 74 analytes in 10 donors from 66 laboratories in seven countries. Clin Chem. 2002; 48: 2008-2016.
9. Ward G, Simpson A, Boscato L, Hickman PE. The investigation of interferences in immunoassay. Clin Biochem. 2017; 50: 1306-1311.

Cite this article

Li H, Joshi U, Iskander F, Alyousef T, Kodumuri V (2018) Increase in Troponin I Levels due to Heterophilic Antibody Interference: Is Influenza Responsible for this False Troponin Elevation? JSM Atheroscler 3(1): 1041.