AUCTORES
Globalize your Research

Cardiology Research and Reports
Rateesh Sareen *

Open Access

Letter to editor

Falsely Elevated Troponin I Levels in Influenza H1N1 Positive Patient

Rateesh Sareen [1*], Shyam Saini [2], G N Gupta [3], Madhulika Sharma [4]

[1] Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India.

[2] Senior laboratory technical manager, Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India.

[3] Consultant & Head Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India.

[4] Sr Consultant & Head, Department of Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India.

***Corresponding Author:** Rateesh Sareen, Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India.

Received date: November 09, 2023; **Accepted date:** December 20, 2023; **Published date:** January 02, 2023

Citation: Sareen R., Saini S., G. N. Gupta, Sharma M., (2023), Falsely Elevated Troponin I Levels in Influenza H1N1 Positive Patient, *Cardiology Research and Reports*. 5(1); **DOI:**10.31579/2692-9759/081

Abstract

An adult male admitted in emergency with complaint of fever and respiratory distress. On work up several fold increase in Troponin I levels were noted. The cardiac work up did not reveal any abnormality. The patient was tested for H1N1 Influenza RNA PCR which came positive and patient was treated with Tamiflu. The spurious high sensitivity Troponin I levels assay mandates that the test result should always be seen in light of clinical scenario as non-cardiac elevations are more frequent as thought.

Keywords: acute coronary syndrome; heterophile antibody; alkaline phosphatase

To the editor

Troponins are single chain polypeptides involved in the regulation of cardiac muscle contraction and are crucial biomarkers in the diagnosis of acute coronary syndrome (ACS). [1] Troponin I (Tn I) and Troponin T (Tn T) exist as two iso forms- skeletal and cardiac form respectively.[2] It is to be noted that currently used monoclonal antibody-based assays do not detect skeletal isoforms therefore their interference is not encountered in assays used for cardiac Troponins. [3]

Cardiac Troponins- Tn I and Tn T are most sensitive and specific markers for cardiac monocyte damage. [4] There are many different assays for cTn I measurement that make cTn I a labile marker and at times is falsely elevated without cardiac cause. The present as case report is one such example that caused diagnostic dilemma to clinical team. It is therefore prudent to make accurate diagnosis backed by clinical history and ECG findings rather than solely relying on biomarkers only.

We present a case of elderly man presenting with chest discomfort, respiratory distress to emergency unit. The initial investigations showed elevated hs Trop I levels without any changes in ECG or cardiac ailment. On further work up the cause of elevated TropnI level was non-cardiogenic most likely H1N1 virus infection.

The patient presented in emergency department of tertiary care hospital in western India with complaints of fever, vomiting and respiratory distress. The laboratory investigations revealed-BUN- 25 mg/dl, Creatinine -0.6 mg /dl, Sodium 133 m mol/liter, potassium 3.3 m mol/liter, chloride 100 m mol/lit, SGOT- 220U/L, SGPT 122 U/L, Total protein-5.1 gm/dl, Albumin 1.8 gm/dl, globulin 3.3 gm/dl, A/G ratio 0.5, Alkaline Phosphatase 102 U/L, Gamma GT-90 U/L, Procalcitonin- 3.52 ug/L & LDH – 319 U/L.

An automated complete blood count (CBC) demonstrated Hemoglobin- 116 g/L (reference range 130-170 g/L), white blood cell count 18.35 x 10 9 /L (reference range 4-10 x 10 9 /L) Platelet count 265 x 10 9/L (reference range 150-450 x 109/L) , Hematocrit 34.3 % (reference range-36%-46%), differential count – Blasts+ Promyelocytes- 12%, Myelocytes-15%, Neutrophils- 87%, Band forms-3% & Lymphocytes-10%.Test for HIV 1 & 2, Hepatitis B and C viral serology were non-reactive. Malarial smears and rapid malarial antigen test were negative. Routine urine and stool examination did not show any abnormal finding. There was strong suspicion of cardiac disease and so an immediate Troponin I was done which was 2725 ng/L and pro BNP – 3540 pg/ml. The elevated Troponin I levels prompted us to refer to cardiologist who on subsequent work up didn't find any cardiac cause for the ailment. A repeat Troponin I level after 12 hours of admission revealed further escalation of Troponin, I levels to 3198 ng/L. The elevated Trop I level without cardiac ailment prompted us to do literature search for causes of falsely elevated Trop I levels. Thereafter the patient was tested for infective viral etiologies COVID 19 and swine flu H1N1.pcr covid WAS NEGATIVE (Mol Bio diagnostics) and H1N1 RNA PCR (Taqman assay)

was positive with ct value 18.4. The additional workup using estimation of carcinoembryonic antigen (CEA), CA-19.9 and anti-nuclear antibody (ANA) were within normal reference range for age of patient. The patient was started on anti-viral Tamiflu and a repeat Troponin I was done after 4 days which decreased to 457.8 ng/L. Sputum, blood and urine culture was negative for any microbial growth.

Cardiac Troponin elevation is seen in other conditions that are not classical MI, these are referred as false positive elevations. [1, 5] (Table-1) that occur in absence of myocyte necrosis.

Table-1 Causes of falsely elevated Troponin I levels	
Interference	Alkaline phosphatase Fibrin Heterophile antibody
Hemolysis	
Renal dysfunction	
Laboratory error	

There is literature evidence to suggest role of interference by Heterophile antibody in serum of patient leading to falsely elevated Troponin elevation.[6] Heterophile antibodies are produced against poorly defined antigens as a result of transfused blood [7], vaccination [8], dietary antigens [9] and therapeutic antibodies [10].

False elevations of Troponin can also be attributed to immunoglobin-Troponin complex referred as macro troponin. In the current case the elaborate cardiac work up did not reveal any cardiac pathology. Infection with H1N1 virus was detected and patient was started on oral Tamiflu, ant viral drug. A repeat Trop I level estimation on day 3 showed falls to more than 75% of initial value suggesting H1N1 as cause of this elevation. The facts are supported by literature studies by Brown et al [11], Pecavar et al [12], Chacko et al [13] , Han et al[14] , Ludwig et al [15] , Wang et al [16] and Greaves et al [17] who have reported Troponin I level elevations in H1N1 infection. However, the rise as seen in our case makes it rare case as the rise of Troponin, I reported in studies was 10% of normal or maximum four times of normal level whereas in the present case the elevation was several folds. The elevated Troponin levels in H1N1 indicate in poor prognosis but fortunately timely anti-viral therapy resulted in good outcome for the patient in current case. In the present case high sensitivity Trop, I test was used which allow accurate detection of Trop I levels whereas literature studies have been done on other contemporary assays with heterogeneous cut offs. [18-20] The elevated Trop I levels in H1N1 infection are indicator of poor prognosis but the timely testing for H1N1 in current case helped clinician to start antiviral Tamiflu immediately and such prompt intervention resulted in favorable uneventful recovery of patient.

The take home message is straightforward that every laboratory investigation should be interpreted in clinical context of patient as over reliance on spurious laboratory result could delay diagnosis and there by affect prognosis.

Sources of funding: Nil

Conflict of interest: None

References:

1. M. Katz, (1992). Physiology of the Heart, Raven Press, New York, NY, USA, 2nd edition.
2. Public health weekly reports for NOVEMBER 11, 1932. *Publ Health Rep*, 47:2159e89.
3. Peretz A, Azrad M, Blum A. (2019). Influenza virus and atherosclerosis. *QJM*; 112:749e55.
4. Thygesen K, Alpert JS, White HD, et al. (2007). Universal definition of myocardial infarction. *Circulation*; 116:2634–2653.
5. D. A. Morrow, C. P. Cannon, R. L. Jesse et al., (2007). National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes, *Circulation*, vol. 115, no. 13, pp. e356–e375.
6. Zaidi A, Cowell R. (2010). False positive cardiac troponin elevation due to heterophile antibodies: more common than we recognise? *BMJ Case Rep*. bcr1120092477.
7. Hawkins BR, Saueracker GC, Dawkins RL, et al. (1980). Population study of heterophile antibodies. *Vox Sang*; 39:339–342.
8. Palache AM, Brands R, van Scharrenburg GJ. (1997). Immunogenicity and reactogenicity of influenza subunit vaccines produced in MDCK cells or fertilized chicken eggs. *J Infect Dis*;176(Suppl 1):S20–S23.
9. Jewell DP, Truelove SC. (1972). Circulating antibodies to cow's milk proteins in ulcerative colitis. *Gut*; 13:796–801.
10. Legouffe E, Liautard J, Gaillard JP, et al. (1994). Human anti-mouse antibody response to the injection of murine monoclonal antibodies against IL-6. *Clin Exp Immunol*; 98:323–329.
11. Brown SM, Pittman J, Miller Iii RR, Horton KD, Markewitz B, et al. (2011). Right and left heart failure in severe H1N1 influenza A infection. *Eur Respir J*; 37:112e8.
12. Pecavar B, Nadrah K, Papst L, Cec V, Kotar T, et al. (2011). Clinical characteristics of adult patients with influenza-like illness hospitalized in general ward during Influenza a H1N1pandemic 2009/2010. Wien Klin Wochenschr; 123:662e7.
13. Chacko B, Peter JV, Pichamuthu K, Ramakrishna K, Moorthy M, et al. (2012). Cardiac manifestations in patients with pandemic (H1N1) 2009 virus infection need in intensive care. *J Crit Care*; 27:106. e1e6.
14. Han J, Mou Y, Yan D, Zhang YT, Jiang TA, Zhang YY, et al. (2015). Transient cardiac injury during H7N9 infection. *Eur J Clin Invest*; 45:117e25.
15. Ludwig A, Lucero-Obusan C, Schirmer P, Winston C, Holodniy M. (2015). Acute cardiac injury events </¼30 days after laboratory-confirmed influenza virus infection among U.S. veterans, 2010-2012. *BMC Cardiovasc Disord*; 15:109.
16. Wang J, Xu H, Yang X, Zhao D, Liu S, et al. (2017). Cardiac complications associated with the influenza viruses A subtype H7N9 or pandemic H1N1 in critically ill patients under intensive care. *Braz J Infect Dis*; 21:12e8
17. Greaves K, Oxford JS, Price CP, Clarke GH, Crake T. (2003). The prevalence of myocarditis and skeletal muscle injury during acute viral infection in adults: measurement of cardiac troponins I and T in 152 patients with acute influenza infection. *Arch Intern Med*; 163:165e8.

18. Fagnoul D, Pasquier P, Bodson L, Ortiz JA, Vincent JL, et al. (2013). Myocardial dysfunction during H1N1 influenza infection. *J Crit Care*; 28:321e7.
19. Ito T, Akamatsu K, Fujita SI, Kanzaki Y, Ukimura A, et al. (2019). Transient depression of myocardial function after influenza virus infection: a study of echocardiographic tissue imaging. *PLOS One*; 14: e0221628.
20. Pizzini A, Burkert F, Theurl I, Weiss G, Bellmann-Weiler R. (2020). Prognostic impact of highly sensitive Troponin T in patients with influenza virus infection: a retrospective analysis. *Heart Lung*; 49:105e9.

DOI:10.31579/2692-9759/081