False Positive Troponin Levels due to Heterophil Antibodies in a Pregnant Woman

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SUMMARY

Positive troponin test results in peripheral blood can be detected either during myocardial injury or from falsely positive test results. In this report, we present the positive results of a troponin test in a 24-year-old pregnant woman referred to the emergency department with atypical chest pain, and the clinical algorithm that we used to make the correct diagnosis. This patient presented with the same complaint of chest pain at different times while positive troponin levels were detected. In the absence of signs of myocardial injury, we suspected that heterophil antibodies were playing a major role. Further examinations revealed heterophil antibodies that could cross react with the troponin tests in peripheral blood.

Key words: False positive troponin; heterophil antibodies.

Introduction

As a result of myocardial infarction, enzymes such as myoglobin, cardiac troponins, creatine kinase, and lactate dehydrogenase rise in the blood. Among these, cardiac troponins play a special role by virtue of their characteristics of being released only from cardiac muscle; increased levels even in minor myocardial injury retain the ability to make a diagnosis with high sensitivity and accuracy. As a result, European and American societies of cardiology have recommended the use of troponin I or T as a diagnostic laboratory criterion of myocardial infarction since 2000.[1] Elevated level of troponin indicates myocardial injury in spite of no information about the cause of the injury.

Apart from myocardial infarction, positive troponin level may also be detected due to myocardial injury or false positive test results.[2,3] In this report, we aimed to present a case with troponin positivity due to heterophil antibodies.

Case Report

A 24-year-old housewife referred to the emergency department with left submammarian chest pain that was confined to a point and increased with leaning forward or deep breathing (November 14th). Due to a positive troponin level she was transferred to the cardiology polyclinic (troponin-I level: 0.20 ng/mL, reference level: 0-0.04 ng/ml) (Table 1).

Her medical history was remarkable for being 20 weeks pregnant. She had no history of heart disease, medication use, cigarette smoking, alcohol, or drug abuse. Functionally, she was in a good status. Her physical examination was unremarkable. Both electrocardiography and echocardiography were negative with respect to perimyocarditis, myocardial ischemia, or myocardial infarction. Other blood tests were normal for creatine kinase (CK), creatine kinase MB isoenzyme (CK-MB), and alkaline phosphatase or rheumatoid factor (Table 2) with false positive potential in result of troponin level. As she revealed she had similar complaints before pregnancy with positive troponin levels (Table 1). In the absence of typical myocardial ischemia, which was not confirmed by electrocardiography, echocardiography or normal range result of the CK and the CK-MB despite troponin-I elevatıon, we concluded the possibility of laboratory error that resulted in a false positive troponin elevation. For increased accuracy of the test result we surveyed the

result in two different laboratories simultaneously (November 15th). The obtained laboratory results showed positive troponin-I levels in our center with normal troponin-T levels in another center. When the same sample was studied using the interference test at our laboratory, the troponin-I level was found within the normal range. The false positivity was attributed to interference of heterophil antibodies and her blood sample was sent to a tertiary center to search for heterophil antibodies.

Discussion

Cardiac troponins are sensitive and specific laboratory markers for myocardial injury and thus replaced CK-MB, the conventional diagnostic marker. Troponins are currently considered the gold standard for the diagnosis of acute myocardial infarction.[1,4] Depending on the cellular damage, cardiac troponins begin to emerge in plasma 4-6 hours after the onset

Table 1. Patient's troponin levels during eight months

Date-Hour	Troponin-I (reference)	CK (reference)	CK-MB (reference)	Troponin-T (reference)	Studying laboratory
April 4th 01:59 p.m.(*)	0.20 (0-0.04 ng/ml)				Our laboratory
April 4th 04:42 p.m.	0.21 (0-0.04 ng/ml)				Our laboratory
April 4th 10:12 p.m.				<0.01µg/L (<0.01µg/L)	1st outside center
November 14th 08:11 p.m.(#)	0.20 (0-0.04 ng/ml)		11 (0-25 u/l)		Our laboratory
November 15th 00:56 a.m.(#)	0.20 (0-0.04 ng/ml)				Our laboratory
November 15th 09:56 a.m.	0.24 (0-0.04 ng/ml)	46 (0-145 u/l)	10 (0-25 u/l)		Our laboratory
November 15th 12:23 p.m.				<0.01µg/L (<0.01µg/L)	2nd outside center
November 20th 03:28 p.m.(#)	0.20 (0-0.04 ng/ml)	53 (0-145 u/l)	11 (0-25 u/l)		Our laboratory

(*): Blood results before pregnancy. (#): Blood results during pregnancy.

Table 2. Other blood results from the patient

Date	WBC (reference)	RBC (reference)	HGB (reference)	HTC (reference)	PLT (reference)	CRP (reference)	ALP (reference)	AST (reference)	RF (reference)
November 20th	7.4 x10⁹ L (4-12x10⁹ L)	4.05 x10¹² L (3. 5-5.2 x10¹² L)	12.1 g/dL (12-16 g/dL)	35.9% (35-49%)	230 x10⁹ L (130-450x10⁹ L)	4 mg/dl (0-5 mg/dl)	52.39 U/L (30-120 U/L)	19 u/l (0-31 u/l)	4 IU/L (0-18 IU/L)

WBC: White Blood Count; RBC: Red Blood Cells; HGB: Hemoglobin; HTC: Hematocrit; PLT: Platelet; CRP: C-reactive protein; ALP: Alkaline Phosphatase; AST: Aspartate Transaminase; RF: Rheumatoid Factor.

of ischemic symptoms and continue to be elevated for 10 days to 2 weeks.[5]

Despite the advantages of troponins, clinicians should keep in mind other processes that elevate troponin levels apart from myocardial infarction.[2,3,6-11] While some of the events with troponin elevation other than myocardial infarction are associated with myocardial injury, some of them occur as a result of troponin tests giving false positive results.

Troponin positivity as a result of myocardial injury may occur with the following: congestive heart failure, coronary vasospasm, cardiac trauma, myocarditis/perimyocarditis, pulmonary embolism, post-cardiac surgery and cardiac ablation, cardioversion and cardiopulmonary resuscitation, sepsis, critically ill patients, end-stage renal disease, arrhythmias, stroke, and epileptic seizures.

False positive troponin testing may result from: heterophile antibodies, Rheumatoid factor, or macroenzymes. Several additional examples of interfering substances are found in the literature;[3,10,11] among which are circulating antibodies from immunotherapies, vaccinations or blood transfusions, fibrin clots, immunocomplexes, and malfunction of the analyzers.

We did not determine any clinical event that might have been associated with elevated troponin levels. Thus, we focused on the conditions with potential false positive troponin results. We ordered another test the same day at an outside center. The troponin-T result of the outside center was normal. Hence, we took a sample from the troponin positive blood sample and sent it to a tertiary center for testing for heterophil antibodies. The latter testing was positive for heterophil antibodies.

It has been reported that heterophil antibodies lead to a false positive result in one of 2000 patients assessed by modern immunoassay methods.[12] This condition may lead to misdiagnoses and unnecessary invasive interventions. Therefore, the clinicians should be vigilant about this interference. In the event of any doubt, the suspicious blood sample should be studied with other devices using at least 2 different methods.[12] Alternatively, this sample may be re-evaluated by adding heterophil blocking reagents.[13]

Heterophil antibodies are formed in human serum against animal immunoglobulins. However, they usually do not lead to any clinical disease state, although they may interact with immunoassays.[14] The effects of heterophil antibodies on the immunoassays have been well documented.[15-17] Heterophil antibodies may arise accidentally or due to occupational exposure to foreign proteins. The chance of heterophil antibody formation increases in people with frequent

contact with animals such as veterinarians, farmers, or pet owners. They may also be formed as a result of administration of animal antibodies in cancer therapy or radiological tumor imaging.

Our patient was a woman living in a rural area where close contact with animals is prevalent. That may have led to development of the heterophil antibodies in this patient.

Conclusion

As in our case, patients with an elevated troponin level but without clinical, electrocardiographic, or echocardiographic findings consistent with myocardial infarction or other conditions that may have elevated troponin levels should be evaluated for the presence of heterophil antibodies before further invasive therapies are commenced. If heterophil antibody positivity is suspected, troponin levels should be re-evaluated with another device or method.

Conflict of Interest

The authors declare that there is no potential conflicts of interest.

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