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Case Report

Erroneously high troponin measurement caused by fibrin clot: Two cases

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Abstract

Acute myocardial infarction is the most common cause of morbidity and mortality in the world. Cardiac troponin measurements play a key role in the diagnosis. However, preanalytical errors as a result of the presence of fibrin or interference due to conditions such as heterophile antibody positivity may cause erroneously high results. Such errors may result in invasive procedures, such as angiography, which may add unnecessary risk. In our hospital, high-sensitivity troponin-I (hs-TnI) was routinely analyzed using a serum separator tube (reference value: female <15.5 pg/mL, male <34.2 pg/mL). This report describes the cases of 2 patients with a false initial troponin measurement: a 19-year-old male patient and a 55-year-old female patient. The hs-TnI value of the male patient was initially measured as 55.5 pg/mL. After the analysis, it was noted that the sample contained fibrin. The sample was centrifuged again and the TnI result was 1.8 pg/mL. Similarly, the TnI result of the female patient was first measured as 90.2 pg/mL. When it was observed that there was fibrin present, the sample was recentrifuged. The revised result was 2.4 pg/mL. The laboratory staff were trained on preanalytical errors, and the use of lithium heparin tubes was implemented in the laboratory as an additional means to eliminate the problem of fibrin interference.

Keywords: Fibrin clot, immunoassay, interference, troponin I

Acute myocardial infarction (AMI) is the most common cause of morbidity and mortality in the world. Cardiac biomarkers reveal cardiac damage and play a fundamental role in the diagnosis of AMI. The primary cardiac biomarkers are cardiac troponin-I (cTnI) and cardiac troponin-T (cTnT). If cTn analysis is not available, the best alternative is creatine kinase-MB [1]. Patients with suspected acute coronary syndrome account for approximately 10% of all emergency patients, however only 5% are ultimately diagnosed with AMI [2]. Cardiac troponins are generally analyzed using immunoassay methods. Many forms of interference in immunoassay methods have been identified. The most common are substances that cross-react with the analyte, heterophilic antibodies, and autoantibodies [3]. Notification of cross-reacting substances is usually provided by the manufacturer in the kit package insert. Microfibrin filaments in serum samples can lead to inaccurately high results in cardiac tests [4]. Mistaken results due to interference can result in unnecessary invasive procedures. High-sensitive cardiac troponin I (hs-TnI) tests can detect troponin levels at lower concentrations. The better precision values of hs-TnI can help diagnose AMI at an early stage [5]. An hs-TnI test provides significant clinical utility for the diagnosis and risk classification of patients with suspected AMI in emergency departments [6].

In our hospital, the standard for hs-TnI analysis was the use of a serum tube with a gel separator and coagulation activator (Vacusera 5 mL CAT serum gel and clot activator; Disera, Izmir, Turkey) and analysis is performed using the Architect Stat high-sensitivity troponin-I reagent and an Abbott Architect I2000 SR autoanalyzer (Abbott Laboratories, Lake Bluff, IL, USA).

Patients and Results

A 17-year-old male patient presented at the internal medicine clinic with abdominal pain. The initial hs-TnI value recorded

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was 55.5 pg/mL (reference value: female: <15.5 pg/mL, male: <34.2 pg/mL). The patient had no known history of cardiac disease, hypertension, or kidney disease. The creatinine value was within the reference range and there was no specificity in the biochemistry tests. After the analysis, it was observed that the sample contained fibrin (Fig. 1). The sample was recentrifuged and analyzed 2 times. The hs-TnI results were 1.7 pg/mL and 1.8 pg/mL and the result was reported as 1.8 pg/mL. Three months later, the hs-TnI result of a 55-year-old female patient who presented at the internal medicine clinic with upper abdominal pain was initially measured as 90.2 pg/mL. The patient had no hypertension or renal disease comorbidities. Careful examination of the sample revealed fibrin strands. The sample was centrifuged again, and the hs-TnI result was reported as 2.4 pg/mL following 2 consecutive analyses.

The patients provided consent for this case report.

Discussion

Preanalytical problems, such as fibrin clots, can occur if insufficient time is allowed for serum specimens to clot adequately prior to centrifugation. Fibrin artefacts may be small fibrous structures or larger, visible clots. These fibrin clots in the serum can significantly alter the troponin results. It has been recommended that the waiting time before centrifugation be increased for samples of patients using anticoagulants [7]. Importantly, neither of our patients had a history of anticoagulant/antiaggregant use. Our review suggested that the first sample was centrifuged prior to the appropriate time allowance for clotting. The laboratory staff were informed about the issue and additional preanalytical phase training was provided. When we checked the turnaround time of the second case, we saw that the sample had been held properly. We sought a more permanent solution because the second case revealed the potential for significant error despite proper procedures.

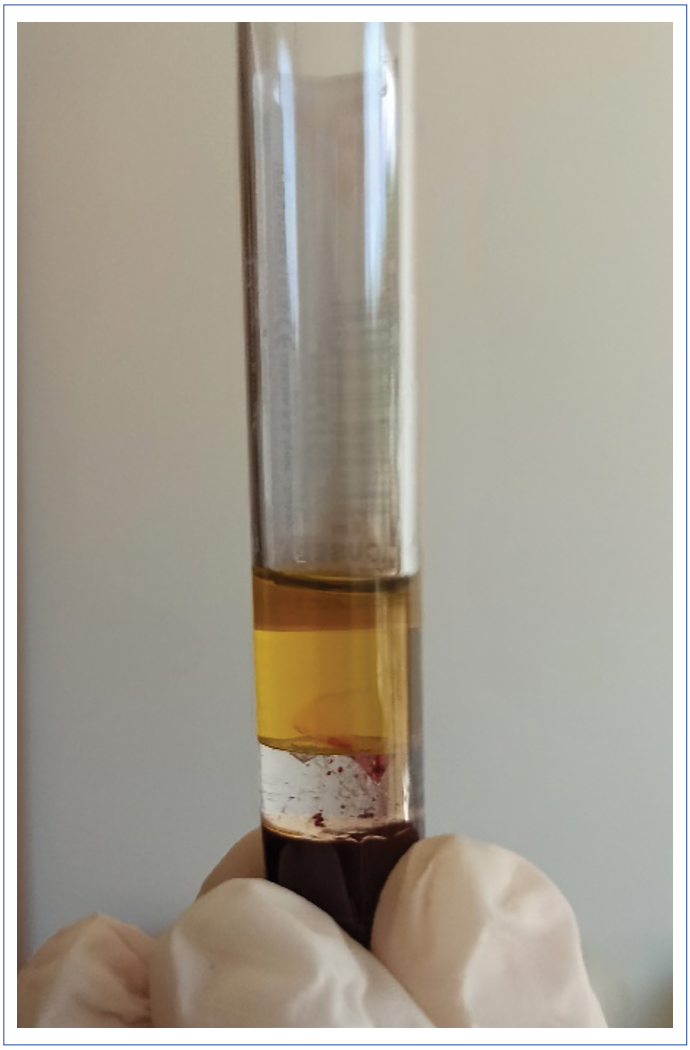

Figure 1. Fibrin clot in a serum sample.

We used serum samples, but examination of the analyzer manufacturer's insert revealed that heparinized plasma was also acceptable. Heparinized plasma measurement results of cardiac troponins may be lower than those determined using serum [8]. However, the difference should not lead to misdiagnosis; both types of samples can be used for cardiac troponin measurements [9, 10]. The use of heparinized plasma is generally preferred in clinical laboratories because it reduces turnaround time [11]. Heparin induces a conformational change of antithrombin III to accelerate the inhibition of thrombin and factor Xa, which is why it is used as an anticoagulant [12]. Therefore, it could also be an appropriate solution to the problem of fibrin clots. We contacted our supplier and initiated the use of lithium heparin tubes (Vacusera 2 mL-LH; Disera, Izmir, Turkey) for hs-TnI analysis.

Fibrin clots may cause erroneous results in insufficient samples or as a result of assay interference. Fibrin clots can also block analyzer probes, leading to subsequent mis-sampling [13]. Under-measuring of the analyte can also occur due to incomplete pipetting. False positivity in troponin contrary to expectation may be seen because the antibody binds nonspecifically to fibrin, or the indicator enzyme is physically captured by fibrin [7].

False-positive results in cardiac troponins due to interference can lead to unnecessary invasive procedures, treatments, and a prolonged hospital stay. It is important for clinicians to contact the laboratory in the event of results that are not compatible with the patient's clinical findings. Heterophilic antibodies are known to cause interference. A heterophilic blocking tube (HBT) is frequently used to prevent this kind of interference [14]. However, case reports have also demonstrated falsely high troponin-I results that did not change with the use of an HBT. Precipitation with polyethylene glycol and troponin-T analysis, which is a different cardiac biomarker, can provide a solution in such instances [15]. We suggest repeat centrifugation as an initial step in the event of unexpectedly high troponin results before implementing additional processes, such as the use of HBT, polyethylene glycol, or performing other kinds of troponin analysis.

Conclusion

Laboratory staff should be educated about the possibility of fibrin-related errors, and samples containing fibrin clots should not be analyzed. We recommend the use of lithium heparin tubes and plasma as a precaution to minimize errors. This method will also help to reduce turnaround time since it does not require waiting time before centrifugation.

Informed Consent: The patients provided informed consent.

Conflict of Interest: None declared.

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