False-positive cardiac troponin T due to assay interference with heterophilic antibodies

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A 38-year-old woman was admitted to the emergency unit with chest pain radiating to her left arm. She had recently suffered from a cold with cough and neck pain lasting for 2 weeks. The patient had a history of deep venous thrombosis during pregnancy associated with APC-resistance. She had neither cardiovascular risk factors nor a history of coronary or cerebral artery disease. The family history was negative for coronary heart disease and stroke.

On admission the patient complained of strong pain in the left side of the chest worsening on inspiration. She had painful musculoskeletal points on the left chest wall and neck, otherwise physical examination was normal. Computed tomography of the chest ruled out pulmonary embolism. Neither electrocardiogram nor echocardiography showed any evidence of perimyocarditis, myocardial ischaemia or cardiac infarction. However, elevated troponin T serum levels (1.76 µg/l) were detected (Elecsys E170, Roche Diagnostic, Rotkreuz, Switzerland), while CK (90 U/l, Modular P, Roche Diagnostic), CK-MB (13 U/l, Modular P, Roche Diagnostic), and myoglobin (29 U/l, Elecsys E170, Roche Diagnostic) were within reference ranges.

Repeat measurements showed that serum concentration of troponin T remained elevated (1.65 µg/l, 1.46 µg/l and 1.75 µg/l after two, six and 48 hours, respectively) while levels of CK, CK-MB, and myoglobin remained within their reference ranges.

In view of the persistently elevated serum concentrations of troponin T without elevation of other cardiac necrosis markers, we decided not to undertake coronary angiography suspecting interference of heterophilic antibodies with the troponin T assay. To show such interference, we treated a serum sample of our patient with heterophilic blocking reagent (Scantibodies Laboratory, Santee, CA, USA) for one hour and measured troponin T again. The troponin T level decreased to 0.18 µg/l upon treatment with the blocking antibody while the same treatment did not alter the troponin T level in a sample from a patient with acute coronary syndrome measured in parallel. These results confirmed antibody interference in the troponin assay. The patient was discharged with the diagnosis of musculoskeletal chest pain.

The origin of the heterophilic antibodies is not clear. However, in a recent review Levinson and Miller argued that they represent natural antibodies that bind their antigen with low affinity [1]. This may explain why the older radioimmunoassay that depend on strong affinity binding of the antibodies were less prone to such interactions than the newer generation immunoassays [1]. These modern immunoassays have been revised by adding non-specific blocking antibodies to the assay to reduce the effect of interfering antibodies [2], however, some patients may exceed the blocking capacity of a specific immunoassay procedure [3, 4].

It is estimated that heterophilic antibodies cause about one false result in every 2000 investigations produced with modern immunoassays [1]. This can result in unnecessary and possibly even harmful diagnostic procedures and/or treatment. Therefore, physicians need to be aware of these interferences with immunoassays, which basically can occur with every immunoassay. Contacting their laboratory directors will allow testing for the presence of such heterophilic antibodies in a patient's sample. The suspected sample can be re-measured with an assay from another manufacturer and will usually give a discordant result, at least when assayed by a different two-site method [1]. Alternatively, the sample can be re-analyzed after pre-treatment with commercially available heterophilic blocking reagents, as presented in this report [5, 6].

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