Falsely elevated troponin levels

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In assessments of chest pain, cardiac troponins have a prominent position. In clinical work we are well aware that conditions other than myocardial infarction can result in an elevated troponin level, but the possibility of a falsely elevated test result appears to be little known.

In this article I present a case history that illustrates the problem of falsely elevated troponin levels and the consequences of disregarding this potential interpretation.

To diagnose a myocardial infarction, an increase and/or fall in troponin values by at least one value > the 99th percentile in a healthy reference population is required, combined with other ischaemic signs or symptoms (1). Troponin T and troponin I are considered equal in diagnostics of myocardial infarction. There is only one manufacturer of tests for troponin T and thus only one reference range. For troponin I, there are a number of manufacturers of tests with varying reference ranges.

The amount of change needed to make a diagnosis of myocardial infarction has been a matter of debate. It has been concluded that a 50% change for values around the 99th percentile is required, and 20% in case of higher levels of troponin (2).

This development has provided more sensitive troponin tests. It has thus become possible to detect an increase at an earlier stage of myocardial infarction, but this comes at the cost of specificity. Increased troponin values normally indicate a myocardial injury, but give no clue to the mechanism of injury. A number of diseases may result in myocardial injury. In cases of severe renal failure, reduced elimination may result in an elevated level. Current troponin tests have a very high sensitivity and may be truly elevated even though other laboratory tests, coronary angiography or radiological examinations reveal no pathological findings. When referring to falsely elevated troponin values here, it is because an alternative test for troponin has returned a normal value.

A case history

A man in his late sixties with diet-controlled diabetes mellitus, moderate chronic obstructive pulmonary disease (COPD), normal renal function and slight hypothyroidism (negative thyroid receptor antibodies (TRAS) and negative anti-TPO) had been repeatedly hospitalised because of dyspnoea and chest pain that gave rise to suspicion of coronary disease.

Over the last 15 years he had been examined five times with coronary angiography, with findings of normal arteries. Four of these examinations had been undertaken in the course of four years, there were 25 values for troponin T in the interval 50–120 ng/l. A number of proBNP values were taken and ultrasound examinations made of his heart. An MRI scan of his heart revealed no signs of myocarditis. When distinguishing between different troponins, it was found that troponin T was elevated at 100 ng/l (upper reference limit 14 ng/l), while troponin I was within the reference area of 26 ng/l (upper reference limit 34 ng/l).

The establishment of a normal level of troponin I reduced the patient's worries, and it was significantly easier to explain the pains as muscular in origin. There have been no subsequent hospitalisations due to this problem. We found no explanation for the falsely elevated troponin T value.

Clinical experience

Troponin analysis is requisitioned even when the suspicion of myocardial infarction or another myocardial injury is very low. This increases the likelihood of finding a falsely elevated test result.

We have suspected a falsely elevated value in cases of atypical or obviously non-coronary chest pain, absence of other diseases that might explain an elevated value, normal ECG and absence of pathology on coronary angiography or an MRI scan of the heart. A small change in value from the first to the second test may produce an initial suspicion that this is not an acute infarction, but several patients with a falsely elevated troponin level satisfied the requirement for a 20% change. In readmissions, elevated troponins at the same level as in previous hospitalisations may have given rise to suspicion of a falsely elevated troponin value.

The suspicion of a false-positive test for troponin T has been confirmed by sending stored serum from the same sample for analysis in another hospital that has used troponin I (ES Vitros). Despite a clearly elevated level of troponin T, the analysis of troponin I from the same sample has been within the reference range.

The literature recommends a broad assessment with a view to heart disease, which often involves both coronary angiography and an MRI scan of the heart (3). These examinations are only undertaken in large hospitals, and transfer of patients for this purpose requires considerable resources.

This case history illustrates the fact that some patients are subjected to extensive examinations because of elevated troponin values. In my experience, some of these patients had symptoms that did not indicate such comprehensive assessment, but where the unexplained elevated troponin values triggered both additional examinations during their hospitalisation and checks-ups after discharge. Patients admitted with chest pains normally have short hospitalisation periods. It is thus desirable to have access to an alternative troponin test that provides an answer within the same day, so as to avoid comprehensive assessments for which the clinical picture and the ECG provide no basis.

Causes and management

Disregarding the possibility of a misplaced test tube, the causes of falsely elevated troponin values are stated as follows (3, 4): Heterophilic antibodies, human anti-animal antibodies, auto-antibodies, fibrin, rheumatoid factor, endogenous blood products such as bilirubin, haemoglobin and lipidemia, a high concentration of alkaline phosphatase, immune complexes and analytical equipment errors. It has been stated that the presence of heterophilic antibodies is relatively common, so this is the most frequent explanation for a false-positive test result (3).

I have found no studies that have compared the tests for troponin T and troponin I with

regard to their vulnerability to a falsely elevated test result. Algorithms have been designed for laboratory personnel as well as clinicians where a false-positive test is suspected (4).

The first step is a new test to see if the result is unchanged, or alternatively a haemolysis. Next, it is recommended to exclude heart disease other than acute coronary syndrome before contacting the laboratory for help with clarification and possibly another immunoassay test. It is stated that troponin I and T may both return false-positive values, but that the prevalence is highly uncertain (3, 4).

It is important to be aware of the possibility of a falsely elevated troponin value. This should be taken into account when the clinical picture is inconsistent with the troponin test result. My experience is that early contact with the laboratory and a check against another method may save the patient unnecessary diagnostic procedures and anxiety.

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