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A case of false positive Troponin I in a patient affected by cryoglobulinemic vasculitis

M. Bellan[1,2], M. Pirisi[1-3], G. Bellomo[4], P.P. Sainaghi[2,3]

[1]Department of Translational Medicine, Università del Piemonte Orientale UPO, Novara, Italy;
[2]Division of Internal Medicine, Immunorheumatology Unit, AOU Maggiore della Carità, Novara, Italy;
[3]IRCAD (Interdisciplinary Reseach Center of Autoimmune Diseases), Novara, Italy;
[4]Department of Health Sciences, Università del Piemonte Orientale UPO, Novara, Italy

SUMMARY

Troponin I (TnI) false positive results have been reported in patients affected by immune disorders.
We report the case of a 74-year-old woman affected by cryoglobulinemic vasculitis, admitted to the Emergency Room because of a lipotimic episode. A marked elevation of TnI plasma concentration was confirmed in multiple determinations, despite the absence of symptoms or electrocardiogram findings suggesting myocardial infarction. TnI plasma concentration was reported normal after re-testing with a different commercial kit.
A false TnI positivity should be considered in patients with immune disorders, especially if seropositive for rheumatoid factor, when the clinical context does not suggest myocardial infarction.

Key words: *Troponin I; vasculitis; cryoglobulinaemia.*

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INTRODUCTION

Troponin I (TnI) assay is an essential diagnostic tool in the workup of myocardial infarction (1). Although the new, high-sensitivity troponin assays offer greater diagnostic accuracy than the standard assays (2), false positive results have been reported on various analytical platforms, leading to a misdiagnosis of acute coronary syndrome, with potentially serious consequences for the patient (3). In the past, several papers reported the possible interference between Rheumatoid Factor (RF) and TnI, in Rheumatoid Arthritis patients (4). Herein we report a case of false positive high-sensitivity TnI test in a patient with cryoglobulinemic vasculitis and high levels of RF.

CASE REPORT

A 74-year-old patient was firstly examined at our outpatient immunorheumatology clinic, because of the onset of skin ulcers, digital necrosis and constitutional symptoms (4-kg unintentional weight loss and night sweats in the previous 2 months). At physical examination, vital signs were normal; mild hepatosplenomegaly was noted, with no significant lymphadenopathy; digit ulcers involving the III finger of the right hand, the IV finger of the left hand, and the V toes of both feet. Palpable purpura was observed on lower limbs bilaterally. The neurologic examination revealed diminished reflexes and loss of sensitivity. She was known to be HCV positive (genotype 2a/c) since 1996.

Laboratory findings were notable for mild normochromic normocytic anaemia (Hb 10.8 gr/dl) and marked erythrocyte sedimentation rate elevation (92 mm/h). Immunoglobulin levels were the following: IgA 35 mg/dl, IgG 550 mg/dl, IgM 467 mg/dl. RF concentration (10,400 UI/ml) and cryoglobulin titre (cryocrit 70%) were strikingly high. An electromyography was performed and revealed a sensory and motor neuropathy.

The clinical picture together with laboratory findings led to a diagnosis of HCV-

Corresponding author
Mattia Bellan
Department of Translational Medicine
Università del Piemonte Orientale UPO
Via Solaroli, 17 - 28100 Novara, Italy
E-mail: bellanmattia@yahoo.it

related cryoglobulinemic vasculitis. Intravenous iloprost was started, together with acetylsalicylic acid and prednisone, with rapid symptomatic relief. Clinical remission was obtained after Rituximab treatment.

One month later the patient was admitted at the Emergency Unit of our Hospital because of a single lipotimic episode, occurred after prolonged orthostatism. Neither chest pains, nor other symptoms were reported. ECG did not reveal any sign of cardiac ischemia. The physical examination was unremarkable. Laboratory findings revealed a significant elevation of TnI plasma concentration (ADVIA Centaur Ultra troponin I assay, Siemens Healthcare) confirmed in multiple determinations, ranging from 3.2 to 10.5 ng/ml, despite normal CK-MB concentration; a question of atypical coronary syndrome was raised.

During the following 10-hour observation the patient remained asymptomatic. She was then admitted to the cardiology Intensive Care Unit and a coronary catheterization was performed; no significant stenosis of coronary arteries was found.

In the following days the patient remained asymptomatic, TnI concentration remained elevated although with wide variations, while CK-MB remained normal (Figure 1). Suspecting a false positive result, a blood sample was sent to a second laboratory using a different commercial kit (COBAS 8000, Roche Diagnostics) where TnI plasma concentration was reported normal. The patient was discharged; at follow-up she remained asymptomatic both for cardiac and vasculitic symptoms.

DISCUSSION AND CONCLUSIONS

The new high-sensitivity TnI assays show a sensitivity around 80-95%, higher than the standard ones, with a specificity ranging 90-95% (1). Many situations can account for false positive results; RF has been shown to cause false TnI determinations, in particular in RA patients (4-6). Commonly, as in our case, these latter interferences can be dependent on the commercial kit used (7, 8). Though well described in RA patients, this is the first reported case of a TnI false positive result in cryoglobulinemia. It has been previously reported that the use of monoclonal antibodies can interfere with TnI dosage; our patient was previously treated with Rituximab. It cannot be therefore completely ruled out that Rituximab treatment could have contributed to TnI false positivity (9).

This report confirms that laboratory tests should always be requested and interpreted on the basis of the clinical picture they are intended to clarify; in this case, history,

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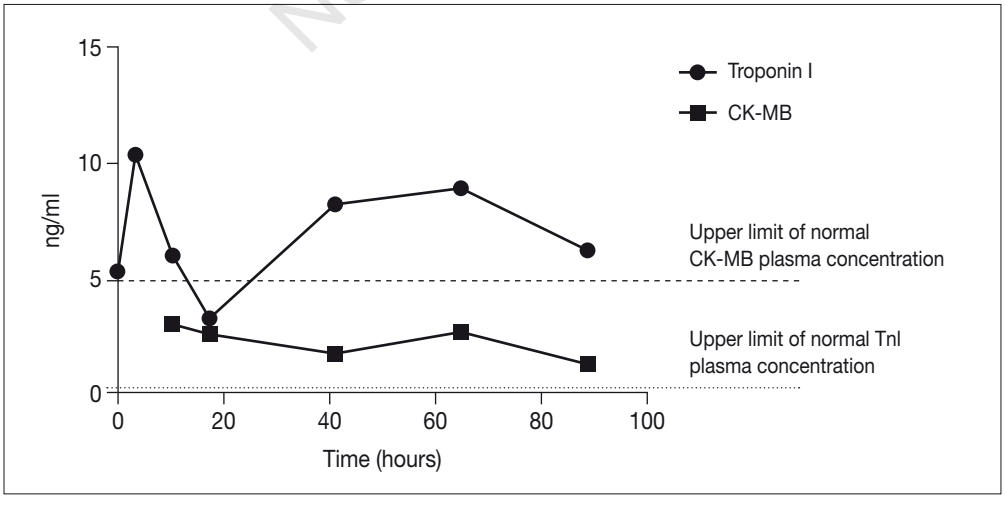

Figure 1 - Temporal trend of CK-MB and TnI plasma concentrations. Note the persistence of normal CK-MB concentrations in association with highly variable TnI plasma concentrations.

physical findings and ECG were not consistent with an acute coronary syndrome, but rather with a vasovagal syndrome. The wide fluctuation of TnI levels, with all other cardiac markers remaining within the normal reference range, was a further clue to false positivity. In these cases, sequential dilutions lead to a non-linear decrease in TnI concentration.

Therefore, a false TnI positivity should be considered in patients with immune disorders, especially if seropositive for RF, when the clinical setting does not suggest myocardial infarction. In this event, retesting by a different assay is indicated. Alternatively, polyetiene glycol can be used to remove RF, avoiding further interferences (10). We advise reporting the occurrence of false positive test at discharge and in follow-up reports, to alert clinicians to scrutinize this possibility in case of future TnI positivity.

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