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Letters

Persistently Elevated Troponin Level Caused by Heterophile Antibodies

Challenge in Everyday Clinical Practice

We read with great interest the case report by Santos et al. (1), published in a recent issue of *JACC: Case Reports,* that showed how the presence of heterophile antibodies is a rare possible cause of false positive troponin levels.

Moreover, according to our experience, an additional challenge in determining the optimal course of treatment in such patients is borderline stenosis of 1 or more coronary arteries. In the context of elevated troponin levels, accompanied by a clinical presentation understood and treated as acute coronary syndrome without ST-segment elevation, borderline 70% stenosis of the circumflex coronary artery found on a coronary angiogram of our patient was considered a "culprit" lesion, and percutaneous coronary intervention with stent implantation was performed. Repeated chest pain and elevated troponin led to another coronary angiogram, which showed no in-stent stenosis or thrombosis. Persistently elevated troponin was then suspected to be false positive resulting from the existence of heterophile antibodies in the patient's serum; and this was proven by measuring both concentration of troponin I (false positive) and troponin T (normal). The patient did not have acute coronary syndrome without ST-segment elevation, and the borderline stenosis of the circumflex artery found in the coronary angiogram was only a coincidence within her moderate cardiovascular risk profile, rather than a culprit lesion.

In this context of chronic basal elevation of troponin inconsistent with other performed diagnostic methods (repeatedly normal echocardiography and electrocardiography findings), even when borderline coronary artery stenosis is found on a coronary angiogram, it is important for clinicians to consider the possibility of heterophile antibody presence as a cause of persistently elevated troponin and avoid misdiagnosis and overtreatment. Furthermore, additional functional tests such as instantaneous wave-free ratio or fractional flow reserve should be performed to estimate the significance of a borderline coronary artery lesion, and imaging methods (single-photon emission computed tomography, cardiac magnetic resonance) should be used for detection of ischemia (2,3). Visually based conclusions regarding the hemodynamic severity of borderline coronary artery stenosis are subjective and possibly inaccurate, and they alter treatment decisions that can be of prognostic significance and cause overtreatment, especially in patients with heterophile antibodies.

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REFERENCES

1. Santos LG, Carvalho RR, Sa FM, et al. Circulating heterophile antibodies causing cardiac troponin elevation: an unusual differential diagnosis of myocardial disease. J Am Coll Cardiol Case Rep 2020;2:456–60.

2. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 2020;41:407–77.

3. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J 2019;40:87–165.

REPLY: Persistently Elevated Troponin Level Caused by Heterophile Antibodies

Challenge in Everyday Clinical Practice

We thank Drs. Merkaš and Lakušić for their interest in our case report (1) and congratulate them for sharing their experience regarding the issue of

persistent cardiac troponin (cTn) elevation secondary to heterophile antibody (hAb) interference.

In their letter, a case-based experience is used to raise an even more challenging scenario: the presence of obstructive coronary artery disease (70% stenosis of the left circumflex artery [LCX]) in a patient with a clinical presentation similar to that of our patient (chest pain, elevated cTn-I, and no ST-segment elevation). Given the assumption of non-ST-segment elevation myocardial infarction (NSTEMI), the LCX stenosis was considered a "culprit" lesion and was successfully treated with percutaneous coronary intervention (PCI). The presence of false positive results justifying persistent cTn-I elevation was suspected following a repeat coronary angiogram that was performed to evaluate new onset of chest pain associated with cTn-I elevation and that was unremarkable. It was proven when a different troponin assay was used. As a consequence, Drs. Merkaš and Lakušić hypothesize that the patient did not experience an NSTEMI and that the intermediate LCX stenosis was probably an incidental finding.

Overall, we find that this challenging case was well managed by our colleagues and congratulate them for suspecting false positive cTn results before proceeding to additional investigation or interventions. Although we agree that the patient did not have an NSTEMI, hAb interference can only be considered likely. As proposed by Mair et al. (2), the patient's blood sample should be treated with interference blocking proteins to confirm such a phenomenon because other analytical constraints may also cause false positive results of a given cTn assay. Regarding the appropriateness of PCI, we agree that functional tests such as fractional flow reserve may be performed to estimate the functional significance of noncritical coronary stenosis, although further studies are needed to assess the validity of culprit vessel identification in patients who have had an NSTEMI (3). Similarly, cardiac magnetic resonance would be helpful for the assessment of ischemia within the LCX territory if PCI was deferred for some reason (e.g., suspicion of false positive results) or if doubts remained following PCI (4), as well as to assess alternative causes of myocardial injury (e.g., myocarditis) (1,2).

In conclusion, the consequences of hAb interference resulting in falsely elevated cTn values may be more pronounced in patients presenting with acute chest pain and noncritical coronary artery stenosis. A high level of suspicion and appropriate complementary evaluation may reduce misdiagnosis and overtreatment, thus avoiding unnecessary prognostic implications.

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REFERENCES

1. Santos LG, Carvalho RR, Sa FM, et al. Circulating heterophile antibodies causing cardiac troponin elevation: an unusual differential diagnosis of myocardial disease. J Am Coll Cardiol Case Rep 2020;2:456–60.

2. Mair J, Lindahl B, Muller C, et al. What to do when you question cardiac troponin values. Eur Heart J Acute Cardiovasc Care 2018;7:577–86.

3. Ihdayhid AR, Koh JS, Ramzy J, et al. the role of fractional flow reserve and instantaneous wave-free ratio measurements in patients with acute coronary syndrome. Curr Cardiol Rep 2019;21:159.

4. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 2020;41:407–77.