



Correspondence

Myocardial injury through serum troponin I and echocardiography in anaphylaxis: Takotsubo cardiomyopathy and the Kounis hypersensitivity-associated acute coronary syndrome

To the Editor,

Measuring of high-sensitivity cardiac troponin levels is essential in the diagnosis of acute myocardial infarction. *Acute myocardial infarction* is defined as myocardial cell death due to prolonged myocardial ischemia. Indeed, in the third universal definition of myocardial infarction [1], detection of rise and/or fall of cardiac troponin above the 99th percentile of the upper reference limit together with ischemic symptoms, electrocardiographic changes of new ischemia, development of pathologic Q-waves in the electrocardiogram, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality is essential for defining myocardial infarction. Based on the above, the third universal definition of myocardial infarction still includes 5 different types of myocardial infarction. Therefore, clinical symptoms, electrocardiography, imaging techniques, and troponin levels should be always used for detecting acute myocardial ischemia. In the very important article published in the *American Journal of Emergency Medicine* [2], Cha et al, measuring troponin levels and using, for the first time, echocardiographic techniques, found that between 300 anaphylaxis cases that were diagnosed in the emergency department (ED), myocardial injury was developed in 7.3% of patients. Various cardiomyopathy, including Kounis syndrome and Takotsubo cardiomyopathy, was also observed in patients with myocardial injury. These findings might have profound clinical, therapeutic, and pathophysiologic implications as far as anaphylaxis, myocardial injury, and Kounis anaphylaxis-associated acute coronary syndrome [3] are concerned. It seems likely that the anaphylaxis, Takotsubo, allergy, and Kounis syndrome complex is under “attack” with all favorable consequences [4]. The study of Cha et al as well as the previous study of Lippi et al [5] published recently come to support previous laboratory and clinical evidence that inflammatory mediators released locally and in the systemic circulation during allergic and anaphylactic reactions are causing myocardial injury implicated in anaphylactic cardiac shock and cerebral hypoperfusion [6].

Indeed, experimental and clinical evidence supports our view that, in anaphylactic reactions, the heart and especially the coronary arteries are the primary target of the released mediators that induce myocardial injury resulting in troponin raising and cardiomyopathy. Emergency physicians and physicians in general should focus their attention on this matter.

In experimental anaphylaxis, the followings have been observed:

1. Primary cardiac reaction caused by the intracardiac release of histamine followed by a secondary cardiovascular reaction caused by the systemic release of anaphylactic mediators [7].
2. Prompt and prolonged decrease in coronary blood flow, abrupt heart rate increase that peaked within 2 min, and transient

increase in ventricular contractile force, followed by a prolonged decrease [8].

3. Heart rate and left ventricular end-diastolic pressure are markedly increased, whereas coronary flow, aortic flow, left ventricular diastolic pressure, and maximal rate of rise of left ventricular pressure (LVtp/dtmax) are profoundly decreased. When a specific platelet activating factor (PAF) antagonist is given before anaphylactic challenge, all of the above are inhibited [9].
4. Acute myocardial ischemia, decrease in cardiac output, initial raise in arterial blood pressure, and increase in left ventricular end-diastolic pressure indicating pump failure are the main findings. The observed pump failure definitely excludes peripheral vasodilatation as a cause of the registered anaphylactic cardiac damage according to the authors [10].
5. Decrease in coronary blood flow, decrease in the maximum increasing rate of systolic left ventricular pressure (dp/dtmax) and increase in coronary vascular resistance as evidence of coronary spasm [11].
6. Anaphylactic hypotension is caused by a decreased in cardiac output via platelet activating factor and histamine release but not by peripheral vasodilatation [12].

There is also clinical evidence that patients with anaphylactic cardiac collapse, manifesting as Kounis syndrome and Takotsubo cardiomyopathy with increased serum troponin, do not respond to intravenous fluid administration and inotropic therapy but require coronary event treatment protocol. This denotes that the heart and especially the coronary arteries are the primary target of the allergic inflammatory mediators that induce coronary injury with increased troponin levels. The following are some clinical examples:

1. Myocardial infarction protocol treatment proved to be life saving in an atopic female nurse, with eczema, asthma, and allergy to milk protein who developed anaphylactic reaction with hemodynamic disturbance due to myocardial stunning leading to reduced cardiac output [13]. Her hemodynamic status was unresponsive to intravenous administration of fluids such as Ringer acetate, antiallergic treatment with adrenaline and corticosteroids, and her condition was complicated with pulmonary congestion and reduced ejection fraction.
2. Acute myocardial infarction protocol treatment with thrombolysis rendered good results in a patient with stent thrombosis after anaphylaxis from snake bite while the patient was not responding to inotropes and fluid expansion [14].
3. In perioperative anaphylactic shock due to gelofusine infusion and increased troponin, treatment with metaraminol and

epinephrine not only worsened the hypotension but annihilated cardiac output within 3 minutes. The patient recovered gradually with stopping gelofusine infusion, administration intravenous antihistamine and corticosteroids, and ongoing inotropic support [15].

In this respect, it is reasonable to suggest systematic measurement of cardiac biomarkers and especially troponin levels in all patients admitted to the EDs with acute allergic, hypersensitivity, anaphylactoid, and anaphylactic reactions and even in those lacking symptoms of myocardial ischemia, to timely identify and appropriately manage a potential cardiac injury [5]. Furthermore, the suggestion by Cha et al that further prospective studies are necessary to investigate serum catecholamine, serial troponin I, echocardiography, and prognosis of cardiac injury in patients with anaphylaxis seems to be worthwhile.

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