

# Acute Myocardial Infarction Induced by Anaphylaxis in China: The Kounis Syndrome

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In the very interesting report published in *Chinese Medical Journal*<sup>[1]</sup> concerning a 65-year-old hypertensive and hyperlipidemic male patient, with stent implantation 5 years previously, the patient developed anaphylactic shock accompanied by chest discomfort, palpitation, itchiness, nausea, vomiting, dyspnea, wheezing, abdominal pain, sweating, pale complexion, dizziness, and syncope following bread and milk consumption. The clinical symptomatology was associated with electrocardiographic and laboratory evidence of acute inferolateral myocardial infarction, and the patient recovered with epinephrine, antiallergic, and myocardial infarction protocol therapy including ticagrelor and Clexane. Coronary arteriography demonstrated lesions in the left trunk and the three coronary branches, but the stented areas were unobstructed. The allergen test revealed a Grade 2 (2.11 kUA/L) for wheat and Grade 0 for milk.

This report, however, raised the following issues as far as anaphylaxis in coronary-stented patients, allergy to food consumption, and the acute myocardial infarction induced by anaphylaxis in China:

1. Stent implantation is a life-saving medical procedure that has become, nowadays, the most frequently performed therapeutic procedure in medicine. The currently used coronary artery stents are the drug-eluting stents and occasionally the bare-metal stents. The drug-eluting stents dispose stainless steel platform that contains nickel, chromium, titanium, manganese, and molybdenum with cobalt or platinum alloy and biocompatible durable or biodegradable polymer combined with the antiproliferative drug everolimus or zotarolimus. The bare-metal stents are made from stainless steel. All stent components including the antiproliferative drugs and the drugs the patients are taking after discharge from hospital (aspirin

and clopidogrel) together with any environmental exposure or food consumption can act as strong antigens, either separately or synergistically, able to induce hypersensitivity or anaphylactic reactions. This "antigenic complex" seems to apply continuous, repetitive, persistent, and chronic hypersensitivity irritation able to induce hypersensitivity inflammation with systemic manifestations and stent thrombosis manifesting as Kounis syndrome.<sup>[2]</sup>

Indeed, the described patient complained of chest discomfort, abdominal pain, dizziness, and repeated wheals involving the whole body, on five occasions in the past, but he did not pay any attention, did not receive any treatment, and did not subject to further tests. The fact that his implanted stents were found unobstructed with the absence of thrombus in the left trunk and three coronary branches could be attributed to the action of the administered platelet aggregation inhibitor ticagrelor and enoxaparin (Clexane).

2. Few cases of Kounis anaphylaxis-associated acute coronary syndrome, Type I and Type II variants, induced by food consumption have been reported so far. Fish, shellfish, milk, rice, and mustard are some of the offenders. In a recent report<sup>[3]</sup> concerning a patient with balloon angioplasty and placement of a drug-eluting stent, Kounis syndrome was developed following anaphylactic reaction, confirmed during hospitalization with oral food consumption test. The culprit was the

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sheep milk. In another report,<sup>[4]</sup> anaphylactic shock was induced in a 65-year-old woman, approximately 30 min after eating Chinese noodles including shellfish. This patient had a previous history of anaphylactic shock after ingestion of shellfish.

The described patient was sensitive to wheat but not to milk and this was not related to any exercise. During exercise, a fall in pH takes place creating an acidic state that may promote mast cell degranulation and induce thrombosis. *In vitro* studies have shown that during exercise, plasma osmolarity is raised and this can increase basophil activation and histamine secretion. A variety of food causes have been associated with food-dependent exercise-induced anaphylaxis.

3. The authors stated that there are no reports of anaphylaxis-induced acute myocardial infarction in China. However, in a viewpoint published nearly 10 years ago in *Chinese Medical Journal*,<sup>[5]</sup> the authors concluded that Kounis syndrome could be considered as part of hypersensitivity following drug-eluting stent implantation that can lead to stent thrombosis, but other causes may play more important role. However, anaphylactic shock associated with Kounis syndrome has been reported recently from the First Affiliated Hospital, Department of Pharmacy, School of Medicine, Soochow University, Suzhou, China, and concerned a 37-year-old woman who was administered cefuroxime intravenously for perioperative prophylaxis.<sup>[6]</sup> In another report from the Third Hospital of the Chinese People's Liberation Army, Baoji, Shaanxi Province, China, anaphylactic shock associated with Kounis syndrome was induced by progesterone capsules.<sup>[7]</sup> Five cases of anaphylaxis-induced Kounis syndrome, some of them complicated with shock, were recently reported from the Department of Cardiology, China-Japan Friendship Hospital, Beijing, China, and were associated with traditional Chinese medicines such as "Ma-Xing shi gan tang," "Ma-Huang" (ephedra), and "Di-Long" (earthworm).<sup>[8]</sup> Several other reports associating Kounis syndrome, not only with anaphylactic shock but also with allergy and hypersensitivity, have been already published concerning patients from China.<sup>[9,10]</sup>

Therefore, Kounis syndrome is not a rare disease but is rarely recognized and underdiagnosed condition. It is anticipated that more reports describing additional etiologies would appear in the future, especially in China, the most populated country in the world!

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### Conflicts of interest

There are no conflicts of interest.

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