

Exercise-induce anaphylaxis, food-dependent exercise-induce anaphylaxis, cholinergic urticaria and Kounis syndrome

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Anaphylaxis is a condition that occurs unexpectedly. It creates fear and uncertainty to both physicians and the public and may progress rapidly in patients of all ages, in both sexes and often in young and otherwise healthy individuals. Exercise-induced anaphylaxis (EIA) is a rare, unpredictable and potentially fatal form of anaphylaxis, which is more common in atopic individuals, and associated with physical activity or exercise. EIA may occur independently of food allergen ingestion, and for a sub-population of patients, both ingestion of a food allergen either pre- or post-exercise and exercise are required to induce food-dependent exercise-induced anaphylaxis (FDEIA).

Such an interesting FDEIA case was published recently in *the Netherlands Journal of Medicine*.¹ The authors report on a 49-year-old male with no cardiovascular disease history, who experienced a previous episode of urticaria during a strenuous cycling trip. This patient also developed anaphylactic shock during physical exercise, that was accompanied by urticaria on his chest and arms, abdominal pain, vomiting and diarrhea. Electrocardiogram and laboratory findings were suggestive of acute ST-elevation myocardial infarction.

This case raises important issues concerning the pathophysiology of exercise, food consumption, allergy, anaphylactic shock, cholinergic, stress-induced, allergy to effort, aquagenic urticaria and the Kounis hypersensitivity-associated acute coronary syndrome.

Indeed, during exercise the following can occur:

1. Mast cell degranulation is facilitated during exercise due to a decrease in pH resulting in an acidic environment.²

2. Tissue transglutaminase enzyme alterations occur during exercise that may cause peptide aggregation, which in turn, increases IgE cross-linking.³
3. A sudden redistribution of blood during exercise transports allergens away from the gut to the skin and/or skeletal muscle, where phenotypically different mast cells reside.⁴
4. Exercise applies an inhibitory effect on gastric acid secretion. This decreases digestion of oral allergens and preserves the structural integrity of the gastrointestinal duct, which leads to continued systemic absorption of the allergens whether it be profilins, lipid transfer proteins or other antigenic determinants.⁵
5. During food intake, substances such as alcohol can damage the ultrastructure of gastric and gut mucosa and induce alterations in their integrity and permeability; these result in endotoxins entering the circulation and could potentially facilitate allergen entry.⁶
6. Experiments have shown that during exercise, plasma osmolarity is raised and this can increase basophil activation and histamine release.⁷

FDEIA has been associated with several causes including disease conditions; environmental factors; foods such as fruits, fish, nuts and vegetables; and drugs. These should be always tested for, in order to identify the culprit.⁸ Wheat and tomatoes are commonly used food items that can induce exercise anaphylaxis and should also always be considered.

The described patient was suspected, correctly, to have suffered EIA provoked by wheat; the patient developed EIA after eating wheat before his cycling trip. The authors also wanted to conduct a food-exercise challenge, however the patient had accidentally challenged himself by eating

bread and dancing before arriving at the hospital. To our knowledge, FDEIA has been associated with acute coronary syndrome and in particular, with the Kounis hypersensitivity-associated acute coronary syndrome only once in the past.⁹

This patient developed urticaria on his chest and arms, abdominal pain, vomiting and diarrhea after warming up the patient's body temperature, however his condition deteriorated and he developed angioedema and collapsed. There is controversy whether peripheral vasodilatation or coronary vasoconstriction is the main cause of anaphylactic cardiovascular collapse.^{10,11} Whereas electrocardiography, cardiac enzymes and troponin were suggestive of myocardial injury, echocardiography did not show any wall abnormalities, and thus excluded takotsubo cardiomyopathy (also known as stress cardiomyopathy). Ideally, coronary angiography would have resolved this problem, had it been recommended.

Systemic manifestations such as abdominal pain, nausea, vomiting and diarrhea associated with effort-induced urticaria are characteristics of so-called cholinergic urticaria, also known as stress urticaria, allergy to effort and aquagenic urticaria. Cholinergic urticaria is a type of physical urticaria characterized by a number of short-lasting, highly pruritic wheals resembling the wheals depicted in the paper by Rosier et al.¹

This kind of urticaria has been attributed to water in sweat (aquagenic) during exercise, which reacts with sebum, forming a compound acting as an allergen that induces the release of histamine.¹²

Effort-induced anaphylaxis associated with allergy and myocardial infarction seem to constitute a clinical complex that needs careful attention and should be always considered. Recognition, diagnosis, prevention and treating this complex is of paramount importance.

DISCLOSURES

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