# Two cases of food-dependent exercise-induced anaphylaxis with different culprit foods

Hassan M.S. Mobayed, Maryam Ali Al-Nesf

#### Abstract:

Department of Medicine, Hamad General Hospital, Doha, Qatar

## Address for correspondence:

Dr. Maryam Ali Al-Nesf, Department of Medicine, Hamad General Hospital, Doha, Qatar. E-mail: mariamali@hmc. org.qa

Submitted: 31-12-2012 Accepted: 09-03-2013



Access this article online

Website: www.thoracicmedicine.org DOI: 10.4103/1817-1737.124443 Food-dependent exercise-induced anaphylaxis (FDEIA) is one of the severe allergic reactions in which symptoms develop only if exercise takes place within a few hours of eating a specific food. It is important to consider FDEIA in cases of unexplained anaphylaxis as reactions can occur several hours after ingesting the culprit food(s). We herein report the first two cases of FDEIA in the Middle East. The first one is induced by wheat, while the other by peanut. The pathophysiology, predisposing factors, diagnosis, and treatment of FDEIA are also summarized here.

#### Key words:

Anaphylaxis, food-dependent exercise-induced anaphylaxis, wheat

#### Introduction

Food-dependent exercise-induced anaphylaxis (FDEIA) is an unusual form of exercise induced anaphylaxis that occurs only when the patient exercises within 2-4 h of ingesting a specific food.<sup>[1]</sup> Neither the food intake alone nor the exercise alone can trigger the anaphylactic reaction. This syndrome is underdiagnosed and many clinicians may not consider it in a patient presenting with anaphylaxis.

We reviewed the literatures; there are no cases of FDEIA reported from the Middle East. This is a report of two interesting cases of FDEIA, one caused specifically by wheat and the other by peanut.

#### **Case Reports**

#### Case 1

A 14-year-old Palestinian female middle school student seen initially in the allergy clinic on October 2009. She described frequent attacks of itchy hives, swelling of lips, and eyelids. They were followed by dyspnea, wheezing, and dizziness spills. She gave history of four attacks over the last year. In all the attacks, her symptoms appeared during physical exertion immediately following the ingestion of her dinner that usually contains wheat bread, cheese, and eggs. Surprisingly, she could tolerate these foods if it was not followed by exercise. Moreover, her symptoms never occurred if a meal did not precede performing the exercise activity. Her last attack was severe and occurred while jogging and running at the backyard immediately after having a slice of vegetarian pizza for which she attended the emergency room (ED).

She gave history of not taking any medication specifically nonsteroidal anti-inflammatory drugs (NSAIDs) before having exercise. Also, the attacks were not related to her menstruation. Review of her past medical history and family history were noncontributory. In the ED, she was treated for anaphylaxis with intramuscular adrenalin and intravenous antihistamine, hydrocortisone, and fluids. And she was instructed to avoid eating cheese and eggs. In the allergy clinic, her physical examination was non remarkable and dermographism test was negative. Her baseline serum tryptase was normal. The serum tryptase was not checked in the ED during the attacks. The allergy skin prick testing for common foods showed a positive reaction to only wheat. A supervised graded oral challenge with wheat at rest was performed and was tolerated without any consequences. She was instructed to avoid any exercise for 4 h after ingestion of food, particularly the wheat. Over the last 2 years of regular followup, she described no single episode of anaphylaxis.

#### Case 2

A 15-year-old Qatari male student was referred to the allergy clinic on January 2011 because of a suspected peanut allergy. He reported three episodes of anaphylaxis associated with the ingestion of peanut in the last 8 months. The first occurred while jogging 3 h, following eating a bar of peanut-containing chocolate. He developed flushing, large plaques of urticarial rash all over the body associated with periorbital facial swelling, shortness of breath, and wheezing. He was brought to the ED and treated for anaphylaxis attack. The second and the third episodes also occurred when he started running 2 h after having a piece of sweet that contains mixed nuts. He can tolerate eating nuts if no exercise is performed and he does not develop any symptoms if he exercises without eating nuts. Medical history is significant for childhood atopic dermatitis, bronchial asthma, and allergic rhinitis. He has strong family history of atopy. His father as well as three of his siblings has asthma and seasonal allergic rhinitis. Physical examination was unremarkable. Allergy skin prick testing for food showed positive reaction to peanut, almond, and hazelnut. A supervised graded oral challenges with peanut, almond, and hazelnut at rest were negative. He was advised to avoid any exercise for 4 h, following food ingestions particularly nuts. He has no attacks of anaphylaxis over the last 1 year of follow-up.

#### Discussion

FDEIA was first described in 1979 by Maulitz *et al.*, as a late allergic reaction to shellfish induced by strenuous exercise.<sup>[2]</sup>

In exercise-induced anaphylaxis type, exercise alone can trigger anaphylaxis. Many patients, however, require one or more cofactors to be present in order to develop symptoms. Food-dependent exercise-induced anaphylactic reactions are becoming more prominent.<sup>[3]</sup>

FDEIA is considered to be immunoglobulin E (IgE)-mediated hypersensitivity reaction to food allergens, because IgE antibodies against the causative food allergens have been detected after skin prick or radioallergosorbent tests in the majority of FDEIA patients.<sup>[4]</sup>

Clinical manifestations of FDEIA are signs and symptoms of anaphylaxis in the setting of physical exertion. Symptoms may begin at any stage of exercise and occasionally occur just after exercise. Symptoms occur only when the person exercises within minutes to a few hours after eating. Wheat, shellfish, tomatoes, peanuts, and corn are the most common foods implicated in FDEIA. However, the disorder has been reported with a wide variety of foods, including fruits, seeds, milk, soybean, lettuce, peas, beans, rice, and various meats.<sup>[4]</sup>

Wheat is the most frequent food that triggers FDEIA in Japan. Studies from Japan showed that wheat is the cause of anaphylaxis in 57% of cases of FDEIA.<sup>[5]</sup> Omeg-5 gliadin which is a component of wheat gluten has been identified as the major allergen in patients with FDEIA.<sup>[6]</sup>

When anaphylaxis is triggered by a specific food, the condition is called specific FDEIA; however, in unspecific FDEIA, susceptible individuals develop anaphylaxis when exercise after food regardless of what food has been eaten.<sup>[7]</sup>

Contributing factors may include use of aspirin or NSAIDs, exposure to high pollen levels, extreme of temperatures or humidity, or even stress or menses.<sup>[8-10]</sup>

The exact pathogenesis of FDEIA is still unknown. Several theories have been proposed to explain FDEIA.

One theory is suggesting the activation of the intestinal enzyme tissue transglutaminase during exercise which will be capable of binding and aggregating gliadin moieties to form large immunogenic complexes that demonstrate increased IgE binding.<sup>[6]</sup>

Another theory is the increased gastric permeability during exercise, which may permit increased entry of intact or incompletely digested allergens into the circulation during exercise but not during rest.<sup>[10]</sup>

The third theory described that blood flow redistribution away from the viscera to the skin and musculature during exercise may carry food allergens to tissues containing mast cells that are not tolerant to those allergens, resulting in an allergic reaction during exercise, but tolerance at rest.<sup>[11]</sup>

Moreover, a 4<sup>th</sup> theory suggests that exercise mobilizes and activates immune cells from gut-associated depots, stimulating proinflammatory responses that are normally countered by anti-inflammatory responses.<sup>[12]</sup>

The diagnosis of FDEIA is usually made clinically, based on a detailed history of the events surrounding the episodes and by excluding other disorders that could mimic it.

Looking for evidence of food-specific IgE to the implicated food, either by skin testing or *in vitro* assays is essential in the evaluation of patients with FDEIA because sensitization to the precipitating food(s) is usually demonstrable.<sup>[7]</sup>

A positive food and exercise challenge confirms the diagnosis but a negative challenge does not reliably exclude the diagnosis. No protocol has been established for food exercise challenge to evaluate patients with FDEIA. The Standard Bruce protocol for stress testing has been used with variable success in eliciting symptoms with exercise challenge.<sup>[4,13]</sup> Thus, until a validated protocol for exercise challenge is established, challenge is not required to confirm the diagnosis.

Treatment of the anaphylactic reaction in FDEIA follows the usual protocol of anaphylaxis management by epinephrine intramuscular, antihistamine, and hydrocortisone. Preventing further attacks is essential and can be done by instructing the patient to avoid eating for at least 4 h prior to vigorous physical exercise. Moreover, carrying self-administered EpiPen (Meda pharma GmBH & co. KG Benzstrasse 1,61352 Bad Homburg, Germany) (an epinephrine autoinjector) is highly advised for any incidental exposure.

In our patients, the diagnosis of FDEIA was not made by the primary care physician or by the emergency physician. The patients have been advised to avoid many foods as cases of primary food allergy. Lack of awareness of the diagnosis of FDEIA by many physicians will potentially lead to wrong diagnoses and management plans, and unnecessarily limit the patient's diet and routine exercise. We are describing the first two cases of FDEIA in the Middle East and we believe that physician awareness and strategies are needed to ensure accurate diagnosis and management of this condition.

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**How to cite this article:** Al-Nesf MA, Mobayed HM. Two cases of food-dependent exercise-induced anaphylaxis with different culprit foods. Ann Thorac Med 2014;9:42-4.

Source of Support: Nil, Conflict of Interest: None declared.

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