

## FOOD-DEPENDENT EXERCISE-INDUCED ANAPHYLAXIS-SEQUENCE OF CAUSATIVE FACTORS MIGHT BE REVERSED

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**Abstract:** We present a case of a 27-years-old female who experienced several episodes of food-dependent exercise-induced anaphylaxis (FDEIA). Besides two typical episodes of FDEIA triggered by a postprandial physical exercise, she also experienced atypical episodes in which the sequence of the causative stimuli was clearly reversed—clinical symptoms which appeared after a prolonged exercise, followed by ingestion of the sensitizing food. This unusual clinical picture entitled us to extend the routine recommendations—avoidance of the coincidence of food allergens intake and exercise accordingly to her history.

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### INTRODUCTION

Food-dependent exercise-induced anaphylaxis (FDEIA) is defined as the occurrence of anaphylactic symptoms in association with postprandial exercise. This classical picture initially described by Maulitz *et al.* [8] was reported in many studies, mainly as case reports [2, 3, 6, 8, 9, 10, 11, 12, 13, 14, 15]. A cornerstone of this syndrome is that physical exercise without ingestion of causative food allergen, as well as ingestion of food allergen without postprandial exercise, are well tolerated. The mechanism of mast cell activation by food allergens is IgE dependent, but the mechanism by which exercise evokes clinical symptoms is not fully understood [2, 5, 7, 13, 15]. Spectrum of the causative food allergens covers a wide range, but the most common in European population are tomatoes, cereals and peanuts [13]. The time elapsed between meal and exercise is usually between 30–120 minutes, and the duration of exercise before the onset of symptoms lasts 10–50 minutes.

Only some subjects experience their symptoms during the recovery phase [13]. In this study we report an unusual case of FDEIA, in whom anaphylactic symptoms appeared not only after postprandial exercise, but also when the food allergen was ingested immediately after prolonged exercise.

### CASE DESCRIPTION

A 27-year-old female with a negative history of atopic diseases, experienced in the last 12 years five incidents of FDEIA following ingestion of different fruits: plums, grapes, cranberries, peaches, blackberries and raspberries. In some episodes those fruits were eaten together, therefore the precise identification of culprit food was uncertain to the patient. It should be pointed out that the patient is a young, physically very active person, frequently performing vigorous physical exercises which were well tolerated unless accompanied by ingestion of the sensitizing foods. Moreover, for many years until now, all these foods were

**Table 1.** Episodes of FDEIA with reversed sequence of triggering factors.

	Episode 1	Episode 2	Episode 3
Physical factor	outdoor exercise	outdoor exercise	indoor exercise
Culprit food	raspberries	peaches	cranberries
SPT to culprit food	positive	positive	positive
sIgE to culprit food	not done	not done	not done
Duration of physical effort	2 hours	3 hours	5 hours
Weather condition	hot weather	hot weather	very hot weather
Intensity of physical effort	high intensity	medium intensity	medium intensity
Onset of anaphylaxis after food ingestion	20 minutes	10 minutes	10 minutes
Onset of anaphylaxis after exercise ending	20 minutes	about 20 minutes	10 minutes
Symptoms of anaphylaxis	generalized urticaria, face and upper limbs angioedema, vomiting, diarrhea	generalized urticaria, face oedema, nausea, loss of consciousness	urticaria on neck and hands

frequently ingested and well tolerated if the ingestion was not accompanied by physical exercise. The patient experienced two typical episodes of FDEIA. The first one occurred 12 years ago after 30 minutes of intensive walking, preceded by eating blackberries. Clinical symptoms of anaphylaxis included generalized urticaria, facial angioedema, nausea, vomiting and weakness. The second episode was precipitated 10 years ago by ingestion of raspberries and prolonged physical exercise started about 3 hours later. After 1 hour of dancing she developed anaphylactic symptoms of medium intensity: disseminated urticaria accompanied by facial angioedema and nausea. In addition, the patient experienced three unusual episodes of FDEIA, described below.

**Episode 1.** Immediately after discontinuation of prolonged exercise lasting 2 hours, the patient ate raspberries. About 20 minutes later she experienced generalized urticaria accompanied by angioedema localized on the face and upper limbs, vomiting and diarrhea.

**Episode 2.** During a hot and sunny day the patient performed an outdoor exercise of medium intensity for about 3 hours and a few minutes later she ate peaches. About 10 minutes later symptoms of a heavy anaphylactic reaction with generalized urticaria, angioedema of the whole face, nausea and loss of consciousness appeared and the patient required emergency room treatment.

**Episode 3.** Following a strenuous and prolonged exercise the patient ate the first meal that day including potatoes, chicken and cranberries. About 10 minutes later, she noticed disseminated urticaria localized on the neck and hands, which were partially reduced by 10 mg of cetirizine. Four hours later she ate white grapes and a shortly afterwards started dancing intensively. A few minutes later she developed a heavy anaphylactic reaction with the symptoms similar to those described in the episode 2. All three episodes are summarized in Table 1.

**Allergological examinations.** Skin testing with a standard set of aeroallergens and food allergens (Allergopharma, Reinbek, Germany) was performed, accompanied by skin testing with fresh extracts of peach, kiwifruit, mandarin, orange, nectarine, blackberry, black and white grape, raspberry, cranberry and pineapple suspended in Coca solution without phenol (50% of 0.9% NaCl and 50% of glycerol) in concentration of 5% (vol/vol). Skin tests were positive to peach, raspberry, cranberry, nectarine, blackberry and black grape. Total serum IgE was 119 kU/L (Immulite 2000, Siemens, Germany). Allergen specific IgE determinations performed with EUROLineScan (Euroimmun Medizinische Labordiagnostika, Lübeck, Germany) were positive to *Alternaria alternata* (0.35 kU/l-class 1), dog and cat hair (0.47 kU/l-class 1). An exercise test was performed with induced neither symptoms of anaphylaxis nor any changes in spirometric values. Due to a possible life-threatening systemic reaction, an exercise challenge after ingestion of food allergens was not performed.

## DISCUSSION

Classical picture of FDEIA and its definition clearly indicate that the occurrence of anaphylactic symptoms is associated with postprandial exercise [3, 6, 8, 9, 10, 11, 12, 13, 14]. Our patient fulfils these diagnostic criteria only in the case of two typical episodes. However, the three episodes of FDEIA described above are characterized by a reversed sequence of culprit stimuli. This “reversed sequence” was clearly reported in episodes 1 and 2, where food allergens were eaten shortly after discontinuation of prolonged exercise. The most complex and difficult for an unequivocal interpretation is episode 3. In the first phase, a long and fatiguing journey (perceived by the patient as a prolonged and heavy exercise) clearly preceded the food intake. The second phase took place 4 hours later and the sequence of stimuli was classical. An important question – whether it was one prolonged episode or two independent ones – is not easy to answer. It seems to be characteristic

for the episodes of “reversed sequence” that the physical exercise was of medium intensity but prolonged in time, even for several hours, and gradually leading to exhaustion. Despite the lack of similar reports of “reversed sequence” of culprit stimuli, clinical picture of all mentioned episodes is very suggestive and, in our opinion, fulfill the criteria of FDEIA. Skin tests were positive to culprit food allergens (peach, raspberry, cranberry, nectarine, blackberry and black grape) and ingestion of them accompanied by physical exercise resulted in symptoms of anaphylaxis, regardless of the sequence of both stimuli. It is well known that aspirin intake facilitates or precipitates symptoms of FDEIA, as does exercise. This effect might be obtained regardless of the time of aspirin intake, i.e. before or together with the food allergen [1, 4, 5, 7]. Thus, it seems very likely that in FDEIA the coincidence of triggering factors, but not their sequence, is of crucial importance.

The aim of this case report is to draw attention to the need for a careful and detailed anamnestic examination in patients with apparent simple food allergy or exercise induced anaphylaxis. It seems reasonable to individualize standard recommendations in patients with unusual sequence of events resulting in a potentially life-threatening anaphylactic reaction. Our patient, in consequence of her uncommon clinical history, has been informed about the nature of FDEIA and instructed to avoid causative food allergens during the 4 hours preceding intended physical activity, while performing it, and for at least 2 hours after its discontinuation.

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