

Anaphylaxis Induced by Exercise and Related to Multiple Food Intake

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ABSTRACT

In some patients, exercise-induced anaphylactic (EIA) reactions occur only when a particular food is eaten before exercise. We describe three patients with EIA induced by different foods. Patients who presented episodes of EIA performed exercise challenges after fasting and 1 hour after a meal without foods suspected of predisposing the reaction. Subsequently, patients performed exercises after separate intake of each suspected food. Patients underwent skin prick tests (SPT) with food extracts. Serum total and specific IgE antibodies to food were determined. No reactions were provoked by exercise tests without prior intake of suspected foods. Eight of 30 food-exercise combination challenges were positive. In Patient 1, tomato, zucchini, and wheat resulted in adverse reactions; in Patient 2, potato, peanuts, and tomato; in Patient 3, rice and peanuts. SPTs and RASTs to foods predisposing the reaction were positive. Food-exercise combined challenge may be useful in identifying foods that favor EIA in children with multiple food-dependent EIA. (Allergy and Asthma Proc 18:245-248, 1997)

Exercise-induced anaphylaxis (EIA) is a distinct form of physical allergy.¹ In some patients, anaphylaxis occurs only when exercise is preceded by the intake of either a specific food (specific food-dependent EIA) or any meal (nonspecific food-dependent EIA).² A few cases of specific food-dependent EIA have been reported from the first description of Maulitz et al.³ Particular foods, such as celery,² shellfish,^{3-5,6} wheat,^{4,7-11} grapes,⁴ nuts,¹² peach,¹² egg,^{6,13} orange,¹⁴ apple,¹⁵ hazelnut,¹⁶ cheese,¹⁷ cabbage,¹⁷

chestnut,¹⁸ rice,¹⁸ tomato,¹⁸ and cuttlefish¹⁹ have been reported to induce the reaction. As other factors, drug intake,^{1,3} cold temperature,¹⁵ menstrual cycle,⁴ dental amalgam,²⁰ and weather conditions^{1,21} have been found seemingly to precipitate EIA.

We previously reported clinical features and reduced pulmonary function in two cases of EIA associated with the ingestion of different specific foods.²² We present our complete series of multiple food-dependent EIA that includes the follow-up of one case and one additional case.

MATERIALS AND METHODS

Patients

The study population consisted of 3 patients (2 male and 1 female) ranging in age from 19 to 23 years. All patients were evaluated at the Department of Pediatrics, University Hospital of Parma, Italy. The department has an intensive care unit. Clinical and laboratory data were recorded prospectively in all patients from the time of enrollment in the study. Patients were diagnosed with EIA according to the following criteria^{1,5,21,24}: 1) episodes of upper respiratory tract obstruction and/or collapse with rash or urticaria, precipitated by exercise; 2) anaphylaxis not experienced in response to warm baths, showers, fever, or other events increasing core body temperature; 3) collapse not due to a dysfunction of an organ, such as the heart, lung, or brain.

In our patients, physical exercise provoked urticaria in 3 cases, angioedema in 3, conjunctivitis in 2, hypotension in 2, rhinitis in 1, dyspnea in 1, and loss of consciousness in 1. One patient had palm pruritus as a prodromal symptom. The interval between eating and exercise varied from 30 to 60 minutes. Symptoms were elicited by dancing and basketball in Case 1, by basketball in Case 2 and by soccer in Case 3. The onset of symptoms occurred after 5 to 30 minutes of strenuous exercise. Foods suspected of inducing the reactions are listed in Table I.

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TABLE I

Results of Food-Exercise Combination Challenge

Patient	Age	Sex	Food	Prodromal Manifestation	Complete Clinical Symptoms
1	19	F	Peach, apple, rice, soy, maize, peas, lentils, spinach, broccoli, artichoke Tomato	Negative Palm pruritus	Negative Rhinoconjunctivitis, generalized urticaria, facial angioedema, swelling of mouth
			Wheat	Palm pruritus	Rhinoconjunctivitis, generalized urticaria, facial angioedema, fall in PEFR (15%) and FEV ₁ (13%), swelling of mouth
2	19	M	Zucchini Wheat, peas, rabbit meat Potato	Negative Palm and leg pruritus	Pruritus Negative Conjunctivitis, lump in the throat, inspiratory dyspnea, fall in PEFR (11%) and FEV ₁ (12%), generalized urticaria, lip angioedema
			Peanuts	Palm pruritus	Generalized urticaria, lip angioedema, fall in PEFR (12.5%) and FEV ₁ (12.1%), dyspnea
			Tomato	Diffuse pruritus	Generalized urticaria, wheezing, fall in PEFR (25%), and FEV ₁ (13.8%)
3	23	M	Beans, peas, peach, cherry, spinach, pear, walnut, plum, oat Rice	Negative	Negative Urticaria, facial angioedema, brassy cough, hoarseness, hypotension
			Peanuts		Urticaria, facial angioedema, pruritus

The patients felt that intake of suspected foods, but not followed by exercise, did not provoke any adverse reaction. A similar exercise never resulted in symptoms without ingestion of suspected foods. No patient experienced anaphylaxis in response to warm baths, fever, or other increases in core body temperature, drug intake, cold temperature, weather conditions, menstrual cycle, or dental amalgam.

Immunologic Studies

Patients underwent skin prick tests (SPT) with a 1:20 (W:v) concentration of food extract (Bayropharm, Milan, Italy). The size of the skin test wheal was compared with histamine, 1 mg/mL, and the diluent. SPTs were considered positive if the diameter of the wheal was greater than 3 mm, after subtracting the diameter of the wheal of the negative control wheal and at least half the area of the histamine standard. Blood was taken to measure both specific IgE antibodies to food by RAST (Pharmacia, Uppsala, Sweden) and total IgE levels by PRIST (Pharmacia, Uppsala, Sweden).

Exercise Challenge

The exercise test consisted of free running for 6 minutes with an increase in heart rate up to at least 170 beats per minute.²³ Pulmonary function was measured with a com-

puterized spirometer (Microloop-Markos). Measurements were performed before running and at 3, 6, 10, and 15 minute intervals after beginning the exercise. Exercise tests were performed if baseline values of PEFR and FEV₁ were at least 80% of predicted values. Blood pressure was monitored during exercise challenges. Beta 2-agonists and inhaled corticosteroids were withheld for at least 12 hours before each testing session. Oral steroids and antihistamines were withheld for 8 days. All exercise challenges were conducted in the same conditions of temperature (20°–22°) and humidity, at the same time of the day. Patients underwent a controlled exercise test after 12 hours fasting. An exercise test was then performed 1 hour after a meal that did not contain suspected foods and 1 hour after eating each suspected food. Exercise challenge tests were performed on separate days.

RESULTS

No reaction was provoked by ingestion of foods alone or by exercise tests performed both on fasting and after taking a meal without suspected foods. Eight of 30 food-exercise combination challenges were positive (Table I).

Patient 1 performed 13 food-exercise combination challenges. Tomato, wheat, and zucchini induced reactions. Five

minutes after running, she developed intense pruritus of the palms, and within a few seconds she presented generalized urticaria as well as facial angioedema, swelling of the mouth, and rhinoconjunctivitis. Airway obstruction on pulmonary function testing was registered after exercises following wheat intake (Table I). Blood pressure was always normal. A year later, she noticed that attacks were elicited also by exercise following the ingestion of zucchini. On the basis of previous medical history, this food had never been considered as suspicious of inducing attacks. The zucchini-exercise combination challenge induced the occurrence of pruritus.

Patient 2 performed six exercise challenges after ingesting suspected foods. Potato, peanuts, and tomato favoured the onset of clinical reactions after running (Table I). Positive exercise challenges resulted in pruritus of the palms followed by generalized urticaria. A few minutes after the end of the exercise following the intake of peanuts, labial angioedema and bronchospasm occurred. After potato-exercise challenge, he presented with conjunctivitis, facial angioedema, and inspiratory dyspnea with the feeling of a "lump in the throat." A fall in peak expiratory flow rate (PEFR) and forced expiratory volume during the first second of expiration (FEV_1) was registered. The analysis of the flow/volume curve showed a slight plateau in the inspiratory loop, which suggested that difficult breathing principally depended on obstruction of the upper airways.⁸ Blood pressure was normal following all exercise challenges.

Patient 3 tolerated 9 of 11 food-and-exercise challenges. Rice gave rise to urticaria and facial angioedema, followed by brassy cough, hoarseness, and hypotension. The ingestion of peanuts before exercise induced facial angioedema, generalized hives, and pruritus.

Patients were treated with antihistamines, corticosteroids, epinephrine, and inhaled salbutamol, which resolved episodes. Patients avoided triggering foods for at least 6 hours before exercise. No further attacks occurred thereafter.

SPTs and RASTs results to foods that predisposed attacks, as showed by challenge, were positive. SPT results to suspected foods with negative food-exercise combination challenge were positive in 20 of 22 (90%) cases. Results of RAST to foods with negative food-exercise combination challenge were positive in 11 of 22 (50%) cases. Serum total IgE antibodies were elevated in two patients.

DISCUSSION

The presence of multiple food-dependent EIAN was demonstrated in our patients. Neither meal nor exercise alone induced symptoms. The intake of either tomato, wheat, or zucchini was a predisposing factor to reaction to exercise in Case 1; the intake of either potato, peanuts, or tomato in Case 2; the intake of either rice or peanuts in Case

3. Several reports²⁻¹⁹ have described patients who were sensitive to a single food. Although our data showed that exercise with prior ingestion of different foods produced anaphylactic symptoms, our findings show that the history was helpful in suspecting triggering foods. However, such foods were confirmed only by challenge tests. This is different from the findings of several investigators,^{1,4} who suggested that negative exercise challenge results did not rule out EIAN. However, studies on larger populations are required to clarify this difference.

In accordance with previous studies,^{3-5,8,14,15} we found that both SPTs and specific IgE antibodies to foods had excellent sensitivity in food-dependent EIAN. However, because of the high false-positive rates, the clinical significance of positive SPT and RAST results should be ascertained by food-exercise combination challenge.

Additional factors favoring EIAN, such as drug intake,^{1,4} cold temperature,¹⁵ dental amalgam,²⁰ weather conditions,²¹ and menstrual cycle⁴ have been reported. We carefully excluded those factors that could predispose EIAN in our population.

Our findings underline that food-dependent EIAN is distinct from other exertion-related syndromes such as cholinergic urticaria or exercise-induced asthma. In our study, no patient presented hives either with warm stimuli such as warm baths, fever, or exercise not preceded by food consumption.^{21,24} Furthermore, urticaria did not occur with stress or anxiety. None of the patients had a history of exercise-induced asthma. We found that dyspnea did not occur during or after exercise unless a particular food was eaten.

The pathogenic mechanisms of food-dependent EIAN remain unclear. Several studies have shown that exercise without food ingestion increases plasma histamine concentrations in some patients both with food-dependent EIAN^{4,6} and with EIAN.²⁵⁻²⁶ Moreover, in a few cases histamine concentration was higher after food-exercise combination challenge than after exercise challenge alone.^{4,6} Our findings are consistent with the hypothesis that food-dependent IgE-mediated reactions may lower the threshold for mediator release from mast-cell, induced by exercise.³ However, exercise did not precipitate the reaction for all foods to which children had an in vivo and in vitro positive tests. We believe that this may be the consequence of poor diagnostic accuracy of these tests.

Our results point out that EIAN can be induced by multiple foods. This finding suggests that more emphasis needs to be placed on assessing the role of foods in patients with EIAN. An accurate identification of precipitating foods by food-and-exercise challenge improves the quality of life of these patients. Prophylactic treatments have not been found to be effective, but avoidance of triggering foods for at least 6 hours before exercise can prevent reactions. In addition, a subject developed EIAN after ingestion of a food that was not suspected before. Therefore, patients should never exercise alone and should always carry epinephrine.

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