

Apple-dependent exercise-induced anaphylaxis

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Exercise-induced anaphylaxis (EIA) is a form of physical allergy occurring in association with physical exercise, and presenting with pruritus, urticaria, and erythema, before progressing to upper respiratory obstruction or vascular collapse. It has been reported in a group of patients in whom ingestion of a specific food or a particular postprandial state is a prerequisite for its development (1–4). We report a patient in whom apple was the triggering factor in EIA.

Case report

A 12-year-old girl was seen at our clinic because of an episode of warmth, intense pruritus of the palms, erythema, facial angioedema, and urticaria, accompanied by dysphonia as well as difficult breathing and weakness. The patient had been playing basketball for 30 min and she had eaten an apple immediately before exercise (she denied having eaten other foods including spices). On admission, she was treated with epinephrine, antihistamines, and corticosteroids. Cutaneous symptoms were relieved, but angioedema persisted for a week.

The patient had a family history of atopy. She complained of mild seasonal rhinitis. Previously she had eaten apples and other fresh fruits without adverse reactions, and a similar amount of exercise had never resulted in symptoms. Neither heat nor cold exposure caused urticaria.

Both physical examination and laboratory assessment were unremarkable during the asymptomatic state.

Total IgE level was 60 kIU/l. Prick tests with inhalants and foods (including birch pollen and cel-

ery) were negative except for *Artemisia vulgaris* pollen. Prick by prick test with fresh apple was positive. Specific IgE determination by the CAP System revealed class 2 against both *A. vulgaris* pollen and apple.

All challenge tests were made on separate days. Informed consent was obtained from the parents before each challenge. An open oral challenge test with apple was negative. The patient was tested for exercise challenge twice on the treadmill of the laboratory (25°C and 50% relative humidity) for 10 min.

The first exercise study was performed with the patient fasting. One hour before the second exercise challenge, she ate an apple. Both tests were negative. Later, for 10 min, she performed a free-run outdoor exercise challenge (11°C and 50% relative humidity) 1 h after eating an apple. Ten minutes after running, she developed intense pruritus of the palms and fingers and rhinoconjunctivitis, and within 5 min she had generalized urticaria with both small and giant wheals involving face, neck, back, and arms as well as facial angioedema. Blood pressure was normal, and no significant changes were seen in pulmonary function. The patient was immediately treated with epinephrine, antihistamines, and corticosteroids. Ten minutes later, symptoms progressed to cough and difficult breathing. An 18% fall in basal FEV₁ was registered. The patient was then treated with inhaled salbutamol and epinephrine, and the episode resolved within 2 h, although angioedema lasted for several hours.

Another outdoor exercise challenge test (10°C and 53% relative humidity) after the intake of other food-stuffs was negative.

Discussion

Exercise-induced anaphylaxis is recognized as a distinct form of physical allergy (5). Little is known about the physiopathologic mechanisms of these reactions. The syndrome appears to encompass a heterogeneous group of patients and reactions. As predisposing factors, sensitivity to some specific food (celery, peach, wheat, shellfish, grape) or food intake itself has been reported (1–4); such cases are called “food-dependent EIA”.

In our case, apple-dependent EIA was demonstrated. This patient had an IgE-mediated sensitization to apple; however, neither apple nor exercise alone induced symptoms. Our findings are consistent with the hypotheses of several other authors (1–4). The apple-dependent, IgE-mediated, immediate-hypersensitivity-type reaction would be sub-threshold without exercise, but, because of the influence of exercise on mast-cell releasability, it becomes clinically overt. However, because the patient’s first episode of EIA occurred when she was exercising in the cold, and the reaction could be reproduced only when accompanied by certain environmental factors such as cold temperature, other nonimmunologic factors may have contributed to mediator release. On the other hand, neither relative humidity nor exercise intensity seemed to influence the test if both factors were kept similar. Additional precipitating factors including spices, drugs, or alcohol intake; lack of sleep; fatigue; phase of the menstrual cycle; and familial background (1, 5) were

excluded. Other mechanisms proposed to explain this syndrome are increased splanchnic and skeletal muscle blood flow and gastrin-induced mediator release in the postprandial phase (3). Although these mechanisms can explain nonspecific food-dependent EIA, in our patient, the intake of different foodstuffs before exercise did not reproduce the syndrome.

The patient was also sensitized to *A. vulgaris* pollen. This sensitization is found in up to 76% of patients with food-dependent EIA (2). However, since the reaction occurred in winter, the potentiation of the reaction by *Artemisia* pollen is unlikely.

We can conclude that, in this case, the anaphylaxis was probably due to a combined effect of apple allergens, exercise, and environmental factors on mast-cell releasability.

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