

CASE REPORT

CASO CLINICO

Two cases of food-dependent exercise-induced anaphylaxis

Due casi di anafilassi da esercizio fisico indotta da alimenti

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Anaphylaxis • Urticaria • Exercise • Food

Parole chiave

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Summary

Exercise-induced anaphylaxis (EIA) is characterized by the clinical features of systemic anaphylaxis after exercise. Food may be a precipitating factor of EIA (food-dependent EIA, FDEIA). Unlike unspecific FDEIA, where the symptoms are independent of the kind of food ingested prior to exercise, specific FDEIA is linked to the ingestion of certain foods before exercise. In this report we describe two patients with EIA triggered by ingestion of specific foods clearly identified by clinical anamnesis and skin tests. The first patient referred two episodes of anaphylactic shock after ingestion of greens and fruits 1 hour before dance exercises; the second patient referred two episodes of urticaria and eyelid angioedema during the second half of a soccer match, after the ingestion of an apple during the break between the first and the second half of the match. In both patients, the history, the clinical data, the temporal relationship among specific food ingestion, physical exercise and onset of symptoms, the negativity of specific food challenge without exercise and of exercise challenge without specific food, the positive skin prick-test for specific foods, the exclusion of additional precipitating factors strongly support the diagnosis of specific FDEIA. In both cases, exercise was not discouraged; the patients were instructed to avoid eating the offending foods at least 6 hours before exercise and to discontinue exercise after development of any unusual symptom similar to those experienced.

Riassunto

L'anafilassi da esercizio fisico (EIA) è caratterizzata da un quadro clinico di anafilassi sistemica dopo esercizio fisico. Uno dei fattori scatenanti la EIA è rappresentato dal cibo (FDEIA). Contrariamente alla FDEIA aspecifica, in cui i sintomi sono indipendenti dal tipo di cibo ingerito prima dell'esercizio fisico, la FDEIA specifica è legata all'ingestione di alcuni particolari alimenti prima dell'esercizio. Riportiamo due casi di EIA scatenati dall'ingestione di specifici alimenti chiaramente identificati con l'anamnesi e i test cutanei. Il primo paziente riferiva due episodi di shock anafilattico dopo ingestione di frutta e verdura 1 ora prima degli esercizi di danza; il secondo paziente riferiva due episodi di orticaria e angioedema palpebrale durante il secondo tempo di una partita di calcio, dopo l'ingestione di una mela nell'intervallo tra il primo e il secondo tempo. In entrambi i pazienti, la storia, i dati clinici, la relazione temporale tra ingestione di alimenti specifici, esercizio fisico e insorgenza dei sintomi, l'assenza di reazione dopo ingestione dell'alimento senza esercizio fisico e dopo esercizio fisico senza ingestione dell'alimento, la positività ai test cutanei per gli alimenti specifici, l'esclusione di fattori addizionali scatenanti, supportano fortemente la diagnosi di FDEIA specifica. In entrambi i casi l'esercizio fisico non è stato sconsigliato, è stato invece consigliato di evitare l'ingestione degli alimenti specifici almeno nelle 6 ore precedenti l'esercizio fisico e di sospendere immediatamente l'attività in caso di comparsa di sintomi inusuali, simili a quelli presentati durante le reazioni.

Introduction

Exercise-induced anaphylaxis (EIA) has been recognized with increasing frequency since its original description in 1979¹. EIA is characterized by the clinical features of systemic anaphylaxis (collapse, urticaria, angioedema, upper respiratory obstruction,

bronchial constriction, gastrointestinal symptoms) after exercise²⁻⁵. General recommendations for patients with EIA include avoidance of all associated conditions known to trigger attacks in each particular patient, including avoidance of aspirin and nonsteroidals before exercise and avoidance of exercise 4-6 h after eating. In fact, intake of food is a well-rec-

ognized precipitating factor of EIA (food-dependent EIA, FDEIA).

Unlike unspecific FDEIA, where the filling of the stomach is responsible for the symptoms independently of the kind of food ingested prior to exercise, specific FDEIA is linked to the ingestion of certain foods before exercise. Numerous foods (celery, eggs, grapes, peaches, shellfish and wheat) have been implicated in FDEIA. However, ingestion of the implicated food without subsequent physical exercise is not sufficient to provoke the systemic allergic reaction. Strenuous exercise is required for the development of symptoms, and typical age of onset is adolescence or young adulthood. Interestingly, cross-reactions between airborne allergens and foods can occur; a case of specific FDEIA after eating snails has been described in a child sensitive to house-dust mites ⁶, and, in fact, IgE cross reactivity has been identified between house-dust mites and snails.

Specific FDEIA is a mast-cell mediated phenomenon and appears to be mediated by IgE. The diagnosis of FDEIA is made primarily on the basis of history and on positivity in skin test and/or RAST for the foods consumed before the EIA episode and may be confirmed by exercise challenge; furthermore FDEIA may be distinguished from cholinergic urticaria due to the presence of systemic manifestations, urticaria characteristics (wheals with a 10-15 mm diameter) and lack of symptomatic response to increases in body temperature. However several confusing factors (in particular, undermined history, multiple suspected foods, problems with masking foods and the lack of a specific diagnostic test) can make difficult a correct diagnosis; for example, Fiocchi et al. ⁷ reported a case of EIA after food contaminant ingestion.

In this report we describe two patients with EIA triggered by ingestion of specific foods, which were clearly identified by clinical anamnesis and skin tests.

Case 1

A 33-years-old female semi-professional dancer referred to our Operative Unit for two episodes of anaphylactic shock after dance exercises. In both episodes the patient had eaten a meal including greens and fruits 1 h before the onset of her training session, during which she had developed difficulty in breathing and loss of consciousness, immediately treated with betamethasone 8 mg e.v. and chlorphenamine i.m. Past medical history was negative for airway allergic diseases. The patient remembered to have experienced several episodes of epiglottic oedema after ingestion of unidentified foods only during the childhood, after which she had been able to consume any food without manifesting symptoms of al-

lergic reactions. In concomitance with the appearance of symptoms, the patient had consumed no drugs, nutraceuticals or dietary supplements; additional precipitating factors (including spice and alcohol ingestion, phase of the menstrual syndrome, fatigue or lack of sleep) were also excluded. Physical examination findings were unremarkable and routine biochemical parameters were in the normal range. Skin prick-test, performed with a common panel of allergens, showed negativity to aeroallergens and positivity to several food allergens, such as apple (++++), peach (++++), soy beans (++++), sunflower seed (+++), hazelnut (++) , peanut (++) , walnut (++) , spinach (++) . The prick by prick test, performed for vegetables that the patient ingested before anaphylaxis, was positive for cabbage (leaf ++++; flower +++, stem ++), swiss chard (leaf ++++, stem ++), spinach (leaf and stem +++) and lettuce (+++). A specific food challenge without exercise and an exercise challenge without specific food were negative. We did not perform a specific food-exercise-challenge for ethic reasons because of the risk of a serious reaction. On the basis of these data, we made a diagnosis of specific FDEIA.

Case 2

A 15 years-old boy referred to our Operative Unit for two episodes of urticaria after exercise. In both episodes he had developed urticaria and eyelid angioedema, without respiratory symptoms, during a soccer match. The patient referred that symptoms had always appeared during the second half of the match, and that there had been no further episodes of allergic reactions during similar soccer matches. The symptoms had been successfully treated with corticosteroid and antihistaminic therapy. An accurate anamnesis revealed that symptoms had developed every time that the patient had eaten an apple during the break between the first and the second half of the soccer match. The patient had a personal history of oral hitch and lip swelling after peach ingestion, but previously he had eaten apples without any kind of adverse reactions. The patient underwent skin prick-test that was negative to common aeroallergens and positive to food allergens, including apple, peach and cherry; specific IgE to these fruits were also positive. A specific food challenge without exercise and an exercise challenge without specific food were negative. A specific food-exercise-challenge was not performed given the objective findings by history and the possibility to easily avoid the specific food before exercise. Physical examination findings were unremarkable and routine biochemical parameters were in the normal range. In concomitance with the appearance of symptoms, the patient had consumed no

drugs, nutraceuticals or dietary supplements; additional precipitating factors (including spice ingestion, fatigue or lack of sleep, environmental and climatic factors, familial background) were also excluded. On the basis of these data, we made a diagnosis of apple-dependent exercise-induced urticaria and oral allergic syndrome to peach. Lipid transfer proteins (LTPs), small molecules of approximately 10 kD and with high stability, are the main allergens in patients sensitive to Rosaceae and not allergic to birch pollen^{8,9}. LTPs have recently been identified as allergens in Rosaceae subfamilies of the Prunoideae (peach, apricot, plum) and of the Pomoideae (apple); in particular, LTPs from apple (Mal d 3) and from peach (Pru p 3) have been characterized¹⁰. Our patient did not refer respiratory symptoms and did not show positivity to inhalant allergens. Thus, although merely speculative at the present time, an hypothesis is that LTPs have a role in apple-dependent exercise induced urticaria, besides that in oral allergic syndrome to peach. We were unable to perform an immunoblotting analysis because the patient's parents denied the consent for taking a new blood sample.

Discussion

In both patients, although a specific food-exercise challenge test (the reference standard for the diagno-

sis of specific FDEIA) was not performed, we believe that the history, the clinical data, the temporal relationship among specific food ingestion, physical exercise and onset of symptoms, the negativity of specific food challenge without exercise and of exercise challenge without specific food, the positive skin prick-test for specific foods, the exclusion of additional precipitating factors strongly support the diagnosis of specific FDEIA. In both cases, exercise was not discouraged; the patients were instructed to avoid eating the offending foods at least 6 hours before exercise and to discontinue exercise after development of any unusual symptom similar to those experienced.

Moreover, patient one was instructed to the importance to have available when exercising self-injecting epinephrine in the format of Epi-Pen.

In our opinion, this report is of interest because specific FDEIA is a unique physical allergy with increasing incidence as the exercising population increases and new foods are introduced on the market. It is evident that physicians can prescribe realistic prophylactic measures only if the trigger of EIA is clearly identified; one has to stress that a diagnostic error can induce unnecessary dietary modifications and may deter patients from participating in sports. Further researches are warranted to identify plant allergens responsible of specific FDEIA and possible cross reactions with environmental allergens.

References

- Maulitz RM, Pratt DS, Schocket AL. *Exercise-induced anaphylactic reaction to shellfish*. J Allergy Clin Immunol 1979;63:433-4.
- Castells MC, Horan HR, Sheffer AL. *Exercise-induced anaphylaxis*. Curr Allergy Asthma Rep 2003;3:15-21.
- Chong SU, Worm M, Zuberbier T. *Role of adverse reactions to food in urticaria and exercise-induced anaphylaxis*. Int Arch Allergy Immunol 2002;129:19-26.
- Okazaki M, Kitani H, Mifune T, Mitsunobu F, Saito S, Asaumi N, et al. *Food-dependent exercise-induced anaphylaxis*. Intern Med 1992;31:1052-5.
- Volcheck G, Li JT. *Exercise-induced urticaria and anaphylaxis*. Mayo Clin Proc 1997;72:140-7.
- Longo G, Barbi E, Puppini F. *Exercise-induced anaphylaxis to snails*. Allergy 2000;55:513-4.
- Fiocchi A, Mirri GP, Santini I, Bernardo L, Ottoboni F, Riva E. *Exercise-induced anaphylaxis after food contaminant ingestion in double-blinded, placebo-controlled, food-exercise challenge*. J Allergy Clin Immunol 1997;100:424-5.
- Diaz-Perales A, Lombardero M, Sanchez-Monge R, Garcia-Selles FJ, Pernas M, Fernandez-Rivas M, et al. *Lipid-transfer proteins as potential plant panallergens: cross-reactivity among proteins of Artemisia pollen, Castanea nut and Rosaceae fruits, with different IgE-binding capacities*. Clin Exp Allergy 2000;30:1403-10.
- Pastorello EA, Pompei C, Pravettoni V, Brenna O, Farioli L, Trambaioli C, et al. *Lipid transfer proteins and 2S albumins as allergens*. Allergy 2001;56:45-7.
- Breiteneder H, Radauer C. *A classification of plant food allergens*. J Allergy Clin Immunol 2004;113:821-30.