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An unusual case of wheat dependent exercise induced anaphylaxis (WDEIA) triggered by Tri a 14 in a pediatric patient: a case report

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Summary

Wheat dependent-exercise-induced anaphylaxis (WDEIA) is a food allergy characterized by anaphylaxis elicited when wheat ingestion is time-related with physical exercise.

We report a case of WDEIA in an asthmatic boy admitted to our Unit with suspected mushroom acute toxicity. The symptoms occurred during a gym session, approximately 2 hours after the ingestion of a meal based on pasta and cooked mushroom found in the family's garden. Acute toxicity due to mushroom ingestion was then excluded. Triptase serum levels resulted elevated in acute phase and normal after 24 hours. Food specific IgE showed a sensitization to lipid transfer protein Pru p 3 and to Tri a 14.

This case highlights that WDEIA is underdiagnosed, especially when patients are firstly visited in Emergency Unit. Moreover, Tri a 14 is seldom described as responsible for WDEIA, compared to omega 5 gliadin.

Introduction

In 1979 Maulitz first reported food-dependent exercise-induced anaphylaxis (FDEIA) in an adult long-distance runner after a shellfish-based meal (1).

Bread wheat (*Triticum aestivum*) is the most widely grown crop worldwide. Moreover, wheat is highly consumed and often used in food preparations (2). In genetically predisposed individuals, wheat can cause specific immune responses, both immediate (IgE-mediated, such as anaphylaxis, FDEIA, rhinitis and asthma, urticaria) and delayed (non-IgE-mediated, such as celiac disease and dermatitis herpetiformis) (2,3).

FDEIA is a special kind of food allergy. In patients with FDEIA, allergic symptoms are elicited when the ingestion of a specific food is time-related with a triggering factor, such as physical exercise (3).

We report a case of WDEIA in a young boy, which was uncommon for age presentation, for the confounding anamnestic data and hospital admission clinical suspicion.

Case report

M.B. is a 13-year-old boy affected by allergic asthma from the age of 7-years-old (sensitization to dust mite and grass pollen) on steroid inhalatory preventive treatment. Skin prick tests and specific serum IgE were positive to grass and birch pollens, alternaria, dust mite. He had no previous history of food allergy of anaphylaxis. M.B. was referred to our Hospital Emergency Department by the Territorial Emergency Unit for vomiting, flushing and breathing impairment. All the symptoms occurred approximately 2 hours after the ingestion of a meal based on pasta with tomato sauce, chard and cooked mushroom found in

the family's garden. No assumption of any other food/juice, alcohol, drugs nor medications (NSAID) was reported, no insect bite was reported.

M.B. initially showed symptoms while he was exercising in gym, running on a tapis-roulant. Emergency Territorial Unit was alerted, suspecting a toxic reaction to mushroom. Inhalatory salbutamol and endovenous administration of saline solution were given on Ambulance.

M.B. was admitted to Hospital in fair general condition, showing a state of anxiety; oxygen peripheral saturation, blood pressure and heart were all within normal range. He had generalized urticaria and initial lips swelling, with no respiratory distress. Endovenous methylprednisolone and oral cetirizine were administered, with progressive resolution of cutaneous manifestations.

Mycologist analysis showed that the mushroom eaten was *Pleurotus ostreatus*, a well-known edible species. Acute toxicity due to mushroom ingestion was then excluded.

Triptase serum levels and specific food IgE test were performed for egg (0.09 kUA/l), peanut (6.99 kUA/l), nut (7.92 kUA/l), milk (0.10 kUA/l), shrimp (1.54 kUA/l), cod (0.12 kUA/l), wheat (4.32 kUA/l), gluten (0.20 kUA/l), omega-5-gliadin (0.07 kUA/l), LTP Tri a 14 (6.68 kUA/l), LTP Pru p 3 (25.1 kUA/l), Bet v2 profilin (0.10 kUA/l), Bet v1 PR10 (0.07 kUA/l), tomato (0.1 kUA/l), and were determined by ImmunoCAP (Thermo Fisher Scientific, Sweden). The involvement of three different apparatus made the diagnosis of anaphylactic reaction more likely. Triptase level was elevated in acute-phase (19 ug/L, normal values < 11 ug/L), whereas the levels were normal 24 hours after the allergic event. These data confirm the diagnosis of anaphylaxis. Food specific IgE, performed during the clinical observation, showed a sensitization to lipid transfer protein Pru p 3 (25 Ku/l) and to Tri a 14 (6.68 Ku/L), which is a wheat lipid transfer protein. The dosage of Tri a 19 Omega 5 gliadin was negative. Prick-by-prick tests with cooked chard, cornmeal mush, nut and hazelnut were performed after 3 weeks, all with positive results, whereas prick-by-prick with tomato were negative. All these foods contain LTP. Prick-by-prick for peach-tea, wheat, peach and apricot jam were negative: they were tested to evaluate the sensitization toward widely consumed food in infancy and to reduce the risk of a relapse. Oral challenge was proposed, but parents did not give their consent. During allergologic follow up, M.B. reported eating wheat daily with no symptoms, but never in relation with physical exercise, as he was instructed not to. Self-injectable adrenaline was prescribed. He was not instructed to avoid chard, that was assumed even before physical exercise, without allergic reactions. Instead, recently he developed generalized urticaria after the assumption of a piece of flat bread 2 hours before a gym session.

Based on patient's clinical history and allergy test results, we made a diagnosis of WDEIA.

FDEIA is a rare yet severe form of IgE-mediated allergy where ingestion of a putative food associated with physical exercise within 4 hours triggers anaphylaxis (2,4). In FDEIA, both food allergen ingestion and physical exercise are independently tolerated, but their association can elicit anaphylactic reaction (5). Various types of food can be responsible of FDEIA. The list of possible triggering food is constantly under revision and influenced by geographical location and local diet (6).

WDEIA is elicited by wheat proteins (7). Palosuo et al. identified a gamma-like gliadin, later classified as omega-5-gliadin (Tri a 19), as the main allergen involved in WDEIA (8). Patients with WDEIA negative for Tri a 19 are described in literature to have sensitization to high-molecular-weight glutenin, alpha-gliadin, beta gliadin or gamma gliadin (8).

Discussion

In our case report, no sensitization against these common wheat antigens was found. Surprisingly, analysis performed in our patient showed a sensitization to a lipid transfer protein (Tri a 14). Tri a 14 is an allergen often involved in Baker's asthma (9), but few cases of Tri a 14 involvement in WDEIA are described. To our knowledge, only one pediatric case was identified in Europe so far (10). In this study, LTP resulted to be a major allergen only in Italian patients. The role of important cereal allergens, such as lipid transfer proteins, is still unknown in wheat (10).

The pathogenesis of WDEIA is still partly unknown. Physical exercise can cause a re-distribution of blood flow or can interact with mastocyte function, leading to a higher bowel permeability to a specific allergen (2,4). According to a recently published review on WDEIA, wheat/exercise challenge is not a necessary diagnostic test if clinical and laboratory data are suggestive of WDEIA (11). To our knowledge, up to now a universally approved challenge-performance protocol has not been validated yet.

Our case report shows how clinical presentation of anaphylaxis can be misleading, especially when multiple confounding factors are present. In case of anaphylactic reaction in allergic patients with a positive personal history for inhalatory sensitization (asthma), food sensitization might be suspected. In acute phase, serum triptase levels must be assessed, as this test and its variation after 12 to 24 hours are of crucial importance in the diagnostic pathway.

WDEIA is underdiagnosed, especially when patients are firstly visited in Emergency Unit, considering that a patient might have tolerated wheat until its association with exercise.

In our patient, both Tri a 14 and Pru p 3 could be responsible for the anaphylactic event described, as they have a 45% homology, but Tri a 14 seems to be most likely involved, considering that the only food containing LTP (except wheat) assumed by our patient was tomato, and specific IgE for tomato resulted negative. What is more, Pru p 3 reactions are almost always im-

mediate, whereas our patient had a delayed reaction. Moreover, wheat is more often involved in exercised induced anaphylaxis. Tri a 14 is seldom described as responsible for WDEIA, compared to omega 5 gliadin. The assumption of chard before physical exercise did not induce symptoms, whereas the assumption of flat-bread in relation with a gym session caused a generalized urticaria.

Further investigation should be advisable, in order to identify the real importance and incidence of Tri a 14 in WDEIA in pediatric patients, especially in Southern Europe.

Patient consent

Obtained.

Conflict of interest

The authors declare that they have no conflict of interest.

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