

C. MICUCCI<sup>1</sup>, D. AMICO<sup>2</sup>, M. BRACONI<sup>2</sup>, C. PAREO<sup>2</sup>, M.E. CIMARELLI<sup>2</sup>, S. SUBIACO<sup>2</sup>

## Exercise-induced anaphylaxis in a cardiopathic patient on chronic aspirin therapy

<sup>1</sup>UOC di Broncopneumologia - Servizio di Allergologia, Ospedale "Carlo Urbani", Jesi (Ancona) Italy

<sup>2</sup>UOC di Broncopneumologia - Ospedale "Carlo Urbani", Jesi (Ancona) Italy

### Summary

*We report the case of a 73 year old man on chronic aspirin therapy who went in anaphylactic shock during his daily farm chores following a meal rich in wheat products. The serum specific IgE assay (ImmunoCAP) showed strong positive specific IgE responses to  $\omega$ -5 gliadin. A two-year period avoiding wheat meals 3 hours prior to exercise, resulted in a lack of further anaphylaxis; this results aided us in making the diagnosis.*

### Corresponding authors

E-mail: corrado.micucci@tin.it

E-mail: donatellaamico@libero.it

### Case report

The specific Food Dependent Exercise Induced Anaphylaxis (s-FDEIA) is a form of EIA in which anaphylaxis develops only if physical activity occurs within a few hours after eating a specific food. Neither food intake nor physical activity by themselves produces anaphylaxis (1). Symptoms may include cutaneous, gastrointestinal, cardiovascular and respiratory manifestations. A recent study has shown that the large majority of s-FDEIAs in Italy are associated with LTP (Lipid Transfer Protein) (2), which represents the second cause of food allergy in Italian adults (3); however,  $\omega$ -5 gliadin is still considered an important causative agent (2). Furthermore, NSAIDs have been identified as important co-factors in the development of post-prandial anaphylaxis in susceptible individuals (4).

A 73 year old man was admitted to our hospital for the rapid onset of hives, itching, abdominal pain, hypotension (60/40

mmHg) and loss of consciousness about two hours after a meal rich in wheat products and during his daily farm chores. He had a history of valvular heart disease and aortic aneurism. He had suffered three more episodes of shock in the preceding ten years. His therapy consisted of 100 mg of aspirin daily. On admission, complete blood count and tests of liver function, coagulation and kidney function were normal, as were serum levels of electrolytes, cardiac enzymes and the D-dimer test. A CT scan was performed to rule out a hemorrhagic shock due to aortic aneurysm rupture. Echocardiography and an electrocardiogram excluded the possibility of a cardiogenic shock. Symptoms were rapidly relieved by treatment with antihistamines and methylprednisolone. The day following admission, skin tests with commercial extracts (ALK-Abellò, Madrid, Spain and Lofarma Laboratories, Milan, Italy) and serum specific IgE assay - ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) were performed. Allergy skin tests were negative, whereas

the serum specific IgE assay (ImmunoCAP) employed to assess serum food-specific IgE concentrations, showed positive results for wheat, gluten and  $\omega$ -5 gliadin. Other specific molecular targets were negative (**table 1**).

In s-FDEIA, patients develop anaphylaxis after eating a specific food and exercising (2). Over the years, several foods such as wheat, shellfish, tomatoes, peanuts and corn have been implicated in this disorder (5). In European countries, vegetables are the most common food allergens (5). In Italy, LTPs seem to represent the major trigger (2). Wheat is the principal food in Japan (5), but a recent report has shown that  $\omega$ -5 gliadin exerts a certain role even in Italian people (2). Aspirin is a known and important co-factor in promoting the disease (4). Multiple theories have been devised to explain FDEIA. Intestinal permeability increases during exercise, allowing allergenic proteins to have greater access to the gut-associated immune system. Non-steroidal anti-inflammatory drugs and alcohol could favor the development of FDEIA by their ability to further increase intestinal permeability (6). Abnormality in the autonomic system (7), changes in processing specific allergens (8) and alteration in the balance between inflammatory and anti-inflammatory responses mediated by physical activity (9), could also account for the abnormal responses observed in the disease.

The patient examined above experienced an anaphylactic shock after the ingestion of a wheat rich meal, during his daily farm work and after his usual postprandial intake of aspirin.

Despite the lack of data on serum tryptase levels, the clinical characteristics and the serum specific IgE assay (ImmunoCAP) results, together with the exclusion of any other possible causes of shock, led us to make the diagnosis of FDEIA certainly

favoured by aspirin intake. The occurrence of a previous crisis with the same symptoms in similar circumstances supported our hypothesis.

Once discharged, the patient was instructed to avoid wheat meals 3 hours prior to exercise and in order to avoid the coexistence of an additional trigger, to interrupt his aspirin therapy after consulting with a cardiologist. No more episodes of shock have occurred in this patient in the last two years.

## References

1. Morita E, Kunie K, Matsuo H. Food-dependent exercise-induced anaphylaxis. *J Dermatol Sci*. 2007Aug;47(2):109-17.
2. Romano A., Scala E., Rumi G., Gaeta F. et al. Lipid transfer proteins: the most frequent sensitizer in Italian subjects with food-dependent exercise-induced anaphylaxis. *Clinical & Experimental Allergy*. 2012;42:1643-53.
3. Asero R, Antonicelli L, Arena A, Bommarito L, Caruso B et al. EpidemAAITO: features of food allergy in Italian adults attending allergy clinics: a multi-centre study. *Clin Exp Allergy*. 2009Apr;39(4):547-55.
4. Fujii H, Kambe N, Fujisawa A, Kohno K, Morita E, Miyachi Y. Food-dependent exercise-induced anaphylaxis induced by low dose aspirin therapy. *Allergol Int*. 2008Mar;57(1):97-8.
5. Morita E, Matsuo H, Chinuki Y, Takahashi H, Dahlström J, Tanaka A. Food-dependent exercise-induced anaphylaxis - importance of omega-5 gliadin and HMW-glutenin as causative antigens for wheat-dependent exercise-induced anaphylaxis. *Allergol Int*. 2009Dec;58(4):493-8.
6. Heyman M. Gut barrier dysfunction in food allergy. *Eur J Gastroenterol Hepatol*. 2005Dec;17(12):1279-85.
7. Fukutomi O, Kondo N, Agata H, et al. Abnormal responses of the autonomic nervous system in food-dependent exercise-induced anaphylaxis. *Ann Allergy*. 1992May;68(5):438-45.
8. Palosuo K, Varjonen E, Nurkkala J, Kalkkinen N, Harvima R, Reunala T. Transglutaminase-mediated cross-linking of a peptic fraction of omega-5 gliadin enhances IgE reactivity in wheat-dependent, exercise-induced anaphylaxis. *J Allergy Clin Immunol*. 2003Jun;111(6):1386-92.
9. Cooper DM, Radom-Aizik S, Schwindt C, Zaldivar F Jr. Dangerous exercise: lessons learned from dysregulated inflammatory responses to physical activity. *J Appl Physiol*. 2007Aug;103(2):700-9.

**Table 1** - ImmunoCAP Specific IgE Blood Test (KU/L)

rTri a 19 ( $\omega$ -5 gliadin)	52.40
rPru p 3 (LTP)	0.03
nGal d 1 (Ovomucoid)	0.01
nAna c 2 (Bromelin)	0.09
nAsp o 1 (a-amylase)	0.03
Anisakis	0.95
Milk	0.03
Egg	0.02
Wheat	9.10
Corn	0.15
Gluten	13.30
Maize egg	0.04
Yeast	0.05