

## References

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## Cow's milk dependent exercise-induced urticaria after oral tolerance induction in an adolescent

To the Editor,

Exercise-induced urticaria (EIU) is a clinical syndrome in which urticaria occurs in association with exercise.<sup>1</sup> EIU may occur independently of food or may require the ingestion of a food allergen prior to exercise, in a process of food dependent exercise-induced urticaria (FDEIU).

During oral tolerance induction (OTI) to cow's milk (CM) in allergic children, many factors have been pointed out as being responsible for a higher risk of allergic reactions with CM doses previously tolerated, being exercise the most common one.<sup>2</sup> However, prospective data concerning this subject after ending OTI are still lacking.

We report the case of a 16-year-old male, referred to our Immunoallergy department in 2002, at the age of eight years, reporting an IgE-mediated cow's milk allergy (CMA) diagnosed at four months of age following an episode of anaphylaxis. Since then he began strict allergen avoidance, although he has experienced four anaphylactic reactions by accidental ingestion of hidden CM. He also reported intermittent asthma and persistent rhinitis plus family history of atopy.

Skin prick tests (SPT) were positive to grass pollens, whole CM, casein,  $\alpha$ -lactoalbumin and  $\beta$ -lactoglobulin (Laboratorios Leti, Madrid, Spain). Total IgE was 262kU/L and sIgE to whole CM 47kU/L, casein 51 kU/L,  $\alpha$ -lactoalbumin 9 kU/L and  $\beta$ -lactoglobulin 2 kU/L, and increased throughout the years, reaching 350 kU/L to whole CM in 2005 (Phadia, Uppsala, Sweden). Oral food challenges were regularly

performed to evaluate tolerance, and consecutively caused anaphylaxis; the last one, at 11 year-old, was positive with 10 mL. Because of this persistency, we decided to start OTI at that age. He was successfully submitted to an eight-week protocol, reaching a daily dose of 200 mL, which allowed a free diet. He was advised to maintain CM ingestion daily, after a meal, and to avoid vigorous exercise in the two subsequent hours. Although he is an athlete, he strictly respected these indications. A few months after OTI, however, he presents reproducible episodes of EIU when the exercise was unplanned and CM ingestion had occurred within the two previous hours. Episodes resolved with anti-histamine and oral corticosteroid. He has no other episodes of urticaria or other symptoms with CM. sIgE to whole CM in 2010 was 2kU/L, to casein 2.5kU/L and the remaining were negative.

CM OTI is an increasingly attractive strategy, and success has been achieved with several different protocols.<sup>2</sup> Long term follow-up is not available since this is a recent procedure, but data point to be generally well-tolerated and safe.<sup>3</sup>

In EIU food can act as a co-trigger; wheat is most commonly reported, but other foods can be implicated.<sup>3</sup> It is hypothesised that in these patients, food-sensitised immune cells are relatively innocuous until they are redistributed into the systemic circulation from gut-associated deposits during exertion,<sup>4</sup> which is probably what occurs with our patient. Similarly, Caminiti et al. described a case of food dependent exercise-induced anaphylaxis in a child successfully desensitised to CM, however he was submitted to a longer OTI protocol of 180 days<sup>5</sup>; although more severe, his episodes were easier to control by his parents, because exercise was planned. We could speculate if this side-effect (anaphylaxis) more severe than just urticaria could be due to different protocols used.

This is the first time, to our knowledge, that FDEIU is described in an adolescent as a side-effect of successful CM OTI, in which episodes are difficult to control because of his age and the unplanned way that exercise occurs. This case report strengthens the fact that the persistency of this CM tolerance is not yet known, and that external factors may be responsible for its breakdown, despite specific IgE decrease.

### Conflict of interests

The authors have no conflict of interest to declare.

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