

Exercise-induced anaphylaxis after consumption of red meat in a patient with IgE antibodies specific for galactose-alpha-1,3-galactose

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Clinical Implications

- Testing for alpha-gal antibodies in patients with exercise-induced anaphylaxis should be considered even if the patient has not exhibited symptoms at times not associated with exercise.

TO THE EDITOR:

In 2009, Commins and Platts-Mills¹ reported a “novel form of delayed anaphylaxis to red meat” related to serum IgE antibodies to the oligosaccharide galactose-alpha 1,3-galactose (alpha-gal) caused by a tick bite from the lone star tick, *Amblyomma americanum*. It is now recognized that IgE antibody to alpha-gal is common in the southeastern United States and is associated with 2 forms of anaphylaxis: immediate-onset anaphylaxis during first exposure to intravenous cetuximab and delayed-onset anaphylaxis after ingestion of mammalian meat.^{2,3} This information has added a new aspect to the care of patients who might otherwise have been diagnosed with idiopathic anaphylaxis, which can be quite frustrating for patients and clinicians alike. In cases of mammalian meat allergy due to alpha-gal, we are now able to provide patients with the answer to the frequently asked question, “What can I do to prevent these reactions?” Not only can we provide them with a diagnosis, but in so doing we improve their quality of life and provide them with the knowledge of what to avoid to prevent these potentially life-threatening reactions.

Although more cases have been recognized and diagnosed since the initial report of anaphylaxis to mammalian meat due to alpha-gal, there are multiple factors that can prevent or delay diagnosis. As Tripathi et al³ noted, “the lack of enthusiasm for this syndrome could be easily understood because its features run counter to many established teachings about food allergy and anaphylaxis.” It is taught that food allergy reactions typically begin within 1 to 2 hours of consumption of the offending food and with every ingestion. However, in alpha-gal–induced mammal meat allergy, the reaction is delayed, and in most cases occurs 3 to 6 hours after consuming beef, pork, venison, or lamb.¹ Many patients do not have positive skin prick test results to meat extracts. Therefore, intradermal testing to meat is now being done.^{4,5} Patients also may be unaware of or fail to recall previous tick bites. In addition, patients may not experience reactions with every ingestion of mammalian meat, which may be due to the type, processing, dose, and/or preparation of the mammalian meat product.⁶ It should be noted that the severity of reactions may worsen over time with continued tick bites.^{3,6} The most commonly reported symptom was itching.⁴

To add to the growing body of knowledge regarding mammalian meat allergy due to alpha-gal, we are presenting a novel case of exercise-induced anaphylaxis (EIA) after ingestion of red meat in a patient with IgE antibodies to alpha-gal. In this case, the reactions also occurred more rapidly than typical alpha-gal reactions, happening in 1 to 1½ hours instead of 3 to 6 hours.

CASE REPORT

Ms L, a 22-year-old white female, presented to our clinic in Huntsville, Alabama, in December 2013 with a history of 2 episodes while running that were consistent with allergic reactions. Before each event she had eaten Campbell’s Healthy Request Italian Wedding Soup and gone for a run. About 30 minutes after eating, she embarked on a 6-mile run. After 3 miles, approximately 1 hour after eating, she developed nondescript feelings of unease but kept running. By the end of the run, she had hives and swollen lips. She took Benadryl and her symptoms resolved. The following week she ate the same soup 1 hour before running. At the 3-mile mark, approximately 1½ hours after eating, she developed hives and swelling. She stopped to call her father, felt progressively worse, and called 911 for transport to the emergency department. Her symptoms at the time included itching so severe that she could not think about anything else, stomach cramps, and headache. Before diagnosis Ms L tolerated the same soup in the absence of exercise. This raises the question of the role of exercise in potentiating or serving as a cofactor⁵ for the development of anaphylaxis reactions to alpha-gal in select patients, as with wheat-dependent exercise-induced anaphylaxis. There is also data that alcohol can increase the likelihood of reactions to red meat and wheat.^{5,7} She denied being stung by any venomous insects at the time, and she stated that she “probably” had tick bites in the past. It is interesting to note that there is a family history of alpha-gal in her father. Although the familial tendency for EIA has been reported in the literature, there have been no reports of familial tendency for mammalian meat allergy due to alpha-gal of which we are currently aware.

Physical examination was unremarkable. Laboratory findings demonstrated galactose-alpha-1, 3-galactose IgE level of 15.80 kU/L, IgE level of 153 IU/mL (<100 IU/mL), and anti-IgE receptor antibody level of 3.1% (0.0%-5.0 %). Trypsinase was drawn at the time of her first visit, 3 days after her emergency department admission, to screen for mastocytosis, and was 3.1 ng/mL (<11.5). Skin prick testing with positive and negative controls using commercial extracts showed no significant reactivity to a panel of 79 foods, including beef and pork, which produced wheal responses of 2 mm. Skin prick testing with commercial extracts often produce negative results and is insufficient for diagnosis. Skin prick tests and intradermal testing using fresh meat extracts are an alternative testing method that may yield more diagnostic value.^{4,5}

Ms L was advised to avoid mammalian meat on the basis of laboratory findings. She started carrying epinephrine auto-injectors with her during exercise and stopped running alone as

recommended. Of note, she is a long distance road and trail runner. She participates in 50K trail runs that take about 5 hours to complete and eats 3 times/hour during these runs. She gradually increased her running distance, while avoiding eating within 4 hours of exercise, and then slowly added foods during her run. Ms L has continued to avoid all mammalian meat products and has successfully completed long runs using other sources of nutrition.

CONCLUSIONS

In conclusion, Ms L's case adds to the growing body of knowledge of alpha-gal allergy, as a novel aspect to this only recently described condition. As alpha-gal allergy joins the list of differential diagnoses for anaphylaxis, it should also be considered in the event of exercise-related anaphylaxis. Clinicians need to simply include IgE to galactose- α -1,3-galactose on laboratory evaluation. An elevated level in conjunction with a suspected allergic reaction is sufficient for a preliminary diagnosis. Patient history of previous tick bites should be documented. Patient education of those with suspected or confirmed red meat EIA should include keeping epinephrine autoinjectors immediately available during exercise, wearing a medical alert, avoiding exercise alone or in unpopulated areas, and avoiding nonsteroidal anti-inflammatory drugs before exercise. It is known that aspirin and nonsteroidal anti-inflammatory drugs increase gut permeability, and therefore thought to potentiate food allergy absorption, resulting in an increase in the severity of anaphylaxis or lower physical exertion required to elicit a reaction.⁸

This newly recognized aspect of alpha-gal allergy—its ability to potentiate EIA—lends urgency to the importance of its identification and appropriate therapeutic intervention as crucial steps in the prevention of casualty.

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