Food-dependent exercise-induced anaphylaxis

Bryanne Minty MD CCFP

Exercise-induced anaphylaxis (EIA) is a rare disorder in which individuals develop immunoglobulin E (IgE)–mediated hypersensitivity in conjunction with exercise, causing anaphylaxis. The lifetime prevalence of EIA is about 0.05%. About 30% to 50% of EIA is food dependent, only occurring with the combination of a specific food and exercise.[1-5] In these patients exercise or food on their own do not cause anaphylaxis; only in combination do they trigger the reaction. The case presented here describes a rare life-threatening diagnosis in a previously well 22-year-old female jogger. Results of standard allergy testing were noncontributory. This case is unique because there are likely multiple triggers that in combination with exercise contribute to the patient developing the anaphylactic reactions. Diagnosis is made by a careful history and an awareness of the combination of food triggers and EIA. Prevention includes avoidance of the combined potential triggers and carrying an epinephrine autoinjector.

Case

A female patient presented after anaphylactic reactions at the ages of 19 and 22 years with unidentified triggers while jogging. The first event occurred in the spring after eating a salad with scallops and shrimp. She reported abdominal cramping within 5 minutes of starting her jog, then within 30 minutes she developed nausea, facial swelling, diffuse pruritus, and difficulty breathing. A passer-by called an ambulance and the patient lost consciousness. On presentation at the emergency department she had profound hypotension and bradycardia. Emergency treatment included epinephrine, intravenous fluids, steroids, antihistamines, and H_2 antagonists. Epicutaneous testing several weeks later revealed a positive reaction to dust mites and mild reactions to spring tree pollen, banana, avocado, and tomato; she did not react to any shellfish, including shrimp and scallops.

The second event occurred while exercising, again in the spring season, after eating curry with vegetables, shrimp, and white fish. She had been jogging for 45 minutes when she developed facial swelling and hives. In the emergency department she also had an episode of emesis and again was profoundly hypotensive. Subsequent repeat allergy testing showed positive reactions to dust mites, cats, birch, maple, rats, oak, elm, and grass. The foods she was tested for that resulted in negative reactions included the most common food triggers: egg, wheat, fish, shrimp, and peanuts. Also, at this time she had a pet rat in her house.

Discussion

To assess the literature MEDLINE was searched from 2000 to 2015 using the MeSH terms *exercise* and *food hypersensitivity* and *anaphylaxis*, identifying 134 articles.

Many different types of foods have been shown to cause food-dependent exercise-induced anaphylaxis (FDEIA), including wheat, shellfish, nuts, tomatoes, peanuts, fish, pork, beef, mushrooms, hazelnuts, eggs, peaches, apples, milk, and alcohol.[1,2] There are also reports in which the ingestion of 2 foods together along with exercise are required to trigger a reaction.[1] Nonfood combination triggers reported include medication (nonsteroidal anti-inflammatory drugs), cold or warm temperatures, menstrual cycle, pollens, and ingestion of dust mites.[1,2] Interestingly, these nonfood triggers are usually cofactors that appear to enhance the anaphylactic reaction but that do not cause the reaction on their own.

EDITOR'S KEY POINTS

- Food-dependent exercise-induced anaphylaxis is rare, and findings of allergy testing might be negative. Particular food triggers are benign unless combined with exercise.
- Prevention involves avoiding the combination of the trigger food and exercise, allowing 4 to 6 hours for digestion of the known trigger food before exercise, and carrying an epinephrine autoinjector during exercise. Treatment includes immediate intramuscular epinephrine injection and emergency department assessment.

POINTS DE REPÈRE DU RÉDACTEUR

- L'anaphylaxie de source alimentaire déclenchée par l'exercice est rare, et les résultats des tests d'allergie pourraient être négatifs. Certains déclencheurs alimentaires sont bénins, à moins d'être combinés à des activités physiques.
- Pour la prévenir, il s'agit d'éviter la combinaison de l'aliment inducteur et de l'exercice, d'attendre 4 à 6 heures pour que soit digéré l'aliment déclencheur connu avant de faire de l'exercice et de se munir d'un auto-injecteur d'épinéphrine pendant l'activité physique. Le traitement comporte une injection intramusculaire immédiate d'épinéphrine, suivie d'une évaluation à l'urgence.

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There is no definite evidence for what mechanisms trigger the allergic reaction, but several proposed mechanisms might help to explain FDEIA. One of the proposed theories is that IgE cross-links with a specific food allergen and, when combined with exercise, it lowers the threshold for mast cell degranulation, histamine and vasoactive mediators are released, and this in turn leads to anaphylaxis.[2,4] Two other proposed mechanisms include changes in pH that might be a trigger for FDEIA[1] and that exercise increases blood flow to muscle, while decreasing circulation to gut mucosa, thus exposing more muscle tissue mast cells to the allergen.[1,4] The reaction usually occurs within the first 30 minutes of starting physical activity.[1] Symptoms include pruritus, cough, chest tightness, angioedema, urticaria, wheezing, and gastrointestinal complaints.[1]

Treatment of EIA and FDEIA involves the same emergent care as for other causes of anaphylaxis (epinephrine, antihistamines, H_1 and H_2 blockers, inhaled bronchodilators, and steroids as needed). Any patient who has self-administered epinephrine should still seek immediate medical care for further monitoring and treatment, as the anaphylactic reaction might have ongoing life-threatening effects.[2] Further preventive treatment of FDEIA involves avoidance of exercise for 4 to 6 hours after ingesting the known food trigger, carrying an epinephrine autoinjector during exercise, lowering the intensity of exercise, and avoiding exercise in extreme weather conditions such as hot and humid or cold temperatures.[4] Taking medications such as antihistamines or H_2 blockers before exercise is still a controversial topic, as there is currently inadequate evidence to support prophylactic treatment.[2,5] A case study described a successful trial of prophylactic omalizumab in a 14-year-old boy with refractory FDEIA. This relatively new recombinant DNA monoclonal antibody, which binds to IgE and mutes its activity in type I allergic reactions, was taken before exercise and reduced this patient's anaphylactic reactions.[6] Another case study in a 47-year-old Japanese man showed administration of misoprostol (a prostaglandin E_1 analogue) before exercise decreased his wheat-dependent anaphylactic reactions, perhaps owing to upregulation of gastrointestinal breakdown of allergic particles.[7]

Conclusion

The patient in this case is a young woman with FDEIA with an unknown trigger. Treating physicians presumed a combination of spring pollen, seafood, and exercise to be the trigger. She has since avoided any exercise for a minimum of 4 to 6 hours after consuming any fish or seafood. As the reactions occurred with both finned fish and shellfish, she was advised to avoid both possible triggers before exercise. She has not had any further anaphylactic reactions and she carries an epinephrine autoinjector while exercising. If she develops recurrent reactions, it might be reasonable to consider prophylactic exercise treatments such as omalizumab or misoprostol for this rare condition.[6,7]

Dr Minty is a staff physician at the Sioux Lookout Meno Ya Win Health Centre and undertook this report while a resident in family medicine at the Northern Ontario School of Medicine in Sioux Lookout.

Competing interests
None declared

Correspondence
Dr Bryanne Minty; e-mail **brminty@nosm.ca**

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