

individuals mediated by Th2 cells, leading to migration of eosinophils to the esophageal mucosa and their activation leading to secretion of proinflammatory mediators, which causes an inflammatory response, muscular contractions, and fibrosis that results in esophageal dysfunction.^{4,5} On the contrary, IBD is considered to be multifactorial, with genetic susceptibility, environmental triggers, gut microbiome, and immune responses interacting with each other to give different phenotypes of IBD.⁶

Despite these differences, there are certain similarities in these 2 conditions that need to be emphasized. First, both conditions have demonstrated genetic predisposition as evidenced of familial clustering and genetic variations.^{7,8} Second, both the conditions have increased the risk of developing other autoimmune conditions, including celiac disease, hypothyroidism, type 1 diabetes mellitus, asthma, and sarcoidosis.^{7,9} Other similarities pertain to their increasing rates of incidence, natural history, effect on quality of life, and possible utility of dietary therapy for treatment.¹⁰ These 2 conditions have been suggested to represent a spectrum of immune-mediated disease because there seems to be an overlap in immune mechanisms among the 2, such as overexpression of interleukin 13.¹

Eosinophilia in the gastrointestinal tract is common in IBD, and the number of eosinophils is dependent on the disease activity.¹¹ Hence, the presence of active IBD (especially Crohn disease) needs to be considered in any patient with increased eosinophils in the esophagus and a history of IBD. Moreover, esophageal eosinophilia in IBD could also be attributable to reflux or concomitant EoE. Recent studies report that patients with coexistent IBD and EoE have a more complicated course, including IBD-related complications, poor response to infliximab, and worse nutritional outcomes.² Given these differences in natural course and treatment options, it is important to determine the cause of esophageal eosinophilia in IBD. Upper endoscopies in all our patients demonstrated characteristic findings diagnostic of EoE, suggesting a coexistence of EoE and IBD.

This report emphasizes that the possibility of concurrent EoE and IBD needs to be considered by physicians, especially when eosinophilia in patients with IBD is isolated to the esophagus and in the presence of other histologic features of EoE. This consideration will help in early diagnosis and appropriate treatment of these patients and in better understanding of the interactions between

these 2 conditions. Further larger studies need to be conducted to determine the association between these 2 conditions.

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Food-dependent exercise-induced anaphylaxis with sensitization to tomato

Diagnostic approach involving food-exercise challenge

Food-dependent exercise-induced anaphylaxis (FDEIA) is characterized by anaphylaxis that occurs during or shortly after exercise following ingestion of specific foods to which a patient is sensitized. Exercise and food are independently well tolerated.¹ Described mostly in adolescents and young adults, FDEIA has an estimated 0.02% prevalence, and several trigger foods have been reported.^{1–3} We describe a case in which tomato was found to be the culprit food and the diagnostic approach used.

A 15-year-old man with a history of allergic rhinitis was evaluated after 3 episodes of anaphylaxis associated with exercise in a 2-month period. He denied chronic urticaria and use of alcohol and

nonsteroidal anti-inflammatory drugs (NSAIDs). Episode 1 consisted of generalized urticaria that progressed to angioedema of the eyelids and lightheadedness in less than 2 minutes that occurred approximately 1 hour after eating dinner and within 10 minutes of jogging. Symptoms resolved 1 hour after the patient self-treated with diphenhydramine and famotidine. Episode 2 occurred 2 weeks later when the patient noticed urticaria on his torso, rhinorrhea, and nausea after jogging 2 miles after having eaten 2 hours earlier. Symptom resolution occurred after self-medicating with oral diphenhydramine. Episode 3 was, according to the patient, the most severe and burdensome. Eight hours after eating and after running 50 to 75 yards, he developed generalized urticaria, rhinorrhea, eyelid angioedema, and itchiness and foreign-body sensation of the throat. He took oral diphenhydramine and



Table 1
Diagnostic Tests Performed and Results

Diagnostic procedure	Results
Skin prick (CE or P+P)/specific	
IgE tests	
Barley	Negative (P+P)/negative
Buckwheat	Negative (P+P)/negative
Egg white	Negative (CE and P+P)/negative
Green pea	Negative (P+P)/negative
Hop fruit	Negative (P+P)/negative
Cow's milk	Negative (CE and P+P)/negative
Oat	Negative (P+P)/negative
Ovalbumin	Negative (CE)/negative
Peanut	Negative (CE and P+P)/negative
Rice	Negative (CE and P+P)/negative
Rye	Negative (P+P)/negative
Tomato	Positive (CE and P+P)/negative
Wheat	Negative (CE and P+P)/negative
Tryptase levels, ng/mL	
Baseline	2.4 (reference, <11.5)
Acute during third episode	10.4 (reference, <11.5)
Challenges	
Exercise challenge ^a	Negative after >20 min of standard Bruce protocol
Exercise-food challenge ^b	Positive after 5 min of standard Bruce protocol

CE, commercial extract; P+P, prick to prick.

^aPerformed after 5-day avoidance of antihistamines, a tomato-free diet of 24 hours, and 8-hour fasting.^bPerformed after 5-day avoidance of antihistamines And avoidance of all foods except for tomatoes, water, and a vegetable-based, wheat-free pasta for 24 hours. Ate fresh tomatoes 4 hours and tomato marinara sauce 10 hours before exercise-food challenge.

sought medical attention at the emergency department. Approximately 45 minutes after symptom onset, when he got to the emergency department, he was asymptomatic. A tryptase sample was drawn, and after 6 hours, during which he remained symptom free, he was discharged.

Anamnesis revealed a wide variety of potential triggers, including egg, dairy, cereals, fruits, vegetables, and legumes. The results of all skin tests to available commercial food extracts were negative except for tomato. However, given the amount of likely culprit foods and the lack of some commercial extracts and to standardize our approach, we decided to try prick-to-prick (P+P) with fresh produces to elucidate a better candidate food for a challenge. Tomato was the only food that tested positive in P+P tests. All serum specific IgE test results were negative. The diagnostic tests and their results are given in Table 1.

After the patient provided informed consent, we performed an exercise challenge (EC) and an exercise-food challenge (EFC) with tomato (Table 1) using the standard Bruce protocol.⁴ During the EC, the patient denied any symptoms after 20 minutes of the standard Bruce protocol at a peak velocity of 10.2 km/h with a 15% inclination of the treadmill. Physical examination findings were unremarkable, without any signs of urticaria, angioedema, or wheezing. Vital signs were stable at a heart rate of 146/min, a blood pressure of 116/78 mm Hg, and pulse oximetry of 99%.

Two weeks after EC, we performed the EFC using processed marinara sauce, which the patient mixed with a vegetable-based, wheat-free pasta and raw tomatoes while considering that potential allergens, such as proteins, might be better preserved in the raw form of the food. We instructed the patient to take 60 mL of marinara sauce before bed without any other foods except water, and raw tomato (approximately 150 g) 4 hours before the EFC with no food intake between the 2 meals. Alcohol and NSAIDs have been described as augmenting factors¹; however, because the patient denied use of either, we did not use aspirin, alcohol, or any other enhancers. Five minutes into the EFC, at 6 km/h with a 5%

inclination of the treadmill, the patient denied being extenuated from the exercise, and vital signs were stable at a heart rate of 127/min, blood pressure of 104/74 mm Hg, and pulse oximetry of 99%, but he reported nasal congestion and developed rhinorrhea and urticaria on all 4 extremities. The procedure was stopped immediately, and symptoms resolved 10 minutes after administration of 0.3 mg of intramuscular epinephrine and 50 mg of intramuscular diphenhydramine.

On the basis of the skin test results, the negative EC results, and the positive EFC results, the patient was diagnosed with tomato-dependent FDEIA. We invited the patient to participate in the medical decision making. The patient had expressed his wishes to continue exercising routinely and his concerns regarding presenting new episodes. We had an open discussion with him and his parents to provide some reassurance regarding the unlikelihood of presenting an episode without the combination of tomato and exercise. An important part of the discussion centered on encouraging his will to continue exercising as long as he avoids tomatoes 6 to 8 hours before working out and does so while carrying an epinephrine autoinjector on which we educated him and his parents. We also discussed allergy emergency action plans and the importance of exercising alongside people familiarized with his condition and the epinephrine autoinjector use.

This case shows FDEIA as a rare condition, but its real prevalence may be underestimated because of the lack of standardized diagnostic tools, such as EC and EFC. FDEIA has been described as a food allergy, with exercise as the most important of several possible augmenting factors, including NSAIDs, alcohol, menses, and infections.¹ It has been suggested that these factors may increase gastrointestinal permeability, thereby increasing allergen absorption, and decrease the activation threshold of mast cells and basophils.^{1,5} None of these theories has been proven.

Meticulous anamnesis and allergy testing are needed to diagnose FDEIA, and they should aim to determine the following^{1,6,7}: (1) anaphylaxis occurs with exertion only when food ingestion preceded exercise, (2) food and exercise are each tolerated independently, (3) sensitization to the culprit food is demonstrable by skin testing or specific serum IgE testing, and (4) no alternative diagnoses explain the condition.

Food sensitization should be demonstrated by skin testing with commercial extracts or IgE immunoassays if available.^{1,6} P+P tests with fresh food are suggested by current practice parameters as a good method for fruits and vegetables and can be helpful when commercial extracts are unavailable and there is reasonable suspicion about a probable trigger.⁸ Skin testing for possible triggers could help reducing the number of challenges needed. This was the case for our patient, who had eaten a vast array of potential allergens before exercise but only tomato tested positive on skin testing, which is why we chose this food for an EFC. Patients with respiratory allergic disease could benefit from skin tests to environmental allergens because these patients may be more susceptible to attacks during pollen season and there have been reports of cross-reactivity and primary sensitizations to pollen allergens, such as profilin.⁹ These patients could consider avoiding exercise under poor environmental conditions, discussing this association with their physician. Regarding diagnosis, a positive EFC result confirms FDEIA. However, the time-frame from culprit food ingestion to stress test and amount of food needed to ingest are unclear; thus, a negative EFC result does not exclude FDEIA.^{6,10} Moreover, these factors might vary among foods and patients. EFCs are not without risk and should be performed by experienced specialists in an adequate environment equipped to identify and treat potential serious reactions.¹⁰

No pharmacotherapy has been proven to work prophylactically; therefore, FDEIA management focuses on avoiding culprit food(s) and other identified augmenting factors 4 to 6 hours before exercise.¹ Another essential part of management should center on patients' will to exercise and their education regarding the use of epinephrine autoinjector and allergy emergency action plans. Future larger studies could help understanding FDEIA and developing diagnostic tools.

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