

Food-Dependent Exercise-Induced Anaphylaxis

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Abstract

INTRODUCTION

Food-dependent exercise induced anaphylaxis (FDEIA) is a form of food allergy induced by exercise. Symptoms can include urticaria/angioedema, respiratory and gastrointestinal manifestations and hypotension/shock. The precise pathophysiology of this rare syndrome is poorly understood.

CASE REPORT

A 61-year-old male patient visiting New York City from North Carolina presented to the St. Vincent's Catholic Medical Center emergency department brought by ambulance. He was admitted after an episode of hives, hypotension and loss of consciousness. After fluid resuscitation and administration of epinephrine, he resumed consciousness and was able to provide a detailed history. He described a wheat allergy that usually presented with hives and had only presented as an adult. The patient appeared to be overweight and somewhat de-conditioned.

He described having a tuna salad sandwich on bread for lunch and proceeding to walk around the city with friends. He has had this exact sandwich many times without any reaction on the skin, or otherwise. The patient began to feel weak, took 180 mg fexofenadine and then lost consciousness. He was brought to the hospital by ambulance.

On admission, the patient described several similar episodes beginning about five years prior in which the patient consumed a slice of pizza and then a biscuit. After that, he had a skin reaction involving hives. The next episode was about 3 years ago, when the patient was visiting New Hampshire. He again ate a slice of pizza, but then proceeded to walk about a mile to his destination. When he arrived, he began to "itch and break-out" on his skin and then his vision became "whited out". He briefly lost consciousness, and felt ill for a few days thereafter.

His laboratory values showed an ImmunocapTM class 1 sensitivity to wheat on specific IgE testing. There was no elevation of tryptase, which was drawn more than 12 hours after admission, and all his other laboratory test values were normal.

The patient was discharged with a prescription for an epinephrine injector, after education on use and indications. He was also advised to avoid wheat containing products for several hours prior to exertion. He was referred to online resources for assistance and further education regarding avoiding wheat-containing products.

DISCUSSION

Exercise induced anaphylaxis (EIA) reports over the past decade have highlighted several important clinical associations. First, EIA is commonly associated with preceding food ingestion and in that case is often called food dependent exercise induced anaphylaxis (FDEIA). In this case, the patient had elevated specific IgE to wheat, and had eaten wheat prior to mild exercise.

Although the precise pathophysiology of this rare syndrome is poorly understood, Cooper et al¹ have proposed that there can be exercise induced modification of previously activated lymphocytes. These sensitized lymphocytes are innocuous when in the gut, but enter the circulation as a result of exercise-associated redistribution of blood flow, and can interact with other immune cells such as basophils and mast cells, which then release a host of cytokines and can lead to systemic anaphylaxis¹.

This syndrome presents several challenges to the clinician: Affected patients may have no symptoms upon exposure to the associated food outside of the context of exercise, and while positive food allergy tests may be observed, gastric distention due to any food ingestion is thought to play a role

in certain patients². Thus an absence of positive food allergy tests, should not prompt the physician to give patient assurances that food ingestion prior to exercise is safe. Secondly the common foods involved may differ in different countries. For example in Japan, the main provocative foods are crustaceans and soybean, whereas in the Western countries celery, wheat, and legumes are the most common, and in Italy, tomato may be a common provocative food². This pattern may more relate to the dietary patterns of different countries. Thirdly, cofactors may be involved in exacerbating FIEIA. Both alcohol and aspirin are examples of this³. Some cases of exercise induced anaphylaxis appear to only occur during cold weather, which suggests environmental factors are involved in certain cases and with co-existing cholinergic urticaria, hot weather is usually more associated with systemic responses.⁴ Fourthly, serum tryptase levels are commonly normal as they were in this patient. Plasma histamine levels may be more useful during the acute event. This situation is similar to that reported in non-exercise associated food anaphylaxis. Finally, the threshold for the degree of exercise provoking the reaction is quite variable⁴. When the threshold is low as in this deconditioned patient, the clinical syndrome may be mistakenly diagnosed as idiopathic anaphylaxis. When the threshold is high or requires other cofactors, monitored exercise challenge may be unable to reproduce symptoms⁵.

Treatment of FDEIA is primarily preventative with the usual recommendations of not eating at least 4-6 hours prior to exercise, and avoiding other known co-triggers⁶. Portable epinephrine and carrying oral antihistamines is also advised. While oral antihistamines taken prophylactically are often inadequate, there have been case reports of successfully using oral cromolyn with antihistamines⁷. Bicarbonate has also been recommended by some authors⁸. In accessing a prophylactic treatment regimen, formal exercise testing in a monitored setting can be useful in identifying the clinical signs consistent with anaphylaxis, but also to discern the type and intensity of exercise that provokes symptoms and to collect plasma before and after/during exercise to measure histamine especially when clinical endpoints are not reached. Although we have not seen any reports of the effects of anti-IgE therapy in FDEIA, in the presence of specific IgE, this would seem to be a potential clinical situation for the use of this medication as a prophylactic (albeit expensive) agent.

FDEIA can be confused with cholinergic urticaria and exercise induced asthma. Cholinergic urticaria can be viewed as another form of physical urticaria. As described in

the literature, different types of physical and non-physical urticaria may co-exist in the same patient. There has been at least one report of a patient who has had both documented cholinergic urticaria and non-cholinergic exercise induced asthma⁹. One characteristic of exercise induced asthma is that serial exercise challenges result in progressively less bronchospasm, the so called "refractory period." This suggests one possible approach to exercise induced anaphylaxis. Progressively higher exertions separated by rests could hypothetically induce tolerance to exercise which might otherwise be provocative if no rest periods were provided. To our knowledge this hypothetical approach has not been studied. It is also conceivable that plasma histamine levels could be monitored as clinical surrogates in this type of challenge procedure, thus aiding the interpretation of the test in the absence of anaphylaxis signs and symptoms

CONCLUSION

The patient's symptoms are consistent with the cutaneous and hypotensive manifestations of FDEIA. FDEIA is a potentially serious syndrome that presents many challenges to the clinician, requires a high index of suspicion and prompt and appropriate treatment. Wheat and other foods are often a trigger. The affected patient needs to be educated on how to avoid future reactions. The precise mechanisms involved in FDEIA are currently under investigation.

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