

Recognizing and managing food-dependent exercise-induced anaphylaxis

Introduction

Food-dependent exercise-induced anaphylaxis is a rare allergy syndrome affecting approximately 0.017% of the population (Aihara, 2007). Food-dependent exercise-induced anaphylaxis is characterized by anaphylaxis to food allergens in the context of specific co-factors such as exercise, alcohol or non-steroidal anti-inflammatory drugs. A characteristic feature of this condition is that exposure to food allergens in the absence of co-factors is often tolerated. This article presents a case of food-dependent exercise-induced anaphylaxis to highlight the key diagnostic and therapeutic challenges and promote awareness of this rare condition among hospital doctors.

Discussion

Food-dependent exercise-induced anaphylaxis was originally described as a delayed allergic reaction to shellfish following strenuous exercise (Maulitz et al, 1979). It is now attributed to a wide range of food allergens, including wheat, shellfish, corn, peanuts and tomatoes. Several augmentation or co-factors have been implicated in lowering the threshold dose of allergen required to trigger anaphylaxis (Wölbing et al, 2013), most notably exercise, alcohol and non-steroidal anti-inflammatory drugs.

The role of these co-factors in promoting anaphylaxis in food-dependent exercise-induced anaphylaxis is not entirely clear, but several models have been proposed. One theory argues that blood is diverted from the gut during exercise, causing relative ischaemia which increases gut permeability and thus the delivery of food allergens into the circulation (Matsuo et al, 2005). Palosuo et al (2003) proposed that exercise activates the gut enzyme tissue transglutaminase which aggregates with omega-5-gliadin to form a high molecular weight complex that binds to immunoglobulin E with high affinity. Finally, exercise-associated changes in blood pH and osmolality could directly reduce the threshold for mast cell and basophil degranulation (Cooper et al, 2007).

The diagnosis of food-dependent exercise-induced anaphylaxis is largely clinical, based on the recognition of systemic anaphylaxis following exposure to a particular food allergen in association with specific co-factors. It is important to know that food and exercise are independently tolerated. The clinical features of anaphylaxis including urticaria, angioedema, breathing difficulties and collapse each have a wide differential diagnosis, and a diagnosis of 'allergic reaction' made in the emergency department is frequently revised in clinic. For example, urticaria may be spontaneous (often having an autoimmune aetiology), physical (resulting from mast cell degranulation in response to physical stimuli), drug-induced in a non-specific manner or associated with

CASE REPORT

A 40-year-old man presented to the emergency department having rapidly developed generalized urticaria, blurred vision and collapse during a 30-minute run. Sixty minutes before these symptoms he had eaten a pain aux raisins pastry (verified ingredients: egg, butter, wheat flour, sugar and raisins). He was successfully resuscitated and discharged.

The patient was subsequently seen in allergy outpatients, where he reported two previous episodes of self-limiting urticaria. The first followed a meal of seafood linguine with wine. The patient was clear that he had always tolerated these meal components in the past. Another occurred while taking diclofenac sodium for musculoskeletal pain, but the symptoms did not appear to have been temporally related to drug ingestion. The patient was non-atopic, with no history of asthma, eczema or rhinitis, and was otherwise fit and well with no regular medication use.

Skin prick testing with commercial wheat flour extract demonstrated a borderline result at 2 mm (diluent negative control 0 mm, histamine positive control 7 mm). Tests with egg white extract and cows milk protein extract were negative. Serological investigation demonstrated weak positive results for wheat-specific immunoglobulin E (4.21 kU/litre), and a strong

positive result to the wheat allergen omega-5-gliadin immunoglobulin E (13.8 kU/litre). Serum levels of tryptase and C4 were within the normal ranges.

This history of anaphylaxis following exposure to wheat and exercise, together with strong positive circulating immunoglobulin E to omega-5-gliadin, was considered diagnostic of wheat-dependent exercise-induced anaphylaxis. The two previous episodes of urticaria – one after wheat and alcohol, the other associated with the use of diclofenac – may also have resulted from food-dependent exercise-induced anaphylaxis.

The condition was discussed as a risk management issue, whereby the risk of anaphylaxis should be minimized without undue restrictions on diet and exercise. The patient agreed to avoid wheat-based products for 2 hours either side of exercise, and avoid taking alcohol and wheat-based products together. He was reassured that he was not allergic to non-steroidal anti-inflammatory drugs, but may wish to use alternative analgesia. He was also provided with adrenaline autoinjector devices and training.

Over 2 years later, this patient continues to enjoy exercise, alcohol and wheat-based products within this suggested framework and has not experienced any further symptoms.

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a systemic disorder rather than allergy, for example connective tissue disease or systemic mastocytosis. A very detailed timeline of clinically significant events and their relationship to food allergens and co-factors is required to reach the correct diagnosis.

Having made a clinical diagnosis of food-dependent exercise-induced anaphylaxis, the next steps are to delineate a specific allergen in the history and test for allergen-specific immunoglobulin E, using a combination of skin prick testing and serology. This patient demonstrated sensitization to the wheat allergen omega-5-gliadin, which is strongly predictive of wheat-dependent exercise-induced anaphylaxis. However, this test is only 80% sensitive, and immunoglobulin E to native wheat extract only 40% sensitive. Some centres have proposed further investigation by a food-exercise challenge test, seeking to reproduce the symptoms in a controlled environment – however, there is no validated protocol for this procedure.

The mainstays of management are the avoidance of culprit foods with associated co-factors, together with the provision of adrenaline autoinjector devices and training. The latter is particularly important as some residual risk will remain unless the culprit

food allergen is completely avoided, which would be unduly restrictive. The required time interval between food intake and co-factor exposure has been identified as 4 hours (Feldweg, 2015), but in reality the interval is variable and personalization is required.

Conclusions

Food-dependent exercise-induced anaphylaxis is a rare disorder of growing global prominence. Awareness of this in the secondary care setting is necessary to facilitate prompt and accurate case detection and to provide appropriate ongoing care. **BJHM**

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Hamman syndrome

Hamman syndrome has a recognized occurrence in labour, describing spontaneous subcutaneous emphysema with pneumomediastinum. The incidence is between 1 in 2000 and 100 000 labours (Jayran-Nejad, 1993).

A 29-year-old primip had a healthy term vaginal delivery with assistance from Kiwi ventouse and episiotomy. The pregnancy was unremarkable except for an earlier episode of mumps.

Two hours after delivery the patient's partner noticed that her cheeks were swollen and palpation confirmed subcutaneous emphysema. She was otherwise asymptomatic with normal chest examination. Chest radiograph (*Figure 1*) confirmed subcutaneous emphysema in the supraclavicular fossae but no evidence of pneumothorax or pneumomediastinum.

The swelling subsided and she was discharged the next day. While distressing, the patient can be reassured of a positive prognosis, usually resolving within a couple of weeks (Seidl and Brotsman, 1994). Concerns centre around the use of Entonox and intermittent positive pressure ventilation. **BJHM**

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LEARNING POINTS

- Food-dependent exercise-induced anaphylaxis should be considered in a patient presenting with anaphylaxis following exercise.
- A careful clinical history is the most reliable method to recognize food-dependent exercise-induced anaphylaxis.
- The diagnosis requires confirmation in a dedicated allergy clinic, supported by skin prick testing and immunoglobulin E serology, to identify the culprit allergen.
- The main principles of management include identification and avoidance of culprit allergens and potential co-factors, and patient education and the provision of adrenaline autoinjector devices with training.

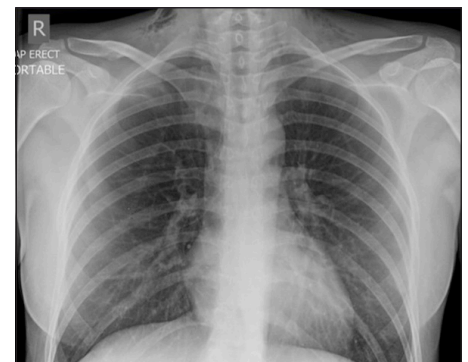
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Images in Medicine

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Figure 1. Chest radiograph showing supraclavicular subcutaneous emphysema.



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