

Handout

Exercise- induced anaphylaxis

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The clinical manifestations of exercise-induced anaphylaxis include flushing, increase warmth, diffuse pruritus, urticaria, angioedema, bronchospasm, hypotension and laryngeal edema which is potentially fatal in athletes. The main differential diagnosis is with cholinergic urticaria. In exercise-induced anaphylaxis, the urticarial lesions are large, with diameters ranging from 10 to 15 mm, opposed to the typically small 1 to 3 mm punctate wheals of cholinergic urticaria. The passive increase of body temperature, not exercise related, is unable to cause exercise-induced anaphylaxis. The differential diagnosis of exercise-induced anaphylaxis also includes exercise-induced asthma, exercise-associated gastroesophageal reflux, systemic mastocytosis, monoclonal mast cell activation syndrome and cardiac conditions like hypertrophic cardiomyopathy and arrhythmias. The most commonly implicated exercise modalities are those requiring running (jogging) and all aerobic exercises (brisk walking, bicycling, racquet sports, vigorous dancing and even gardening). Cytoplasmic mast cell degranulation with massive release of mediators of anaphylaxis, especially histamine, occur. Skin biopsies showed degranulation of dermal mast cells following attacks. Mast cell clonality (twitchy mast cells) with C-kit mutations and consequent mast cell hyperresponsiveness may potentially be present. Family predisposition is uncommon. Exercise induced anaphylaxis may display food dependence, with or without specific IgE sensitivity. The most commonly implicated foods are wheat (omega-5 gliadin), shellfish especially shrimps, celery, corn, cow's milk, mite contaminated wheat flour and peanuts. Curiously, in these patients, aerobic exercises alone, as well as the ingestion of the allergenic foods without associated exercises, do not cause this syndrome. The synergistic effect of both inducing factors is necessary for the occurrence of the anaphylactic manifestations. There may be drug dependence in exercise-induced anaphylaxis: NSAIDs, aspirin, antibiotics (cephalosporins), and the so-called "anticatabolic energizer supplements", such as beta-hydroxymethylbutyrate. Sometimes only marked exercise-induced angioedema with no systemic manifestations occurs. In exercise-induced anaphylaxis there is a higher prevalence of personal and or family atopy. Syncope is seen in 1/3 and laryngeal edema in 2/3 of the cases. It is postprandial, non specific, in 54% and with drug dependence in 13% of the cases.

EXERCISE-INDUCED ANAPHYLAXIS

- **IDIOPATHIC / PRIMARY (FOOD INDEPENDENT)**
- **WITH IgE FOOD DEPENDENCE**
- **WITHOUT IgE FOOD DEPENDENCE (POSTPRANDIAL)**
- **WITH DRUG DEPENDENCE**

The natural history of exercise induced anaphylaxis shows a trend towards stabilizing. This improvement might be associated with adaptation in the practice of exercises, such as avoidance of eating for 4-6 hours prior (more important) and after physical exertion, avoidance of eating the triggering foods and in temperate areas of the planet avoidance of physical exercise when there is high environmental exposure to pollens (exercising indoors). It is also advisable to avoid exercising in extreme weather conditions (hot, cold or humid). Patients perhaps should also not exercise after allergen immunotherapy and after taking NSAIDs/aspirin. Anti-IgE (omalizumab) as a mast cell stabilizer with downregulation of the high affinity IgE receptors (FcεRI) may have a potential role preventing these anaphylactic episodes. The diagnostic tests consist in programmed running or in standard treadmill exercises for about 30 minutes. A negative test nevertheless does not rule it out. The same is true for serum tryptase elevation. Therapeutic measures include prophylaxis, already mentioned, the possible use of oral anti-H1 antihistamines, preferably those with less or non sedating properties, with conflicting data and yet no established proof and also potentially precluding the recognition of anaphylaxis by masking the early dermatological symptoms and signs, montelukast and the immediate availability of self-injecting epinephrine (EpiPen). Anti-H2 may also interfere with the normal digestion of food allergens. Individuals presenting this kind of physical allergy should always be advised to be with someone else when performing exercises who is also familiar with the use of self-injecting epinephrine, to carry a cell phone, to be near emergency medical facilities and to wear some sort of medic alert identification (bracelet for instance) informing the problem. It is very important to immediately stop exercising at the onset of symptoms. Scaled and supervised exercises may induce effective physical tolerance but more studies are still needed. Exercise-induced anaphylaxis is estimated to be about 2.36-5% of all cases of anaphylaxis. A personalized anaphylaxis emergency medical action plan should always be established for the affected individuals.