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CASE REPORT

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Sudden Death Associated with Food and Exercise

ABSTRACT: Exercised-induced anaphylaxis occurs in conjunction with significant physical exertion. Anaphylaxis occurring when an individual exercises within a few hours of ingesting a particular food is an unusual variant. Cardiovascular symptoms can be the sole manifestation of exercise-induced food allergies, in which case death may mimic sudden cardiac death during physical exertion due to other pathologic causes. We report the sudden and unexpected death of an individual following the ingestion of hazelnuts and almonds, to which the individual was not previously known to be allergic. The decedent collapsed during vigorous dancing. The death was not associated with cutaneous or laryngeal manifestations of anaphylaxis. Awareness of the variable manifestations of food-precipitated anaphylaxis is necessary to correctly establish the diagnosis. An elevated serum tryptase level may be indicative of an allergic reaction, and allergen-specific IgE levels may be used to confirm the particular antigen.

KEYWORDS: forensic science, exercised-induced anaphylaxis, food allergy, sudden death

The sudden and unexpected death of an individual during exercise is a well-known phenomenon to the forensic pathologist. The nature of the pathologic process involved is sometimes elusive, particularly in cases where the heart shows no structural abnormalities.

Anaphylaxis is an acute and potentially life-threatening allergic response resulting from generalized mast cell degranulation with the systemic release of chemical mediators, including vasoactive substances (1,2). These vasoactive substances are responsible for the clinical manifestations of the allergic response, such as smooth muscle spasm resulting in bronchospasm, mucosal edema and inflammation. The cardiovascular system may also be involved, with symptoms including tachycardia, hypotension, cardiac dysrhythmias, and complete cardiovascular collapse (2–4). Clinical signs and symptoms are usually rapidly progressive, beginning within minutes or sometimes within seconds of the antigen exposure, although reactions may be delayed for several hours or in rare cases even up to 24 hours (2,3).

Food allergies are hypersensitivity reactions to food and are mediated by IgE antibodies (5,6). In adults, most food allergies are associated with nuts, fish, and shellfish (4,6). Hypersensitivity reactions can also be precipitated by strenuous physical activity. Symptoms of exercise-induced anaphylaxis (EIAn) may range from mild skin manifestations to life-threatening cardiac arrhythmias (7–10). Exercised-induced food allergy is a variant of EIAn that occurs when the exercise is temporally related to the ingestion of a particular food (11,12). Exercise alone does not produce the anaphylactic response, and the ingested food allergen does not elicit an allergic response in the absence of exercise (4,8,13).

We report a case of anaphylaxis occurring during exercise that was precipitated by the ingestion of nuts to which the decedent was not previously known to be allergic.

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Case History

The deceased was a 19-year-old male with a past medical history significant for asthma treated with Pulmicort and Albuterol inhalers and allergies to peanuts and walnuts who died while attending a wedding reception. He had eaten the main meal, and had no complaints. He then ate the dessert, which was a praline mousse in a chocolate shell with a liqueur sauce. Shortly after eating the dessert, he felt that his throat was closing, and his lips began to swell. These were reportedly similar symptoms to those that he had previously experienced after ingesting peanuts. He immediately washed his mouth out with water and proceeded to the kitchen to see if the ingredients of the dessert included peanuts. The only nuts listed on the prepackaged dessert were almonds and hazelnuts. He continued to experience respiratory difficulty, but began to relax when he was reassured that there were no peanuts or walnuts in the dessert. He then attempted to dance, but developed worsening respiratory distress while dancing. Dyspnea progressed in spite of his use of his inhaler. Because of his dyspnea, he asked that his father call for an ambulance and then collapsed. The rescue unit responded and found him unresponsive with an agonal EKG rhythm. His face was cyanotic and his skin was pale and dry. Resuscitation attempts were unsuccessful, and he was pronounced dead at the hospital.

Autopsy Findings

Postmortem examination performed 14 h after the death revealed a well-developed, well-nourished male weighing 154 lb and measuring 68 in. in height. The upper chest and lower neck had palpable subcutaneous air. The right lung was hyperexpanded and the left lung was collapsed. The reported swollen lips were not present at autopsy. The larynx and trachea showed no evidence of swelling or obstruction. Mild submucosal hemorrhage was present just below the vocal cords, consistent with resuscitative efforts. The lungs showed histologic changes of chronic asthma, including thickened basement

membranes, mucus gland hyperplasia and scattered eosinophils. No other significant anatomic findings were identified.

Postmortem toxicologic studies revealed a blood alcohol level of 0.07 G/dL and the presence of lidocaine. No other drugs were detected. A tryptase level obtained on postmortem blood was elevated at 56 mg/L (reference range 0–13.5 mg/L). Immunoglobulin studies revealed a total IgE of 2830 U/L (reference range <180 KU/L). The peanut IgE was greater than100 KU/L, hazelnut IgE 70 KU/L and almond IgE 20.7 KU/L, all interpreted as being very high levels.

Discussion

Anaphylaxis is the most dramatic of the hypersensitivity reactions (14). The term anaphylaxis refers to an IgE-mediated generalized mast cell degranulation (1). An individual may develop IgE antibodies to a specific antigen, such as a food protein. When there is a subsequent exposure to the antigen, the IgE cross-links with the antigen on the surface of the mast cells, leading to degranulation and the release of mast cell products. In addition to the IgE-specific mechanism, mast cells can be activated by non-immunologic mechanisms. Direct activators of mast cells include medications such as opiates and narcotics, radiocontrast material, and other low molecular weight chemicals. If IgE activates mast cell degranulation, the reaction is termed anaphylaxis. If it is activated by non-IgE-mediated mechanisms, then the reaction is termed anaphylactoid (3).

A wide variety of chemicals are released by mast cell degranulation. These chemicals include vasoactive substances such as histamine, leukotrienes, eosinophilic chemotactic factor, neutrophilic chemotactic factor, and platelet activating factor. These vasoactive substances are responsible for the clinical manifestations of the allergic response, leading to smooth muscle spasm, mucosal edema and inflammation, and increased capillary permeability.

Mast cells also release additional mediators that may be useful in making the diagnosis of an allergic response, although they may not be involved in the clinical symptomatology. Most notably, tryptase is an enzyme found almost exclusively in tissue mast cells and is released from the immunologically activated mast cell. Beta tryptase is more specific for mast cell activation than alpha protryptase (15). Tryptase has been used as a marker for human mast cells, and may indicate that these cells have been degranulated when it is elevated in the serum of plasma. Tryptase levels are therefore useful in confirming death from anaphylaxis. Elevated tryptase is detectable within 30 min of the onset of anaphylaxis and peaks 1 to 2 h later (16). The level of tryptase in the circulation is useful as a diagnostic correlate in the evaluation of mast cell disease (17). Tryptase levels are useful even when serum is not obtained until many hours after death. The blood for tryptase determination should be obtained from the femoral vessels. Heart blood tryptase levels have been reported to be elevated in 22% of control cases and femoral blood tryptase elevated in 10% (18). Kemp (15) reported elevated tryptase levels in 12% of otherwise healthy individuals dying from conditions other than anaphylaxis. Tryptase can therefore not be used in isolation to establish a diagnosis of anaphylaxis, but must be interpreted in light of the postmortem examination and the clinical scenario.

Laboratory tests for allergen-specific IgE antibodies should be obtained in suspected cases of anaphylaxis (19,20). Detection of the specific IgE antibodies provides evidence of a previous sensitization to an allergen (20). It allows for the determination of the type of antigen that may be responsible for the anaphylactic reaction. Allergen-specific IgE may be detected in postmortem serum, even after several months of refrigerated storage (16).

Hypersensitivity reactions vary in severity, but the symptoms typically involve the cutaneous, respiratory, and gastrointestinal systems (6). Symptoms of anaphylaxis include urticaria, angioedema, flushing, dyspnea, syncope, and gastrointestinal manifestations (21). The cardiovascular system may also be involved, with symptoms including tachycardia, hypotension, cardiac dysrhythmias, and complete cardiovascular collapse (2–4). The cardiovascular system alone is involved in some allergic reactions (19). The hypotension associated with an anaphylactic reaction may be severe and unresponsive to treatment. (21). Deaths due to anaphylaxis may result from airway obstruction secondary to laryngeal and upper airway edema or bronchospasm. Often death results from cardiovascular collapse and shock, rather than asphyxia (15,22). Many patients will have no specific gross pathologic findings at autopsy. In other cases, there may be postmortem findings that are suggestive of asthma, such as hyperinflation of the lungs or mucus plugging (15,16,22).

It is estimated that food allergies affect approximately 2% of the general population and 8% of children (2,3), and that approximately 100 to 125 individuals die each year in the United States as a result of food-induced anaphylaxis (4,19). While any food protein has the potential to trigger an immunologic reaction, there are only a few foods that are responsible for the vast majority of food-associated hypersensitivity reactions and severe anaphylaxis (4,6). In children, these include milk, eggs, soy, nuts and wheat. Most food allergies in adults are associated with peanuts, tree nuts, fish and shellfish. Food allergies may result in acute symptoms, such as hives and anaphylaxis. They may also cause or exacerbate chronic diseases, such as asthma, atopic dermatitis, or gastrointestinal disorders (6).

Strenuous physical activity can precipitate a hypersensitivity reaction known as exercise-induced anaphylaxis (EIAn). This is characterized by the development of pruritis, flushing, angioedema, generalized urticaria, respiratory distress and cardiovascular collapse during exercise (8,9). Symptoms may range from mild skin manifestations to life-threatening anaphylaxis (10). The clinical features are indistinguishable from those associated with allergens, such as food or insect stings (7). Exercised-induced anaphylaxis may mimic cardiac arrhythmias that may be due to other pathologic processes, such as coronary arteriosclerosis. When EIAn includes skin and respiratory manifestations, the reaction can be distinguished from a sudden cardiac event due to underlying cardiac pathology. However, anaphylactic shock may result in a cardiac arrhythmia in the absence of cutaneous and respiratory symptoms, and may result in an acute myocardial infarction due to coronary artery vasospasm (21). Therefore, an anaphylactic reaction should be considered in the differential diagnosis for sudden cardiac deaths during exercise. The symptoms of EIAn may not always be reproduced with the same level of exercise for the same time period in a particular individual, suggesting that other factors may play a role in the development of the anaphylactic response.

Food ingestion is a well-recognized associated factor in the exacerbation of exercised-induced anaphylaxis (7,14). Exercise-induced food allergies are being recognized with increasing frequency (7). Food-dependent EIAn occurs when exercise follows the ingestion of a particular food or foods (12,23). Kidd and colleagues (11) reported four such cases. In three of their cases, symptoms occurred if celery was ingested prior to exercise. The fourth individual developed anaphylaxis if the ingestion of any food preceded exercise within 2 h. Truwit (12) studied 54 cases of food-dependent EIAn, reporting that tomatoes, celery, and peanuts were the most common triggers.

Most individuals experiencing food-dependent EIAn have eaten within a few hours of exercising (9,19). This is due to a synergistic effect between the allergen-specific IgE from the recent food ingestion and exercise (9). The individual can ingest the food with no allergic symptoms, and can exercise without invoking symptoms.

There is only a problem when the person exercises after having ingested the food allergen within the previous few hours (19). A variation of food-dependent exercise-induced anaphylaxis has been described by Aihara and co-workers (23), who reported a case of EIAn that required the simultaneous intake of two separate foods to provoke the anaphylactic response. In rare cases, the ingestion of any food prior to exercise may lead to anaphylactic symptoms (11,19). There are also reported cases where the ingestion of food shortly followed the exercise (8).

The ingestion of ethanol may exacerbate food-dependent EIAn by allowing increased absorption of the food allergen, resulting in the greater likelihood of an anaphylactic reaction in a person who is sensitized to that food allergen (6). It is recommended that exercise be avoided 4 to 6 h after eating or after the ingestion of alcohol (7,9). The use of aspirin has also been reported as an exacerbating factor in food-dependent EIAn, presumably by increasing gut permeability and thus allowing food allergens to be more readily absorbed (9).

The present case illustrates anaphylaxis occurring after an individual consumed a dessert containing hazelnuts and almonds. Although the decedent had a history of allergies to peanuts and walnuts, he was not known to have other food allergies. The temporal relationship to vigorous dancing indicates that exercise may have been a causal factor. Symptoms preceded the exercise, but significantly worsened when he began to dance. Ethanol consumption and chronic asthma may have also had contributing roles. Symptoms involved only the cardiovascular and respiratory systems, with cardiorespiratory arrest occurring in the absence of cutaneous manifestations of anaphylaxis. Postmortem studies revealed an elevated tryptase level as well as elevated levels of peanut, hazelnut, and almond IgE. The deceased had no underlying cardiovascular pathology.

Although autopsies in the majority of cases of sudden death occurring during exercise reveal underlying cardiac pathologies, including cardiomyopathies and coronary artery disease (24), in occasional cases no abnormalities are found on gross or microscopic examination of the heart. The differential diagnosis of sudden unexpected death during exercise should include exercise-induced anaphylaxis and anaphylactic food allergy, particularly in an individual with a history of asthma, allergies, or other atopic disorders. In suspected cases of anaphylaxis, postmortem testing should include quantitation of tryptase and allergen-specific IgE antibodies (20).

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