

Fatality in a Teenager Secondary to Exercise-Induced Anaphylaxis

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ABSTRACT

This case report documents the events surrounding the death of a teenage youngster while running track. The patient was a known, moderately severe asthmatic with a history of exercise-induced bronchospasm as well as allergic asthma and rhinitis. His death, however, was characterized at postmortem by severe laryngeal edema and only modest evidence of chronic asthma.

INTRODUCTION

EXERCISE-INDUCED ANAPHYLAXIS has been described as a syndrome characterized clinically by generalized body warmth, pruritis, and erythema sometimes progressing, on further exercise, to urticaria, laryngeal edema with stridor or hoarseness, colic, and finally vascular collapse.⁽¹⁻⁷⁾ No deaths have been attributed to the condition to date, but studies of patients with this condition have been associated with elevations of serum histamine and alterations to mast cells, suggesting that it is an IgE-dependent physical allergic reaction.

Exercise-induced asthma is a well-recognized condition characterized by worsening wheeze 1-10 minutes after completion of strenuous physical exertion. There does not appear to be an immunologic cause. Most investigators attribute the problem to dry cold air acting as an irritant to the bronchi. The problem can be reproduced by exposure to cold dry air or by exercise. The severity of the bronchospasm is proportional roughly to the severity of the exercise. Preconditioning and prior treatment with bronchodilator or chromolyn lessen the severity. Death from exercise-induced bronchospasm has not been reported.

This case report details a death occurring during a track meet in an asthmatic known to have exercise-induced asthma, but in whom the death was thought to be due to acute laryngeal edema.

CASE REPORT

SC (birthdate 11/5/70) was 17 years, 5 months of age at the time of his death. He was a known asthmatic who had been followed in our office regularly since the age of 5 years.

Events of the day of his death are as follows. At 7:00 AM, he arose, took 450 mg theophylline (Theodur), which he was taking regularly at 12-hour intervals for 5 days. He took one 500-mg tetracycline capsule, which

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he took regularly (1/day) for acne, washed his face carefully, and applied erythromycin-benzoyl peroxide gel. No details relative to breakfast and lunch were available, although it is known that he drank one large bottle of Gatorade just before the track meet in midafternoon. The weather was cold (45°F) and very windy. SC completed one race without incident (<1 mile) but reported that he did not "feel well" thereafter. No observers reported flushing or hives. He indicated later that he felt better and participated in a 2 mile race, which he reportedly ran well, but collapsed on the infield within two laps of finishing. An eyewitness stated that he rolled over without speaking, raised his left shoulder, and lost consciousness. Several athletic trainers, off-duty paramedics, and coaches administered CPR, but he never regained consciousness and was pronounced dead 1 hour after arriving at the nearest emergency room (30–45 minutes away from the scene).

An autopsy was performed at King's Daughter's Hospital, Madison, Indiana, the next day, and the findings and a wet specimen of the larynx and surrounding tissue were later reviewed at the pathology department of the Children's Hospital Medical Center in Cincinnati. Findings are as follows: The pleural and pericardial cavities were normal, without evidence of bleeding or pneumothorax. All heart valves were normal, no arteriosclerosis was noted, and the muscles of the right ventricle appeared slightly hypertrophied. The entire larynx was described as edematous, and the vocal cords admitted only the tip of a scalpel. No attempts to intubate had been made. The tracheobronchial tree contained a large amount of bloody fluid. The lungs grossly appeared to be "wet and bloody" with reduced crepitation. No food was present in the esophagus or stomach, but some bloody fluid was present. No bleeding sites were noted. No other gross abnormalities or malformations were noted. Microscopically, a moderate infiltrate of chronic inflammatory cells was noted beneath the epithelium of the larynx, and there was moderate to severe edema and focal areas of hemorrhage beneath the laryngeal epithelium. The pulmonary blood vessels were congested, and some hemorrhage was present in the alveoli. Mild hypertrophy of the peribronchial muscles was present. A moderate amount of chronic inflammatory cells was present around some bronchi. The bronchi contained blood and mucinous material. Other unrelated findings included the presence of granulomas in the lymph nodes, kidney, liver, and spleen that were thought to represent healed histoplasmosis. The cause of death was believed to be asphyxia secondary to severe laryngeal edema. Chronic laryngitis, bronchitis, and asthma were secondary diagnoses. Circular marks from attempts at resuscitation were noted; no notation was made of urticarial lesions. Blood was drawn and given to the state police for toxicologic examination, but no report is available. Plasma histamine levels are also not available.

Over the years during which he was followed for asthma, SC often required prolonged treatment with theophylline and inhaled bronchodilators (usually albuterol). He also required several short courses (5 days) of corticosteroids for acute attacks plus treatment with nebulized bronchodilators. Early in life, his weight increments were small, but he experienced a normal pubertal growth spurt and remained in the normal percentiles. He was unable to take karate because of increased wheeze. He frequently used inhaled corticosteroids (beclomethasone or triamcinolone) at our direction for a few months, and fair compliance was suspected. His school attendance was adequate, but often he missed 14–28 days/year because of his asthma. He was seen 12 days before his death with a moderately severe bout of asthma (daily wheeze, difficulty sleeping), PEF 370 L/minute, and was given aerosol Isoetharine and methyl prednisolone by inhalation (repeat PEF 530). He was placed on triamcinolone inhalations qid and theophylline 450 mg q12h. The patient had no known sensitivity to sulfites, food, or insect stings. He had never had sensitivity to medications. He was not known to have taken any other drugs. There was no family history of anaphylaxis or urticaria/angioedema.

DISCUSSION

Episodes of exercise-induced anaphylaxis have been described as being food related by some authors. Several patients with known hypersensitivity to foods seem to have episodes of anaphylaxis triggered by ingestion of that food with concurrent or subsequent exercise. Shellfish,^(8,14) celery,^(9,12) wheat,^(10,13) and sulfites⁽¹¹⁾ have been implicated. Other episodes of exercise-induced anaphylaxis have been described occurring after the ingestion of any food.^(9,15) Novey et al.⁽¹⁵⁾ studied a patient with exercise-induced anaphylaxis using exercise challenges after (1) fasting state with heat-dissipating clothes, (2) fasting state with

FATALITY AFTER EXERCISE-INDUCED ANAPHYLAXIS

heat-retention clothes, and (3) after a meal. They noted that symptoms of syncope, hypotension, pruritis, erythema, urticaria, and angioedema were observed only after food intake. In this patient, plasma histamine levels and levels of C4, C4d, and C50 were normal, suggesting no allergic mechanism. They concluded that at least part of the mechanism for postprandial exercise-related syncope can be attributable to shift of blood flow to the splanchnic and skeletal muscle.

Careful studies by Sheffer et al.⁽¹¹⁾ in seven individuals with exercise-induced anaphylaxis did demonstrate a significant increase in plasma histamine levels in those individuals who demonstrated clinical symptoms. These episodes subsided in 20 minutes, and no pulmonary function abnormalities were noted. Later studies by Sheffer et al.⁽¹⁶⁾ showed loss of electron density, fusion of granule membranes, and decrease in number of intact granules per cell in cutaneous mast cells after episodes of exercise-induced anaphylaxis. They conclude that exercise-induced anaphylaxis is a distinct form of physical allergy. Sonin et al.⁽⁶⁾ reported three cases of multiple physical allergies, two of whom had exercise-induced anaphylaxis.

Grant et al.⁽¹⁷⁾ described exercise-induced anaphylaxis in a male patient plus two brothers, the father, two paternal uncles, and a paternal grandfather. Longley and Panush⁽¹⁸⁾ described two siblings with exercise-induced anaphylaxis who share the HLA haplotype (A3-B8-D3) with their atopic father. The implications are that there may be a familial pattern to this syndrome.

In discussing prevention and treatment, Ahmed et al.⁽¹⁹⁾ describe a possible role for calcium ion antagonists (nifedipine, verapamil) in the prevention of exercise-induced asthma and anaphylaxis, since mediator release from mast cells, synthesis of newly formed chemical mediators, airway smooth muscle contractions, and nerve impulse conduction are all dependent on the availability and flux of calcium ions. An inhalable form of verapamil (methoxy verapamil) has been found to be more effective than verapamil and comparable or more effective than chromolyn sodium in preventing antigen-induced bronchoconstriction. Studies of efficacy in prevention are likely to follow.

CONCLUSION

To my knowledge, this is the first report of a fatality of this type. It seems probably that additional cases will be forthcoming in view of the increasing awareness of the syndrome of exercise-induced anaphylaxis.

Awareness of the possibility of such an event is the most important lesson. Sheffer,⁽²⁰⁾ who has written most extensively about this problem, suggests that exercise-induced anaphylaxis-prone patients ought to avoid foods, drinks, and pharmaceutical agents (particularly ASA) for 4–6 hours before exercise. Prompt recognition of the anaphylactic episode with ready accessibility of resuscitative equipment and medication may have prevented this death. The presence at athletic events of a health care provider capable of providing an airway to the patient in an emergency may be a desirable goal. Perhaps we should insist on identifying cards or bracelets for these individuals and the provision of epinephrine, with careful instructions regarding dosages and technique to be used, by the coach or trainer.

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AUSDENMOORE

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