

An Unusual Case of Anaphylaxis

Mold in Pancake Mix

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Anaphylactic reactions involve contact with an antigen that evokes an immune reaction that is harmful. This type of reaction is a rapidly developing immunologic reaction termed a *type I hypersensitivity reaction*. The antigen complexes with an IgE antibody that is bound to mast cells and basophils in a previously sensitized individual. Upon re-exposure, vasoactive and spasmogenic substances are released that act on vessels and smooth muscle. The reaction can be local or systemic and may be fatal.

The authors report the death of a 19-year-old white male who had a history of “multiple allergies,” including pets, molds, and penicillin. One morning, he and his friends made pancakes with a packaged mix that had been opened and in the cabinet for approximately 2 years. The friends stopped eating the pancakes because they said that they tasted like “rubbing alcohol.” The decedent continued to eat the pancakes and suddenly became short of breath. He was taken to a nearby clinic, where he became unresponsive and died. At autopsy, laryngeal edema and hyperinflated lungs with mucous plugging were identified. Microscopically, edema and numerous degranulating mast cells were identified in the larynx. The smaller airways contained mucus, and findings of chronic asthma were noted. Serum tryptase was elevated at 14.0 ng/ml. The pancake mix was analyzed and found to contain a total mold count of 700/g of mix as follows: *Penicillium*, *Fusarium*, *Mucor*, and *Aspergillus*. Witness statements indicate that the decedent ate two pancakes; thus he consumed an approximate mold count of 21,000. The decedent had a history of allergies to molds and penicillin, and thus was allergic to the molds in the pancake mix. The authors present this unusual case of anaphylaxis and a review of the literature.

Key Words: Anaphylaxis—Tryptase—Sudden death.

The differential diagnosis of acute-onset shortness of breath includes pulmonary embolism, status asthmaticus, acute myocardial infarction, drug reactions, and anaphylaxis. Systemic anaphylaxis, a type I hypersensitivity reaction, is an acute allergic reaction that results from the rapid release of active mediators from tissue mast cells and peripheral blood basophils (1). Anaphylactic reactions can cause variable combinations of symptoms, including cutaneous urticaria, laryngeal edema, rhinorrhea, conjunctivitis, bronchospasm, abdominal cramps, nausea, vomiting, diarrhea, arrhythmias, and hypotension (1,2). Most reactions are due to insect stings, foods, immunotherapy injections, or medications.

The prevalence of anaphylaxis is unknown. Unlike many disorders, there is no requirement to report such reactions to any national registry (3). The postmortem diagnosis of anaphylaxis is not an easy task when the history of events is not witnessed and is further complicated by the fact that the classic signs, such as laryngeal edema, pulmonary hyperinflation, and tissue eosinophilia, are inconstant findings (4). The use of serum tryptase levels, a neutral protease released from mast cell secretory granules, has been helpful in aiding in the diagnosis of anaphylaxis. The following case report is of an anaphylactic death after the ingestion of 2-year-old pancake mix with an elevated mold count.

CASE HISTORY

Clinical Course

The decedent was a 19-year-old white male who had a history of multiple allergies with resultant reactive airway symptoms, which were usually relieved with an albuterol inhaler. Allergies included pets (dogs and cats), molds, and penicillin. While home on vacation from college, he and two friends were eating pancakes made with pancake mix that had been previously opened and had a date of expi-

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ration 2 years prior. The friends stated that they stopped eating the pancakes because they tasted like "rubbing alcohol." The decedent continued to eat and finished two pancakes. Minutes later, while watching television, the decedent became short of breath, which was not relieved by his inhalant. He asked his friends to take him to a medical clinic not far from the home and was reported to become slightly cyanotic during the ride. He was able to walk into the clinic and suddenly collapsed in cardiopulmonary arrest. He failed to respond to resuscitative efforts and was pronounced dead.

Autopsy Findings

The body was that of an obese, young white male with head and neck cyanosis without evidence of injuries. Removal of the chest plate revealed hyperinflated lungs. The right and left mainstem bronchi contained thick mucus secretions, as did the smaller airways upon sectioning. The larynx and epiglottis were mildly edematous on gross examination. The remainder of the organs were in normal anatomic position and grossly unremarkable.

Microscopic examination of the lungs revealed thickened bronchial basement membranes, hypertrophy of bronchial muscle smooth muscle, alveolar capillary hyperemia, and increased size of submucosal glands, consistent with a history of chronic asthma (Figs. 1–2). Numerous eosinophils were noted as well (Fig. 2). A Giemsa stain of the larynx and epiglottis showed increased numbers of mast cells, many of which were degranulating, within an edematous submucosa (Figs. 3–6).

Toxicologic examination revealed a negative blood alcohol and a negative urine drug screen. The

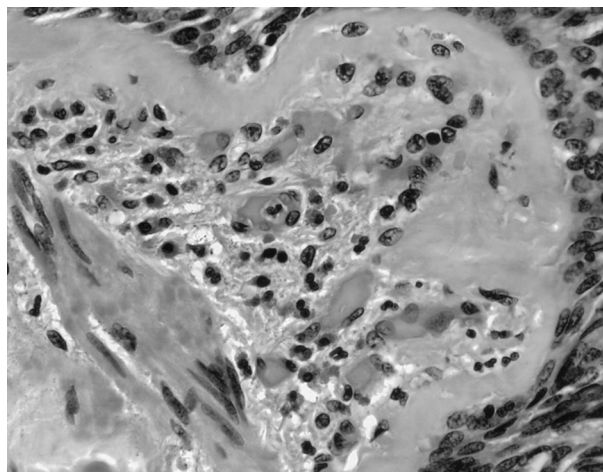


FIG. 2. Hematoxylin and eosin–stained section of lung at higher power (40×) showing the thickened basement membrane and the numerous eosinophils.

serum tryptase level was elevated at 14.0 ng/ml (normal value reported as < 11.4 ng/ml).

The pancake mix was sent to the South Carolina Department of Health and Environmental Control for examination. The total mold count was 700/g of mix with the breakdown as follows: *Penicillium* species 100/g, *Fusarium* species 200/g, *Mucor* 100/g, *Aspergillus flavus* group 200/g, and *Aspergillus niger* group 100/g. According to the nutritional labeling on the box, one pancake would contain 15 g of mix if the directions for preparation were followed. The decedent reportedly consumed two pancakes, ingesting approximately 30 g of mix for a possible total mold count of 21,000.

With the reported history of events, the decedent's history of multiple allergies, an elevated tryptase

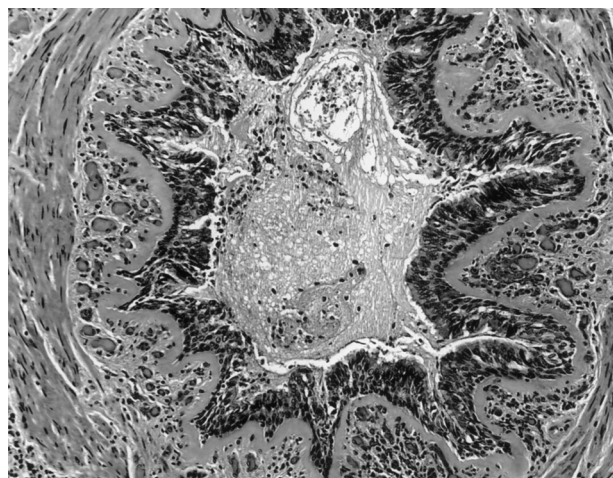


FIG. 1. Hematoxylin and eosin–stained section of lung showing mucus plugging, numerous eosinophils, thickened basement membrane, and increased smooth muscle, consistent with a history of asthma (10×).

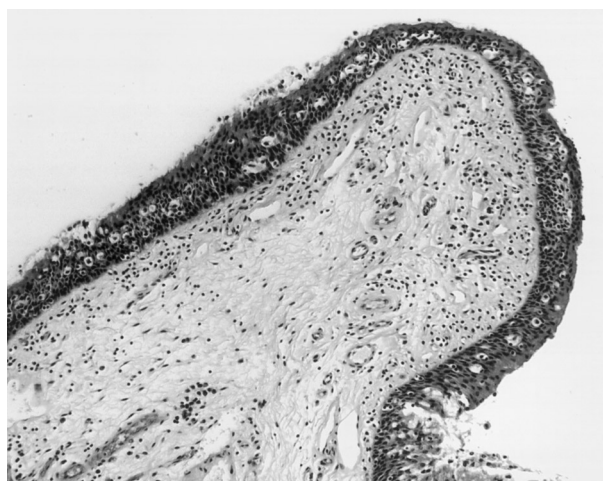


FIG. 3. Section of larynx (hematoxylin and eosin) shows edema and a mast cell infiltration (10×).

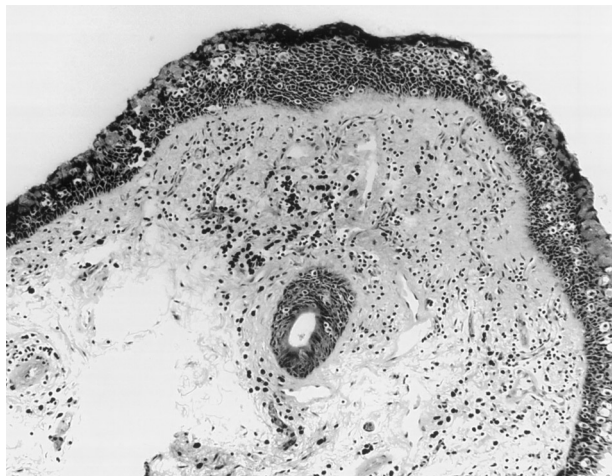


FIG. 4. Section of larynx stained with Giemsa. Note the numerous mononuclear cells infiltrating the lamina propria (10×).

level, and an elevated mold count in the pancake mix, the cause of death was determined to be anaphylaxis due to an allergic reaction to molds.

DISCUSSION

Anaphylaxis is a rapidly developing immunologic reaction occurring within minutes after the combination of antigen and antibody bound to mast cells and/or basophils in individuals previously sensitized (5). Mast cells are found predominately near blood vessels and nerves and in subepithelial sites. Their cytoplasm contains membrane-bound granules that possess a variety of biologically active metabolites. IgE antibodies bind to mast cell surfaces by plasma membrane-bound Fc receptors,

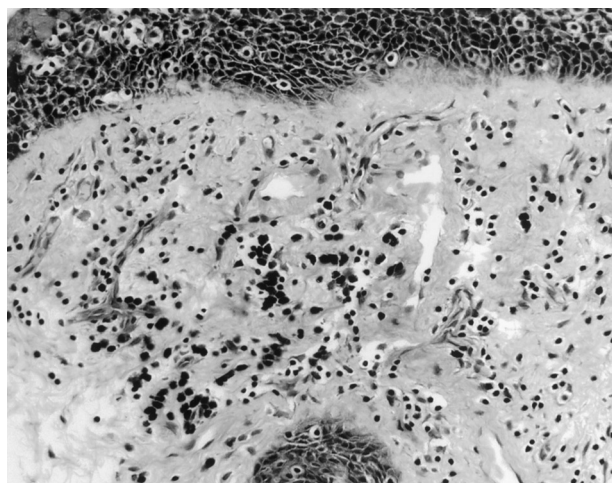


FIG. 5. Larynx stained with Giemsa depicting the marked infiltration of mast cells (20×).

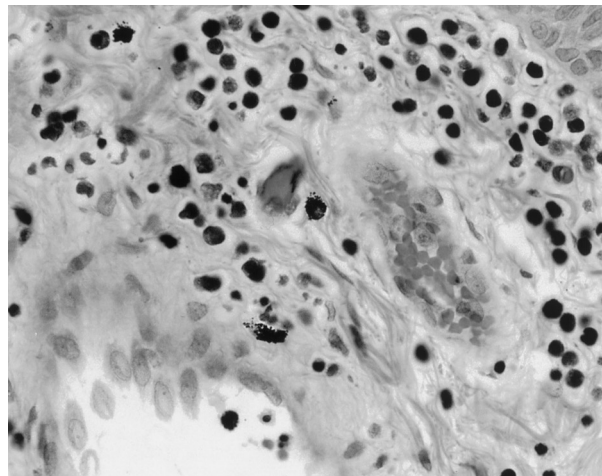


FIG. 6. Giemsa stain highlights the degranulating mast cells in the larynx (40×).

and activation of mast cells occurs when the bound IgE antibodies are crosslinked by binding to multivalent allergen (1).

Anaphylaxis is an uncommon but well-recognized cause of sudden death, resulting from respiratory or cardiac arrest in severe reactions (2). Death is usually attributed to airway obstruction secondary to laryngeal edema, bronchospasm, or mucus plugging. Cardiac arrest can occur with or without respiratory difficulty as the result of either direct effects of the mediators of anaphylaxis on the heart or shock resulting from peripheral vasodilation (2).

Previous studies of fatal cases of anaphylaxis revealed that symptoms developed within 20 minutes in 86% of the cases, and death occurred within 30 minutes in 33% of the cases and within 1 hour in 50% of cases (6). Respiratory distress and circulatory overload were the presenting symptoms in 37% and 33%, respectively, and skin symptoms were the presenting symptom in only 7% of the cases (6). It is important to realize that the absence of cutaneous symptoms does not rule out anaphylaxis. The symptoms of anaphylaxis are generally related to the gastrointestinal, respiratory, cutaneous, and cardiovascular systems (7). The sequence, timing, and severity of symptoms vary from one individual to the next (7). In the current case study, the victim, who lacked cutaneous symptoms, began to experience respiratory difficulty minutes after the ingestion of several pancakes and died within 1 hour.

The classic postmortem findings of anaphylaxis, such as laryngeal edema, pulmonary hyperinflation, and tissue eosinophilia, are subjective and inconsistent (4). A recent study showed that 23 of the 56 anaphylactic deaths studied had no macroscopic postmortem findings of anaphylaxis (2). Thus, it

may be speculated that anaphylaxis can be an unrecognized cause of death in individuals dying unexpectedly (8). In cases in which there is no macroscopic evidence of anaphylaxis, laboratory testing is a useful adjunct for elucidating the etiology. The investigation of possible anaphylactic deaths can be facilitated by the measurement of serum tryptase levels (8). Tryptase, a neutral protease released from mast cell secretory granules when these cells degranulate, is found almost exclusively in tissue mast cells, thus making it a specific marker for systemic mast cell events (8,9). Serum tryptase elevation in postmortem sera has been shown to reflect antemortem mast cell activation, which is compatible with an anaphylactic reaction (9,10). Elevated tryptase levels have been obtained up to 24 hours post mortem (10). The individual in this case report had an elevated tryptase level of 14 ng/ml (reference range, <11.4 ng/ml) at 5 hours post mortem, indicating a systemic mast cell event. Elevated tryptase levels have been identified in specimens from individuals who have died from nonanaphylactic causes, so an elevated postmortem level cannot be used to establish the cause of death as anaphylaxis without additional supportive findings or information (9). The diagnosis of anaphylaxis in this case report was not made on an elevated tryptase level alone but by using the autopsy findings and case history in conjunction with laboratory results. The tryptase test does remain useful in evaluating unexplained deaths, when other clinical information suggests an anaphylactic reaction.

Most anaphylactic reactions are due to insect stings, food allergies, or pharmaceuticals. We present an unusual case of anaphylaxis to molds in pancake mix in an individual with a history of mold allergies. It was determined that the decedent was not

allergic to eggs, which are a component of the pancake mix. In this case, the clinical history, macroscopic findings, microscopic findings, elevated tryptase level, and an identifiable allergen were used in conjunction to make the postmortem diagnosis of an anaphylactic reaction. It is important in cases of suspected anaphylaxis to obtain the substance in question and have it tested to possibly determine the suspected allergen that caused the reaction. In the current case, it was determined that the excess mold in the outdated pancake mix was the probable allergen. The luxury of having all these findings are not present in many cases of anaphylactic deaths, showing the importance of using gross findings, microscopic findings, medical history, event history, and laboratory testing in the evaluation of possible anaphylaxis.

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