COMMON ERRORS IN INTERNAL MEDICINE

ASTHMA OR ANAPHYLAXIS?

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Food-induced anaphylaxis often is mistaken for severe status asthmaticus, and laboratory studies aren't helpful in differentiating the two.

Two hours after eating a buffet dinner at a Thai restaurant, a 20-year-old woman presents to a hospital emergency department (ED) with sudden onset shortness of breath, wheezing, diffuse pruritus, nausea, and abdominal cramps. She has difficulty speaking, but a review of her medical record reveals that she has a history of moderate, persistent asthma; atopic dermatitis; and peanut allergy.

Her family physician is on hospital grounds and called to the ED. She and her two children—a two-year-old, who is allergic to cow's milk, and a two-month-old infant, whom she is breastfeeding—have been seeing this physician for the past few years. Over that period of time, family health care has consisted of routine immunizations and well baby examinations, which have revealed no evidence of asthma or atopy on the part of either child. As detailed in her asthma care plan, the mother uses the short-acting, inhaled beta-agonist albuterol; the long-acting, inhaled beta-agonist salmeterol; and the inhaled corticosteroid fluticasone, all at doses and intervals determined by her symptoms and peak expiratory flow measurements.

Her blood pressure is 100/64 and her respiratory rate is 26 breaths/min. Her peak expiratory flow rate is 250 L/min. Arterial blood drawn as she breathed room air shows that her pH is 7.4, partial pressure of oxygen is 85 mm Hg, and partial pressure of carbon dioxide ($PaCO_2$) is 40 mm Hg. Her chest X-ray, complete blood count, and CHEM-7 are normal. She responds quickly to IV methylprednisolone and repeated nebulized albuterol and ipratropium.

After two and a half hours of treatment and observation in the ED, the patient feels fine and wants to go home. In light of her rapid improvement, normal blood gas values, and on the advice of her family physician, she is discharged with instructions to add a tapering dose of oral prednisone to her usual asthma regimen.

About 90 minutes after discharge, she returns to the ED in severe respiratory distress, requires endotracheal intubation, and is admitted to the intensive care unit (ICU). The ICU resident who takes over her care orders a beta-tryptase level measurement to determine whether her acute symptoms might be an anaphylactic reaction to something she ate. This measurement is within normal limits.

Several days later, when her symptoms, spirometry, and peak-flow measurements have returned to baseline, the patient is discharged on her usual regimen of salmeterol, albuterol, and flutica-

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sone—with the addition of the bronchodilator theophylline 200 mg/day orally and the corticosteroid prednisone 60 mg/day tapered over 19 days to 5 mg/day. In light of the patient's normal serum beta-tryptase level, the physician characterizes her acute illness as a severe asthma exacerbation.

CAN YOU IDENTIFY THE ERRORS?

The main error in this case was excluding the possibility of an anaphylactic reaction on the basis of a normal serum beta-tryptase level. Neither the family physician nor the ED and ICU staff members realized the significance of the patient's peanut allergy. All, therefore, missed opportunities to counsel her about dietary modifications that could mitigate the development of food allergy in her young children, strategies for preventing anaphylactic reactions, and steps to take in case of an accidental ingestion. Other errors include the failure to recognize the patient's potential for a biphasic reaction and the danger signified by "normal" arterial blood gas studies within the context of tachypnea—the two errors that led to her premature discharge from the ED.

GETTING TO THE ROOT OF THE PROBLEM

Anaphylaxis is a severe, systemic, allergic reaction.[1] Food allergy is the leading cause of anaphylaxis treated in hospital EDs in the United States and many other westernized countries.[2] Any food can precipitate an anaphylactic reaction at any age, but food allergy most often develops in the first three years of life and decreases with age.[2] Foods introduced in the first year of life are thus most likely to induce hypersensitization.[3]

Up to one third of those who have fatal or near fatal anaphylactic episodes have biphasic reactions.

Peanut-induced anaphylaxis is an immunoglobulin (Ig) E-mediated condition estimated to affect 1.5 million people and cause 50 to 100 deaths per year in the United States.[4] A national survey indicated that about 1.1% of Americans, or three million people, are allergic to peanuts, tree nuts, or both.[5] In a prospective, descriptive analysis of 544 pediatric cases from a series of 703 patients with food allergies confirmed by challenge, five allergens were responsible for more than three quarters of the food allergies: eggs (36%), peanuts (24%), cow's milk (8%), mustard (6%), and cod (4%).[3] Peanut was the most common allergen for children over the age of three.[3] Wheat and soy are also common allergens.[6] Individuals typically outgrow sensitivities to eggs, milk, wheat, and soy—but not to nuts and fish.[2,6] Fatal food-induced anaphylactic reactions most commonly occur in teenagers and young adults following ingestion of peanuts or tree nuts.[2]

Food-induced anaphylaxis often is mistaken for severe status asthmaticus or an acute cardiovascular event. Laboratory studies aren't helpful in distinguishing food-induced anaphylaxis from these conditions because serum beta-tryptase, a hallmark of the mast cell activation associated with anaphylactic reactions, usually remains at a normal level in patients with food-induced anaphylaxis.[2] This condition, therefore, is diagnosed primarily on the basis of clinical symptoms, presumed exposure to an allergen, and patient history.

Like this patient, people who have life threatening reactions to food usually have asthma and a history of atopy (including atopic dermatitis) or food allergy as young children. Although similar to anaphylaxis from other causes, food-induced anaphylaxis often includes in its early stages such symptoms as oral pruritus or tingling; pharyngeal pruritus and a sensation of airway tightening; colicky abdominal pain; nausea and vomiting; or cutaneous flushing, urticaria, or angioedema.[2] Such critical symptoms as severe bronchospasm may develop within minutes of allergen ingestion or after a few hours.

Double-blind, placebo-controlled food challenges are the gold standard for diagnosing food hypersensitivity, but they're costly and dangerous because they can trigger severe reactions.[7] Consequently, the diagnosis of peanut allergy usually is based on history, a skin prick test, and a specific IgE assay.

When treating patients for anaphylaxis, it's important to keep in mind that up to one third of those who have fatal or near fatal anaphylactic episodes have biphasic reactions. These patients seem to have recovered fully when severe bronchospasm suddenly recurs. Typically, the recurrence is more refractory to standard therapy than the initial symptomatology, often requiring intubation and mechanical ventilation. The mechanism un-

derlying the biphasic phenomenon is unknown, but it appears to be more common in cases in which therapy is initiated late and presenting symptoms are very severe.[2]

It's also critical to interpret blood gas studies within the clinical context in which they're performed. Although a $PaCO_2$ level of 40 mm Hg generally is considered within normal limits, a person who is tachypneic at 26 breaths/min would be expected to have respiratory alkalosis with a $PaCO_2$ in the high 20s or low 30s from hyperventilating. In this setting, a normal $PaCO_2$ indicates serious airflow obstruction and a risk of respiratory failure.

The likelihood of experiencing an anaphylactic reaction is influenced by age (with children under age four being at highest risk) and route of exposure (with parental exposure associated with highest risk).[2] Prior exposure—particularly if it occurred within the preceding five years—increases risk, as does a history of anaphylactic episodes.[2,6] The amount of antigen to which the individual is exposed also influences risk, with greater amounts making an anaphylactic reaction more likely.

GOOD NEWS IN TREATMENT

In a multicenter, phase II study, TNX-901, a monoclonal antibody to IgE, increased the threshold of sensitivity to peanut antigen to a level that should afford protection from unintended ingestions.[8] There were no serious adverse effects of TNX-901, though one patient developed hypotension in response to a food challenge and required overnight hospitalization.[8] In September 2002, the FDA granted TNX-901 fast-track status to expedite review for approval. Phase III studies, however, which would establish dosage and indications, were put on hold pending patent litigation.[8]

Other investigational avenues include immune tolerance induction through one of two possible approaches, both of which have produced encouraging results in animal models. The first uses recombinant peanut antigens that have a reduced capacity to be bound by IgE. The other uses short synthetic peptides that involve T cell specificity but cannot crosslink IgE. If safe and effective in humans, these agents might be even more useful than anti-IgE therapy.[8]

Currently, peanut allergy treatment consists of teaching patients and their families how to avoid the accidental ingestion of peanuts, recognize early symptoms of an allergic reaction, and manage the early stages of an anaphylactic reaction with liquid diphenhydramine and epinephrine self-injection. Patients commonly are advised to wear medical identification bracelets, carry an epinephrine injection kit, and, in view of the risk of a biphasic reaction, follow each epinephrine injection with an ED visit.[8]

Early diagnosis and patient education on avoidance and treatment are imperative. Advise patients to check all food labels for peanuts and to avoid such high risk dining behaviors as eating from a buffet or in an ice cream parlor or sampling unlabeled desserts.[2] Alert patients traveling to developing countries that, due to differences in international methods of processing and filtering nut oils from nutmeats, oil products that are safe in one country may be unsafe in another.

In the event of accidental exposure and anaphylactic symptoms, the patient should be brought to an ED as quickly as possible and treated with epinephrine, antihistamines, supplemental oxygen, intravenous fluids, nebulized albuterol, and corticosteroids, as appropriate. Because of the risk of a biphasic reaction, the patient should be observed for at least four hours before being discharged with a short, tapering course of prednisone and an antihistamine.[2]

The United Kingdom's Department of Health and many allergists in the United States recommend that women with a personal or family history of atopy reduce the risk of sensitizing their children by avoiding peanuts and tree nuts during pregnancy and lactation and refraining from giving peanut products to their children for the first three years of life.[2,8] Pregnant and lactating women soon may be advised to avoid transdermal exposure as well, given observational evidence linking the use of creams containing peanut oil to the development of peanut allergy in childhood.[8,9] Likewise, parents should avoid giving peanuts to children who express an allergy to milk or eggs during their first year of life, since one third of them will develop other food allergies.[2]

Any patient who has had an anaphylactic reaction to peanuts should be evaluated for tree nut allergies as well. About one third of patients with a peanut allergy are allergic to at least one tree nut.[2] Children under the age of five years who are allergic to peanuts should avoid all nuts because they are at risk for developing new nut sensitivities and likely would have difficulty accurately differentiating peanuts from tree nuts in various products. ●

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