Clinical manifestations of immunoglobulin E–mediated food allergy, including pollen–food allergy syndrome

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ABSTRACT

Immunoglobulin E-(IgE) mediated food allergy affects people of all ages but does not have a consistent presentation and may result in various manifestations, even for an individual. The onset of symptoms is usually quite rapid, minutes to a few hours after consumption of the allergen, although exceptions exist. Cutaneous and gastrointestinal symptoms are the most common clinical manifestations; however, they are not present in all allergic reactions. Clinicians, particularly those in emergency care settings, need to be aware that the lack of cutaneous manifestations does not exclude the possibility of anaphylaxis. It is extremely unusual for food allergy reactions to present with isolated upper or lower respiratory symptoms, nor is chronic urticaria a manifestation of food allergy. Clinical manifestations of IgE-mediated food allergy range from mild to severe and, in rare cases, can be fatal. Mild, localized reactions, such as those that occur in pollen–food allergy syndrome, occur in individuals with sensitization to pollens. A small proportion of patients with this syndrome develop anaphylaxis. Alcohol, medications (nonsteroidal anti-inflammatory drugs, antacids), physical exertion, increased body temperature, acute infection, and menstruation are factors that are known to augment the severity of food-induced allergic reactions.

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Immunoglobulin E– mediated food allergy (IgE-FA) is the most common type of food hypersensitivity and is distinguished by its characteristic pathophysiology and clinical presentation. The diagnosis of IgE-FA requires the presence of specific immunoglobulin E (IgE) to a food (sensitization) as well as clinical symptoms on exposure to the food (see Schuler et al. Food Allergy diagnosis and differential diagnosis.). IgE-FA typically presents with symptoms that occur reproducibly on eating a food; onset is soon after ingestion, generally within minutes to 2 hours.

Clinical symptoms typically involve the skin, respiratory, gastrointestinal, and cardiovascular systems, and result from tissue mast cell and circulating basophil mediator release (Table 1).[1] Cutaneous symptoms, such as acute urticaria, flushing, and angioedema, represent the most common manifestation of IgE-FA. Chronic urticaria is not a manifestation of food allergy (FA). Approximately one-third of children ages < 5 years and with moderate-to-severe or refractory atopic dermatitis have IgE-FA. However, FA is rarely a primary trigger, and atopic dermatitis flares often reflect the waxing and waning natural history of the disease as opposed to a food-specific response. Ocular symptoms include conjunctival injection, periorbital edema, watery discharge, chemosis, and pruritus.

Respiratory manifestations include both upper and lower airway signs and symptoms. Rhinorrhea, nasal congestion, sneezing, and pharyngeal pruritus, as well as hoarseness, stridor, and laryngeal edema, can occur. Lower respiratory symptoms include dyspnea, cough, and wheezing. Of note, isolated respiratory symptoms (*i.e.*, asthma exacerbation in the absence of other symptoms or allergic rhinitis) are rarely due to IgE-FA, with the exception of occupational allergic rhinitis and asthma in food industry workers. Baker's asthma is an example of IgE-mediated allergy to inhaled wheat proteins.

Oral pruritus, dysphagia, abdominal pain, nausea, vomiting, and diarrhea are gastrointestinal features of IgE-FA. Of note, oropharyngeal symptoms (pruritus, burning, mild swelling) can occur as part of systemic IgE-FA or as a manifestation of pollen-FA syndrome (PFAS) (see below). As with other features of IgE-FA, the onset of gastrointestinal symptoms occurs minutes to a few hours after exposure, with the exception of diarrhea, which can occur 2 to 6 hours after ingestion. Chronic gastrointestinal symptoms are not characteristic of IgE-FA but can be seen in other forms of food allergy (*i.e.*, eosinophilic gastrointestinal disease; see Brown-Whitehorn T, Spergel JM. Food allergy and eosinophilic gastrointestinal disorders.). Severe repetitive vomiting that occurs 2–6 hours after eating, particularly in infants and toddlers,

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Table 1 **Symptoms of immunoglobulin E–mediated food allergy reactions***

Target Organ	System
Cutaneous	Erythema
	Pruritus
	Urticaria
	Morbilliform eruption
	Angioedema
Ocular	Pruritus
	Conjunctival erythema
	Watery discharge
	Periorbital edema
Upper respiratory	Nasal congestion
	Pruritus
	Rhinorrhea
	Sneezing
	Laryngeal edema
	Hoarseness
	Dry staccato cough
Lower respiratory	Cough
	Chest tightness
	Dyspnea
	Wheezing
	Intercostal retractions
	Accessory muscle use
Gastrointestinal	Angioedema of lips, tongue, or palate
	Oral pruritus
	Nausea
	Abdominal pain
	Reflux
	Vomiting
	Diarrhea
Cardiovascular	Tachycardia; bradycardia, late finding in cardiovascular collapse
	Hypotension
	Dizziness
	Syncope
	Loss of consciousness
Miscellaneous	Uterine contractions
	Sense of impending doom

**From Ref. 1.*

and without skin or respiratory symptoms characteristic of IgE-FA, should prompt consideration of food protein–induced enterocolitis syndrome, a non–IgE-FA (see Anvari S, Davis CM. Food protein-induced enterocolitis syndrome.).

Cardiovascular findings in IgE-FA include tachycardia, arrhythmia, hypotension, shock, and cardiac arrest. Bradycardia can be seen in patients who have progressed to cardiovascular collapse. Neurologic manifestations can include a sense of impending doom, near-syncope, syncope, dizziness, and seizure (secondary to poor perfusion and hypoxia). Anaphylaxis represents the most severe manifestation of IgE-FA and is a serious allergic reaction that is rapid in onset and can be life threatening (see Hearrell M, Anagnostou A. Food allergy: Diagnosis and management of anaphylaxis.). It often involves a combination of cutaneous, respiratory, gastrointestinal, and cardiovascular findings, and can lead to hypotensive shock and death. Cutaneous findings are not always seen in anaphylaxis.

Although rare, FA-induced fatal and near-fatal reactions are reported. Fatal food reactions usually progress very quickly, with an onset of symptoms within 30 minutes and death in < 1 hour. In the vast majority of cases, the affected individual has had a previous but not necessarily severe reaction to the same food allergen. Adolescents and young adults are the most commonly affected individuals, and patients with uncontrolled asthma are at increased risk.[2,3] In addition, most such reactions occur outside of the home. Peanut, tree nuts, fish, and shellfish are the most frequently implicated allergens in fatal and near-fatal reactions.

A lack of readily accessible epinephrine is consistently associated with an increased risk of a fatal reaction.[2,3] Personalized treatment plans should address modifiable risk factors, including attention to risk-taking behavior, asthma control, and previous reaction history. It is important to note, however, that reaction severity is unpredictable, and a history of mild reactions does not imply that future reactions will be mild. Nor do reactions necessarily become more severe over time. Patient education must include the indications for and the method of use of self-injectable epinephrine, stressing the importance of the early use of epinephrine for progressive or systemic reactions.

Multiple variables can affect the presentation and severity of an FA reaction, including the amount of allergen ingested, manner of preparation, food matrix, stomach contents, asthma control, and host factors.[1,4] For example, extensively baked forms of egg and milk may be tolerated by individuals who react to less cooked forms.[1,4] In addition, several co-factors can augment the allergic response, including alcohol, certain medications (non-steroidal anti-inflammatory drugs and [NSAIDs], antacids), exercise, increased body temperature, acute infection, and menstruation.[5]

Food-dependent exercise-induced anaphylaxis (FDEIA) is a unique type of IgE-FA in which symptoms typically occur only when an individual exercises or performs physical activity 2 to 4 hours after ingestion of a specific food or, in some patients, after eating any food. Neither exercise nor food ingestion in isolation triggers symptoms. FDEIA is most often seen in adolescents and young adults. Common triggers include wheat, other grains, peanut, tree nuts, and seafood.[6] Wheat is the

Table 2 **Pollen and food associations in pollen–food allergy syndrome**

Pollen	Food
Birch tree	Pitted fruits (apricot, cherry, peach, plum), apple, pear, kiwi, carrot, celery, parsley, peanut, soybean, almond, hazelnut
Timothy and orchardgrass	Peach, watermelon, orange, tomato, white potato
Ragweed	Melons (cantaloupe, honeydew, watermelon), banana, cucumber, white potato, zucchini
Mugwort weed	Bell pepper, broccoli, cabbage, cauliflower, chard, garlic, onion, parsley

most common culprit in FDEIA, and determination of the antigen has led to this FDEIA subtype's designation as "omega-5 gliadin allergy." Interestingly, in this disorder, reactions do not occur every time exercise follows wheat ingestion but other co-factors (alcohol, NSAIDs) may be present.[7] Clinical manifestations of IgE-FA reactions can differ by age. Children ages < 2 years more commonly experience gastrointestinal and cutaneous symptoms, whereas cardiovascular symptoms are less frequent. In adults and children ages > 2 years, cutaneous, gastrointestinal, and respiratory symptoms occur more frequently. Fatalities in children are mainly due to respiratory compromise, whereas cardiovascular involvement more often leads to death in adults.[8]

The majority of IgE-FA reactions resolve within hours. Although infrequent, biphasic reactions may occur and are characterized by the recurrence of symptoms (without re-exposure to the allergen) 4–8 hours after the initial reaction. It is important to monitor patients for 4–6 hours after an initial acute reaction because the manifestations of delayed-phase reactions can be severe. With regard to biphasic allergic reactions after a single food exposure, recurrence of symptoms or a second reaction does not typically occur > 24 hours after the initial allergic reaction. IgE-FA is not associated with prolonged allergic symptoms that last days to weeks nor with conditions such as chronic urticaria, chronic rhinitis and/or nasal congestion, and other persistent respiratory symptoms (postnasal drainage, throat clearing, cough, wheeze).

PFAS is a subtype of IgE-FA characterized by the rapid onset of symptoms that occur in the proximal gastrointestinal tract after consumption of raw (but not cooked or processed) plant-based foods, such as fruits, vegetables, legumes, tree nuts, herbs, and spices. Oropharyngeal pruritus is the most frequently reported symptom; pruritus of the nose or ears, throat tightness, nausea, dysphonia, and dysphagia may also occur. Of note, up to 2% of patients may develop anaphylactic shock. PFAS occurs in patients with seasonal allergic rhinitis and/or sensitization to pollens. PFAS affects adults more than children and varies geographically, depending on endemic pollinating plants. Birch, mugwort, and ragweed are the most common pollens associated with PFAS.[9] Common food pollen relationships are shown in Table 2.

In summary, the clinical expression and severity of IgE-FA vary significantly. Both patient-specific and food-related factors exert influence over the development and extent of food-induced reactions. Clinicians need to consider such factors in their assessment of patients with suspected FA because successful management is dependent on identification and avoidance of triggers as well as appropriate treatment of acute allergic reactions.

CLINICAL PEARLS

- IgE-FA presents with characteristic cutaneous, gastrointestinal, respiratory, and cardiovascular signs and symptoms that occur reproducibly and rapidly with ingestion of a food allergen.
- Clinicians should not discount the possibility of food-induced anaphylaxis if cutaneous manifestations are absent.
- Isolated respiratory symptoms (allergic rhinitis, asthma) are rarely a manifestation of FA, nor is chronic urticaria.
- Factors that can augment the allergic response include alcohol, certain medications (NSAIDs, antacids), exercise, increased body temperature, acute infection, and menstruation.
- Poor asthma control and delayed epinephrine administration increase the risk of near-fatal and fatal anaphylaxis.
- PFAS is usually associated with mild, localized, and transient symptoms but can progress to anaphylaxis in a small number of individuals.

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