CLINICAL VIGNETTE

Adult-onset Peanut Allergy due to Severe Oral Allergy Syndrome

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A 31-year-old female presented with concern for peanut allergy. She tolerated peanuts without reaction until three months prior to presentation when she noted immediate mouth and throat pruritus following ingestion of peanut butter. She denied associated immediate urticaria, tongue/throat angioedema, shortness of breath, nausea, vomiting, and diarrhea. Her symptoms resolved within an hour without treatment. She ate peanut butter for seven days with progression to a sore throat by the end of the week. Two weeks later, a bite of a peanut butter cup caused immediate throat pruritus and tongue angioedema. She immediately took diphenhydramine 50 mg and symptoms resolved within 1 hour. Since her reaction to peanut, she had eaten and tolerated tree nuts, seeds, cow's milk, hen's egg, wheat, soy, finfish, shellfish, and legumes. She had no history of atopic dermatitis, asthma, urticaria, and autoimmune disease. Past medical history was notable for chronic rhinitis with symptoms of sneezing, rhinorrhea, and ocular pruritus alleviated with cetirizine and fluticasone nasal spray daily. She had no prior allergy testing. Family history was notable for both parents and two siblings with allergic rhinitis. Psychosocial history was unremarkable.

Vital signs were within normal values. Physical examination was unremarkable, except for pale nasal mucosa, moderate inferior turbinate hypertrophy, and cobblestoning of the posterior oropharynx. She had skin prick tests to aeroallergens, oral allergy pollens, and peanut, along with serum IgE level to peanut and peanut components. Results revealed negative peanut serum IgE and components (Ara h 1, Ara h 2, Ara h 3, Ara h 8 and Ara h 9); positive skin prick tests to grass pollens (Bermuda, Timothy, Johnson, Orchard), weed pollen (yellow dock), dust mites, cockroach, cat, dog, and borderline positive to peanut. Based on the patient's clinical history and test results, the conclusion was that she had severe oral allergy syndrome due to cross-reactivity between orchard grass pollen and peanut protein. This is consistent with a secondary IgE-mediated food allergy.

This case demonstrates the importance of differentiating immunologic versus non-immunologic food-induced adverse reactions, recognizing cross-reactive food allergens and co-allergens, and understanding the natural history of an IgE-mediated primary and secondary food allergy. The exact prevalence of food allergy is uncertain due to variations in study definition. Published prevalence rates are highest when based on self-reported food allergy, around 12-13%, compared to 3-4% when diagnosed by the gold standard of clinically observed oral food challenge. Current literature suggests that food allergy affects 1 to 10% of the population, with national surveys showing a 3-fold increase in peanut allergy prevalence since the 1990s.[1]

Food allergy is defined as a reproducible adverse immunological response to ingested food proteins. One exception being mammalian meat carbohydrate as a causative allergen. The most common type of food allergy is IgE-mediated, with immediate onset of symptoms within two hours of ingestion. Symptoms include urticaria, angioedema, respiratory distress, nausea, vomiting, diarrhea, mental status changes, and hypotension. Symptoms may progress to anaphylaxis. Disorders such as atopic dermatitis, eosinophilic gastroenteritis, and eosinophilic esophagitis have mixed IgE-mediated and cell-mediated mechanism of reactivity to food and are not included in this discussion of IgE-mediated food allergy.We use the term "food allergy" to refer only to IgE-mediated food allergy.

Development of IgE-mediated allergy begins with sensitization to the food with the production of food-specific IgE antibodies. On subsequent exposure to the allergenic food, the food-specific IgE antibodies bind to and activate basophils and mast cells, causing the release of histamine, prostaglandins, and leukotrienes with resultant allergic symptoms. It is important to understand that sensitization to specific foods can occur without development of a clinically significant allergic reaction. Therefore, a subject may have a positive skin test or specific IgE to a particular food allergen; without an immediate hypersensitivity reaction to food consumption.

IgE-mediated food allergy is not synonymous with other adverse food reactions. These include food intolerance, food sensitivity defined as difficulty digesting or metabolizing a food, such as lactose intolerance, gluten intolerance, non-celiac gluten sensitivity, celiac disease, reactions to pharmacologically active food components such as tyramine or caffeine-induced jitteriness, food sensitization (positive skin prick or food serum IgE level in the absence of IgE-mediated symptoms), gastrointestinal diseases that respond to dietary changes, and other non-life threatening food-related symptoms. The gut is rarely the only organ affected by IgE-mediated food allergy, as gastrointestinal manifestations are frequently associated with cutaneous symptoms. In general, food allergy tends to occur in those with other atopic diseases, specifically atopic dermatitis, asthma, and allergic rhinitis. Allergies to foods are more generally prevalent in children than in adults, with the exception of shellfish, fruits, and vegetables.

Cross-reactivity is a contributing factor in food allergy. For example, if an aeroallergen is sufficiently similar to a food allergen by either molecular structure or protein sequence, the food allergen can elicit an IgE-mediated reaction based on this similarity. "The aeroallergens identified include plant (pollen-food syndrome and associations), fungal and animal (invertebrate, mammalian or avian) origin (Table 1)."[2] The patient with a food allergy can be sensitized to both labile and stable components of an allergen. "The aeroallergen proteins vary in stability with the linear epitopes showing stability with heating, cooking, storage, and digestion while the conformational epitopes are less stable and tend to lose their allergenicity in the cooking and preservation process."[3] Our patient had positive specific IgE to orchard grass pollen and peanut. Orchard pollen is homologous to peanut and likely contributed to the resultant IgE-mediated symptoms with peanut ingestion.

Co-allergy is another contributing factor in food allergy. This refers to patterns of reactivity to multiple foods not attributable to IgE antibodies to homologous proteins. Available data suggest that 20-68% of patients with peanut allergy are co-allergic to tree nuts.[4] Guidance on tree nut avoidance should be individualized. However, due to concerns about cross-contamination, avoidance of all nuts is advised in young patients. For our patient, co-allergy is not a concern since she has a pollen-food syndrome caused by primary sensitization to orchard grass pollen which is cross-reactive with peanut proteins.

Lastly, the natural history of food allergy varies based on the food allergen. Adult food allergy may be due to persistent food allergy from childhood, or it may develop as an adult due to loss of immunologic tolerance or via aeroallergen sensitization. When food allergy arises from aeroallergen sensitization, it is called a secondary food allergy as the reactions are due to cross-reactivity from structurally related allergens in the culprit food. In contrast, primary food allergy results from gastrointestinal sensitization to culprit food proteins. Adult-onset food allergy tends to remain throughout life. In a 2014 retrospective study of 1,111 adults with food allergy, 15% (171) were first diagnosed at $\geq$ 18 years old. The subjects' ages when the first reaction occurred ranged from 18-86 years, with the majority of the reactions occurring in their early 30s. Women (64%) had more reactions than men (36%). The most common food allergens were: shellfish (54%), tree nut (43%), finfish (15%), soy (13%), and peanut (9%).[5] Based on the above, our patient whose IgE-mediated food allergy symptoms began at 31 years old, is likely have persistent peanut allergy.

This case illustrates the complexity of making the diagnosis of an IgE-mediated food allergy in the adult patient. A food allergy cannot be definitively determined based only on results from skin testing or specific IgE testing to the suspected food allergen. Each patient must first be evaluated with careful exploration of the patient's history, the exact sequence of events and symptoms that led to the suspected food allergy, and physical examination. This is then followed by targeted testing if warranted. Use of food allergy skin prick test or serum IgE level is not advised to evaluate adverse food reactions in the absence of IgE-mediated symptoms. Per the Allergy & Immunology Practice Parameters, non-validated or unproven tests, such as specific IgG to foods, hair analysis, cytotoxicity assays, and applied kinesiology provocation, are also not recommended. In our case, results from testing suggest that sensitization to orchard grass pollen is the likely cause of the IgE-mediated symptoms to peanut ingestion.

To manage her severe oral allergy syndrome, the patient was advised to restrict peanuts from her diet. She was prescribed an epinephrine auto-injector due to throat angioedema. Avoidance measures emphasized the following: "peanut dust does not aerosolize (airborne particle), peanut butter vapors contain no protein, surfaces can be effectively abated of residue (clean with soap and water), and skin contact might cause local irritation but not systemic reactions. Thus, the risk of reaction in public from casual exposure is low, except in instances when peanut is directly ingested (eaten or placed in the mouth). Studies show that most people with peanut allergy can safely eat highly refined peanut oil however avoidance of cold-pressed, expelled or extruded peanut oil—sometimes called gourmet oils is advised."[1]

Our patient was able to manage her symptoms with strict avoidance successfully and remained symptom free at her follow up visit six months later.

Table 1.

Aeroallergen origin	**Food allergy syndrome**
Plant	Pollen food syndrome and associations ● birch-apple, cypress-peach, celery-mugwort-spice syndromes ● mugwort-peach, mugwort-chamomile, mugwort-mustard, ragweed-melon-banana, goosefoot-melon associations
Fungi	*Alternaria*-spinach syndrome
Animal	● dust mite-shrimp syndrome ● cat-pork syndrome ● bird-egg syndrome

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