Friday 24 May 2024

Plant based food allergy syndromes

The principal IgE mediated food allergy syndromes are:

- Pollen food allergy syndrome
- Primary peanut/tree nut allergy syndrome
- LTP allergy syndrome
- Food dependent exercise induced allergy syndromes

Pollen food allergy syndrome

Introduction

Pollen food syndrome (or oral allergy syndrome) describes a localized food allergy which may occur due to cross-reactivity between aeroallergens, such as birch pollen, and raw vegetables, fruits, and nuts. It is the most common food allergy affecting pollen sensitised children and adults who usually have a history of seasonal allergic rhinitis. Symptoms, usually mild or moderate, generally occurs within minutes of eating plant foods and are limited to the lips tongue, mouth and throat. In Northern Europe birch tree pollen is the major sensitising allergen. Pollen food allergy syndrome affects 2% of the UK population; 40% of children and 70% of adults with IgE birch pollen antibodies have the pollen food allergy syndrome. The pollen food allergy syndrome is caused by IgE cross reactivity between pollen and heat labile, protease sensitive food allergens. It is essential to distinguish pollen food allergy syndrome from a primary peanut, tree nut, or fruit allergy, or to non-specific lipid transfer proteins (another highly cross-reactive protein present in most plant foods) as there are significant differences in management between these conditions.

Clinical history

The diagnosis of birch/grass pollen allergy syndrome can be based solely on the clinical history using the following set of questions. If the answer to the following 5 question is yes, then the diagnosis is almost certainly pollen food allergy syndrome.

- Are the food provoking symptoms raw fruits, raw nuts, raw carrot, or celery?
- Are the same trigger foods tolerated when well-cooked or roasted?
- Do symptoms occur immediately or within a few minutes of eating?
- Are symptoms limited to lips, mouth, tongue, throat and include tingling, itch and swelling?
- Have you got a history of seasonal hayfever?

Birch pollen — with apple, apricot, cherry, pear, peach, plum, carrot, celery, parsley, almond, hazelnut, peanut and soya milk.

Timothy grass (a common agricultural grass) — with peach, watermelon, orange, tomato, kiwi, and aubergine, bell peppers, chilli, potato and Swiss chard.

Investigations for pollen food allergy syndrome

If there is no clinical history of seasonal allergic rhinitis, clinician can request a specific tree or grass IgE blood to confirm presence of sensitisation (IgE antibody) and make a diagnosis of the pollen food allergy syndrome.

We recommend referral to an (adult) allergy clinic for advice on investigations and management
Reactions not confined to the oro-pharynx, severe symptoms (significant throat, tongue swelling, respiratory and cardiac symptoms need for emergency therapy) or atypical symptoms triggered by raw foods. We recommend referral to an allergy clinic for advice on investigations and management.
Symptoms after ingestion of cooked/processed fruits and vegetables, smoothies, juices or soya milk
If the history is uncertain as to whether reactions also occurs to roasted hazelnuts, almonds, walnuts, Brazil nuts or peanuts either on their own or when present in composite foods such as chocolates, spreads, desserts or snacks.

Patients with reaction reported to cashew, pistachio, macadamia sesame seeds, beans, lentils, chickpeas should be referred to an allergy clinic. Referral to an allergy clinic is recommended if plant foods are causing symptoms with possible nutritional consequences or in cases where the allergic reactions are causing anxiety, needing the reassurance of a specialist opinion or if there are aversive behaviours restricting diet and quality of life due to a perception of multiple allergies.
Young children with reactions to kiwi, bananas and melon need further investigation as pollen food allergy syndrome is less likely.

Primary peanut and tree nut allergy

Introduction

Primary nut allergy affects over 2% of children and 0.5% of adults. Infants with severe eczema and/or egg allergy have a risk of peanut allergy. Primary nut allergy most commonly presents in the first five years of life, often after first known ingestion with typically rapid onset IgE mediated symptoms. Clinical diagnosis of primary nut allergy can be made a combination of clinical history and evidence of nut sensitisation shown by either positive skin prick test or positive IgE blood test. The main differential is pollen food allergy syndrome which presents with usually mild oro-pharyngeal symptoms in the context of hayfever or pollen sensitisation.

Clinical presentation

Clinical history is the cornerstone of diagnosis. Immediate reaction to peanut on 2 separate occasions has an 80% ~~of~~ probability for predicting primary nut allergy. A clinical history alone however is not enough to make a diagnosis of nut allergy. Nut allergy presents with a rapid onset of IgE mediated symptoms within minutes of ingestion. Nature of symptoms is often related to site and amount of exposure and ingestion of large quantities usually leading to more severe reactions. It is rare for a severe reaction to occur following cutaneous exposure. Following ingestion, immediate mucosal symptoms of oral itch and swelling of the lips are common. Young children may not be able to describe symptoms, and will often spit out food and become distressed. Peanut allergen is absorbed rapidly across oral mucosa, and gradually through the gut, causing cramping central abdominal pain, often accompanied by profuse vomiting. Generalised urticaria, angioedema, rhino-conjunctivitis can occur. More severe reactions include a sensation of throat tightening, wheeze, and breathlessness. Collapse due to hypotension is a rare presentation but can be secondary to hypoxia as a result of respiratory failure. Young children may not be able to describe symptoms of upper airway constriction but suggestive features include change in pitch of voice, hoarseness or loss of voice, stridor, excessive drooling and breathlessness.
Tree nuts (such as Brazil or cashew) cause symptoms of airway narrowing more often than peanut, and cashew nut is associated with more severe reactions. Allergic reactions may be more severe in adults compared to children.
Primary nut allergy and pollen food allergy syndrome can co-exist and care must be taken not to confuse primary nut allergy causing only oral symptoms as PFS.

Investigations for primary peanut and tree nut allergy

A diagnosis of primary peanut and tree nut allergy requires evidence of IgE sensitisation by either skin prick and/or blood test. We recommend referral to an **(adult)** allergy clinic for all suspected cases of primary peanut and tree nut allergy

Primary peanut allergy

Typical clinical history and either positive SPT or specific IgE against Ara h 2/Ara h 6 (component tests). Limited specificity and positive predictive value and poor positive Likelihood Ratio (range 1.29-2.81) of whole peanut allergen extract means that current positive threshold (value >0.35KU/L) is not a reliable biomarker of peanut allergy. Component allergen tests are probably the more reliable test to confirm primary peanut allergy syndrome. The peanut birch pollen homologue, Ara h 8, has limited sensitivity and specificity for secondary peanut allergy; may be positive in those with primary nut allergy who are sensitised to birch pollen. It should only be tested in those with suspected PFS who have a negative peanut Ara h 2, Ara h 6 Ara h 1, Ara h 3, and Ara h 9. We recommend that all patient with a history of suspected primary peanut allergen are referred to an allergy for a comprehensive assessment of their symptoms including component allergen tests and advice on further management.

Primary tree nuts allergy

Hazelnut allergens Cor a 9 and Cor a 14 are the best markers of primary hazelnut allergy in children and adults. If they are negative and the PR10 allergen Cor a1 is positive, this confirms a diagnosis of PFS since Cor a 1 has good sensitivity but poor specificity. Walnut Jug r 1 and Brazil nut Ber e1 have best diagnostic accuracy for primary nut allergy. We recommend that all patient with a history of suspected primary tree nut allergen are referred to an **adult** allergy for a comprehensive assessment of their symptoms including component allergen tests and advice on further management.

Lipid Transfer Protein Allergy Syndrome

Introduction

Lipid transfer proteins (LTP) are proteins found in plant based foods including fruit, vegetables, nuts and cereals. They protect plants against insects and bacterial and viral infections. Sensitisation to lipid transfer proteins can cause allergic reactions in some individuals cause. LTP allergy syndrome was originally described in Southern Europe. However it is increasingly recognised as a cause of food allergy in the UK. Although any plant food can potentially cause allergic reactions, the common culprits include apples, peach, other stone fruits grapes, peanuts, walnuts, hazelnuts, almonds, dried fruit peel and tomatoes. Most LTP content is found in the peel and pips of plant foods. Tree nuts, peanuts, apples stone fruit (peaches) and tomatoes are the most common food triggering LTP syndrome in the UK. The prevalence of this condition is not known, however it affects adults more than children.

Clinical features

Symptoms of LTP allergy syndrome are highly variable, ranging from mild oral pharyngeal symptoms to urticaria and anaphylaxis. The LTP allergy syndrome arise from a cross reactive immune response between pollen and plant food allergens. Plane, olive and cypress tree pollens and as well birch and mugwort aero-allergens are associated with the LTP syndrome. In many cases reactions only occur if there is an additional co-factors such as exercise, stress, or drinking alcohol or taking NSAID within the previous four hours. Cannabis may also be a co-factor or a sensitising agent triggering LTP allergen induced symptoms. Lipid transfer protein allergens are resistant to digestive enzymes and are heat stable. This means that allergic reaction can occur with raw, cooked, roasted, processed, juiced, canned, dried, fermented or crystalised foods. In Spain, non-specific peach lipid transfer protein Pru P3 is the dominant sensitising antigen although this is less likely in the UK. There is some debate as to usefulness of peach Pru P3 as a biomarker of the LTP syndrome in the UK. Expert opinion suggests that additional testing for food allergen LTP components including walnut (Jug r3) London plane tree (Pla a3), mugwort (Art v4) as food thought to be triggering allergic reactions, to capture full spectrum of this condition in affected patients.

Investigations

All patients with suspected LTP allergy syndrome should be referred to and adult allergy clinic for further assessment and management.

Food dependent exercise induced allergy syndromes

Clinical features

Food-dependent exercise-induced wheals, angioedema, and anaphylaxis remain insufficiently characterized. Most patient present with anaphylaxis however about 16% may experience either urticaria and/or angioedema. Almost all symptomatic patients will have exercised within 4 hours of eating and develop symptoms within 1 hour after exertion. A recent literature review found that duration from eating to exercising from 5 minutes to 6 hours (median 1 hour) and from exercising to symptom onset varied between 5 minutes to 5 hours (median 30 minutes). Wheat is the most common culprit food (65% of cases) followed vegetables (9.4%), seafood (8.7%), legumes (7.3%), and fruits (6.3%). Many different types of physical exercise triggered food-dependent allergic reactions, including running, walking, and playing football/soccer. Over half of patients with food-dependent exercise-induced allergic reactions are atopic and 1 in 3 patients has a history of urticaria. Aspirin, NSAID, warm weather and menstruation are the most common augmenting factors for food-dependent exercise allergic disorders. Other reported co-factors include alcohol and proton pump inhibitor drugs.

Investigations

The differential diagnosis of food dependent exercise induced allergic disorder includes primary food allergy exacerbated by exercise, LTP syndrome in particular, exercise induced anaphylaxis, cholinergic urticaria, mastocytosis, exercise-induced asthma or cardiovascular disorders. The allergist/immunologist will also assess for rare or cryptic allergen exposure (e.g. hydrolyzates, gal-alpha-gal or macrogols). 90% of patients have only 1 culprit food. Careful history along with skin prick test, prick-to prick test, and serum-specific IgE measurements will identify most cases. Baseline tryptase is useful to exclude systemic mastocytosis and alpha tryptasaemia which may modify presenting features allergic disorders. Omega-5 gliadin has been associated as the major allergen in wheat dependent exercise induced anaphylaxis although a negative omega-5 gliadin does not rule out this condition. Occasionally oral food challenge or oral food challenge with exercise is required to make a diagnosis of food dependent exercise-induced allergic disease. Patients who no longer eat culprit foods before exercise cease to develop food-dependent exercise-induced allergic reactions

All patients with suspected food dependent exercise induced symptoms should be referred to an adult allergy clinic for investigation and advice on further management.

Sources of information and support for patients

The Allergy UK factsheets on food allergy covers multiple different specific food allergies.

Anaphylaxis UK (anaphylaxis.org.uk) provide very useful factsheets covering severe allergic reactions British Dietetic Association patient leaflets on food allergy and food intolerance.

The patient information leaflets food allergy and intolerance, Nut allergy and Oral Allergy syndrome available on the www.patient.info website.

References

National Institute for Health and Care Excellence (NICE) guideline *How should I assess a person with suspected food allergy* [NICE May 2023]

National Institute for Health and Care Excellence (NICE) guideline *Food allergy in under 19s: assessment and diagnosis* [NICE, 2018a]

The British Society for Allergy and Clinical Immunology (BSACI) guidelines *Guideline for the diagnosis and management of peanut and tree nut allergy* [Stiefel, 2017].

The British Society for Allergy and Clinical Immunology (BSACI) *guideline for the diagnosis and management of pollen food syndrome in the UK* [Skypala, 2022]

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