Grass pollen allergy as an anaphylaxis cofactor during peanut oral immunotherapy

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Grass pollen allergy, typically associated with non–life-threatening symptoms, such as rhinoconjunctivitis, is one of the most common allergies worldwide.[1] Rarely, anaphylaxis occurs after grass pollen exposure in children.[2] Oral immunotherapy (OIT) for the treatment of food allergy has been gaining popularity in the last decade as evidence on methodology, effectiveness, and safety has progressed.[3,4] Studies have revealed that patients with peanut allergy on OIT with seasonal allergic rhinitis experience dose-related adverse events more frequently with seasonal patterns.[5,6] Nevertheless, pollen allergy as an anaphylaxis cofactor while on peanut OIT (POIT) has never been described.

We report a 7-year-old female of Japanese genetic ancestry from Victoria, British Columbia, Canada, with anaphylaxis at 21 months old who presented with vomiting and cough after ingesting a small amount of peanut butter. Skin prick testing result revealed that she was sensitized to peanut (10 mm), and her peanut-specific serum immunoglobulin E was greater than 100 kU/L. She had severe infected atopic dermatitis and moderate allergic rhinoconjunctivitis that worsens during grass pollen seasons and was treated intermittently with desloratadine only. She was sensitized to multiple aeroallergens, including dust mite (4 mm), grass (10 mm), birch (3 mm), and weed (4 mm) pollen, compared with the negative control.

The patient began POIT treatment at 4 years of age based on published protocol in preschool children.[3] She developed 4 episodes of anaphylaxis: 2 during the build-up phase and 2 during the maintenance phase (Fig 1). They were all managed with intramuscular epinephrine injection, antihistamines, and a short course of oral corticosteroids. The first episode occurred after 1 hour, on the first day of updosing from 12 mg to 25 mg peanut protein. Her POIT updose was administered in office after 2 weeks on her previous dose and was given immediately after a snack. The second episode of anaphylaxis that occurred in the clinic during the build-up phase was caused by a parental peanut dosing error. The other 2 episodes occurred 1 and 14 months after starting maintenance phase, which were during the grass pollen season in Victoria between May and July. The latter 2 episodes occurred 4 and 1.5 hours after the ingestion of maintenance dose of peanut. These episodes were not related to recent missed doses, intercurrent illnesses, physical activities, or an empty stomach. Except for these acute episodes of anaphylaxis, the patient only developed mild symptoms during POIT dose escalation and continued maintenance dosing of 300 mg peanut protein daily.

Because our patient's grass pollen allergy was likely to be an extrinsic factor driving anaphylaxis while on POIT, her parents were advised for 2021 to follow grass pollen count reports in Victoria. Because she has already been on antihistamines, a plan following her last anaphylactic episode was made to reduce her dose of POIT to 150 mg of peanut protein when the grass pollen level is moderate or higher and continue on 300 mg peanut protein daily once the grass pollen season is over.

Our patient developed breakthrough episodes of anaphylaxis between May and July in 3 consecutive years, during the typical grass pollen season in Victoria, Canada.[1] The anaphylaxis episodes occurred in the latter part of the each grass pollen season (mid-June to July) suggesting a priming effect and particular risk owing to accumulated exposure and inflammation later in the season. Although it is possible that these 3 episodes of anaphylaxis occurred during the same 3-week period in 3 consecutive years randomly, this likelihood is quite low (0.33% = $3/52 \times 3/52$). This case demonstrates the importance of considering the seasonal timing of anaphylaxis while on OIT, and the role of grass pollen sensitization and exposure as a possible additional extrinsic anaphylaxis risk factor.

Cofactors are exposures to extrinsic factors that lower the threshold dose to an antigen causing anaphylaxis at a dose of the antigen which would previously be tolerated or only induce mild reactions. Nevertheless, the pathophysiology remains uncertain. Common cofactors include exercise, drugs, alcohol, viral infections, hormones, emotional stress, exposure to specific additional allergens, and concomitant diseases, such as mastocytosis.[7] In an adult POIT study, there was a 45% reduction in threshold dose after exercise and sleep deprivation.[8] Large-scale randomized controlled trials during and outside of the grass pollen season for children with and without grass pollen allergy undergoing OIT are warranted to confirm that grass pollen is a potential anaphylaxis cofactor for OIT patients.

This is the first report of grass pollen as an anaphylaxis cofactor in a patient undergoing oral immunotherapy to food based on temporal correlations with the grass pollen season. We predict that additional aeroallergens, such as other species of pollen, dust mite, and cockroach, will be identified as cofactors in future cases as well. Exposure to animal dander (Cat) has already been identified as an anaphylaxis cofactor for OIT patients.[9]

Allergists may wish to reinforce the use of epinephrine autoinjectors for children that have revealed sensitivity to cofactors, especially during pollen season, following a pass of an oral food challenge to a full serving of peanut. Alternatively, it may be advisable to perform the oral food challenge during the peak pollen season if the intent is to reassure the patient they can tolerate peanut as desired, without a concern for aeroallergen cofactors. Studies have revealed that the risk of OIT discontinuation because of adverse events is lower with antihistamine cotreatment.[10] More evidence is needed for whether antihistamine use in OIT patients would benefit breakthrough anaphylaxis owing to cofactor exposures, and whether performing concurrent aeroallergen immunotherapy in children with aeroallergen allergies undergoing food OIT could reduce the risk of breakthrough allergic reactions.

As more pediatric patients are offered OIT for their food allergies, we will see patients who previously tolerated a dose of their allergen have anaphylaxis even while on maintenance dosing owing to cofactor exposure. Although preschool POIT has been found to be safe, anaphylaxis while on maintenance occurs in approximately 0.8% of these children per year.[4] A thorough consideration of possible anaphylaxis cofactors is essential for patients. This will enable allergists to provide risk reduction strategies through cofactor avoidance, immunotherapy to the

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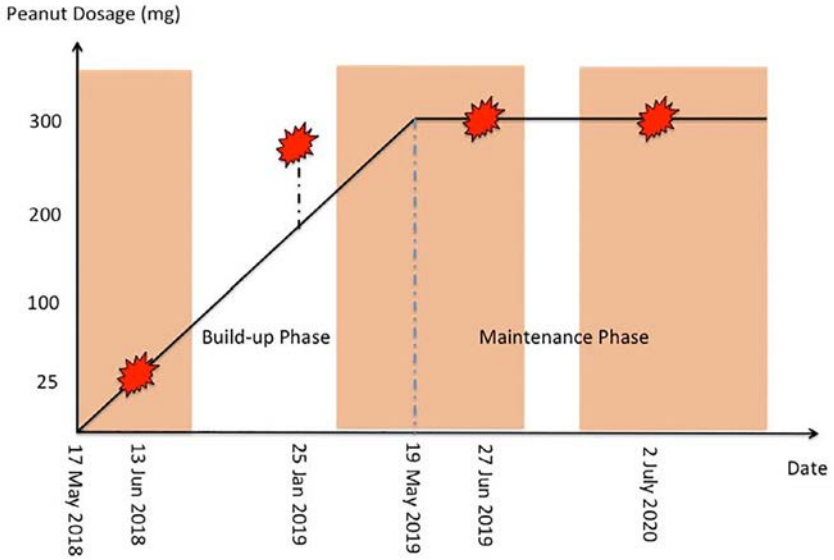

Figure 1. Schematic diagram of the anaphylaxis episodes (red stars) in relationship to the peanut oral immunotherapy and grass pollen seasons in Victoria, Canada (orange boxes). The blue dotted line represents the transition point from the updosing to maintenance stage of oral immunotherapy.

aeroallergen cofactor, or adjusting the OIT doses when cofactor exposure is inevitable.

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Perioperative anaphylaxis to intravenous vancomycin in a pediatric patient with previous topical exposures

Vancomycin is a glycopeptide antibiotic often implicated in hypersensitivity reactions. Immunoglobulin E (IgE)–mediated anaphylaxis to vancomycin is rare, and vancomycin is more frequently described as causing "red man syndrome"—characterized by immediate-onset erythema, pruritus, and sometimes hypotension—secondary to non–IgE-mediated histamine release (ie, by Mas-related G protein-coupled receptor-X2).[1,2] A recent systematic review of vancomycin hypersensitivity identified only 7 cases of presumed IgE-mediated reactions, none of whom were children.[3] We present a case and stepwise diagnostic evaluation of a pediatric patient who experienced cardiac arrest secondary to anaphylaxis to intravenous vancomycin after sensitization by topical vancomycin in the perioperative setting.

An 8-year-old girl with congenital scoliosis and intermittent asthma presented to the operating room (OR) for a spinal-growing rod revision. She was not taking medications and had no personal or

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