
Case report

Late diagnosis of tree nut and sesame allergy in patients previously sensitized but tolerant to peanut

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Background: Recent studies have indicated that tolerance to peanut can occur in patients with a history of peanut allergy. Tree nut and sesame allergies have been reported to occur at increased incidence in patients with peanut allergy. Although the coexistence may be simply due to a predisposition to food allergy in these individuals, cross-reactivity has been demonstrated between peanut and tree nuts and between peanut and sesame seed.

Objective: To describe 3 patients previously sensitized but tolerant to peanut who were subsequently diagnosed as having either tree nut or sesame allergy.

Methods: All the patients had a clinical history of peanut sensitivity and underwent follow-up peanut skin testing to commercial extracts using a bifurcated needle followed by a graded peanut challenge. One patient had a previous positive radioallergosorbent test reaction to sesame and underwent a graded sesame challenge.

Results: All the patients had negative peanut challenge results. Two patients subsequently had exposure to tree nuts at home and had systemic reactions and positive skin test reactions to the incriminated tree nut. One patient had a positive challenge reaction to sesame.

Conclusion: Demonstration of tolerance to peanut may falsely reassure patients and physicians that patients no longer need to avoid tree nuts or sesame. Tree nut and sesame allergies can exist or develop in patients despite the development of tolerance to peanut.

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INTRODUCTION

Studies in the past 7 years^{1,2} have indicated that tolerance to peanut can occur in patients with a history of peanut allergy. It is estimated that 20% of children outgrow their peanut allergy.³ These studies have been based on results of food challenges, often on patients whose skin prick test or peanut specific IgE reactions are positive. Several years after these studies, there were additional studies^{4–7} of patients whose peanut allergy recurred. In a study⁸ of 68 patients who outgrew their peanut allergy, the recurrence rate was found to be 8%. In these studies, patients who consumed peanuts infrequently had an increased chance of a recurrence of their peanut allergy. It has been recommended that patients who outgrow a peanut allergy eat peanut frequently and continue to carry self-injectable epinephrine for at least 1 year.

Tree nut and sesame allergies have been reported to occur at increased incidence in patients with peanut allergy. The coexistence of peanut and tree nut allergy has been reported in 20% to 50% of patients.^{9,10} Sesame allergy has also been increasing and also seems to have an association with peanut allergy. In a study¹¹ of 531 patients sensitized to sesame seed,

448 were also sensitized to peanut. This study was based on skin test results, which do not necessarily correlate with clinical symptoms. In another study,¹² 84% of patients with reported sesame allergy also reported allergy to peanut or tree nut. Follow-up studies that include peanut and sesame challenges are needed to confirm the association of peanut and sesame allergies in these patients. Although the major peanut allergen, Ara h 1, and the major walnut allergen, Jug r 2, are members of the vicilin seed storage family, they show no significant IgE cross-reactivity.¹³ Although the coexistence may be simply due to a predisposition toward food allergy in these individuals, cross-reactivity has been demonstrated between peanut and tree nuts and between peanut and sesame seed. Cross-reactivity between peanut and tree nuts does not seem to be related to the major peanut allergen, Ara h 1, but to other homologous proteins unrelated to their taxonomic relationship.¹⁴ Two sesame seed allergens have been identified that belong to the family of seed storage proteins. One of these allergens (Ses i 3) is a 7S vicilin-type globulin. Both Ara h 1, the major peanut allergen, and Jug r 2, the major walnut allergen, are also 7S vicilin-type globulins. Whereas Ses i 3 has only 36% homology with Ara h 1, the major peanut allergen, it shares an IgE-binding site with Ara h 1.¹⁵ The relevance of the homology is not clear because cross-reactivity using patient sera has not been demonstrated.

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We describe 3 patients with a history of sensitization to peanut but documented tolerance to peanut who were subsequently diagnosed as having either tree nut or sesame allergy. In all cases, tree nuts and sesame were previously being avoided because of the association with peanut and tree nut or sesame seed allergy.

CASE REPORTS

Case 1

A 2½-year-old boy was seen for evaluation of peanut allergy. He had his first reaction to peanut butter at 8 months old, with facial swelling and wheezing. His second exposure was at 2½ years of age, with facial, hand, and foreskin swelling and wheezing. Review of systems was significant for eczema. His medical history was significant for a hospitalization for pneumonia at 9 months of age. Family history was significant for a mother with childhood "allergies" and a father with seasonal allergic rhinitis. Results of initial skin prick testing using a bifurcated needle were positive to peanut (3×16 mm).

At the age of 4 years, he was seen after an acute wheezing episode and was diagnosed as having asthma. At 8 years of age, he had successfully avoided peanut since his previous reaction. Results of skin prick testing to peanut were now negative, which was confirmed with a negative peanut challenge reaction using a previously reported procedure.² He ate small amounts of peanut infrequently after that. At the age of 11 years, he ate half of a chocolate chip cookie with peanut butter chips and ground walnut. He developed throat swelling, vomiting, and lethargy. Follow-up skin tests results were positive to walnut (5×25 mm), pecan (4×15 mm), and hazelnut (8×24 mm) and negative to peanut, almond, Brazil nut, and cashew. He is now sensitized and seems to be allergic to walnut and not peanut.

Case 2

A 14-year-old boy presented with a history of peanut allergy. At the age of 2 years he had gagging, throat closing, and hives to peanut. At the age of 6 years, he was working on a peanut butter bird feeder project at school and developed gagging, choking, hives, and difficulty breathing. He was treated with epinephrine in the emergency department. He then consulted with an allergist and underwent skin testing to peanut, tree nuts, and seeds, all of which had positive results. In the next several years, he developed extreme anxiety regarding his food allergies. When he accidentally ingested a sesame seed roll, he complained of throat itching, although it was unclear whether this was due to his anxiety or an allergic reaction to sesame seeds. Review of systems was significant for seasonal allergic rhinitis and sensitization to animals. His medical history is significant for asthma. He was hospitalized several times as a toddler for asthma, but he denies any symptoms since the age of 7 years.

The patient refused skin testing owing to anxiety over a potential systemic reaction to the extract. The results of ImmunoCap (Pharmacia Diagnostics AB, Uppsala, Sweden) showed sensitization to peanut (1.19 kU/L) and sesame seed (0.43 kU/L). Other tree nuts and seeds (cashew, pistachio, hazelnut, almond, pecan, pumpkin seed, and poppy seed) were negative

(<0.35 kU/L). The patient was subsequently challenged to peanut at 14 years of age, with negative results. His anxiety level improved, and he ate peanut-containing foods on a regular basis. Five and a half months later, at his request, he underwent a graded sesame challenge. He ingested ⅜ tsp of tahini and 1½ tsp of sesame seeds. He complained of throat itching and then developed erythema on his neck and urticaria on his chest consistent with a positive challenge result.

Case 3

A 17-month-old boy was first seen for evaluation of food allergy. He had a history of projectile vomiting after ingesting various formulas, with a few choking episodes and cyanosis. He was admitted to the neonatal intensive care unit and ultimately did well with a casein hydrolysate formula. He had a history of emesis to foods containing eggs and had urticaria when he ate his sister's cereal with milk. He had 1 small bite of a peanut cracker but otherwise was avoiding peanut butter. Review of systems was significant for atopic dermatitis and gastroesophageal reflux. His medical history was unremarkable. His family history was significant for a mother with allergic rhinitis and a sister with asthma. Physical examination revealed lichenification on the extensor surface of the wrists and hands and was otherwise unremarkable. Skin prick test results were positive to milk (7×30 mm), egg (9×28 mm), and peanut (5×20 mm) and negative to soy. The patient was given soy formula in the office, which he tolerated. It was recommended that he avoid milk, egg, peanut, and tree nuts.

Skin prick test results remained positive at follow-up visits. He had vomiting after an unintentional ingestion of milk and vomiting and urticaria after an unintentional ingestion of egg at the age of 2 years. He developed allergic rhinitis and asthma at the age of 4 years that was well managed with montelukast and intermittent cetirizine treatment. He had a negative milk challenge result at the age of 4½ years, a negative egg challenge result at the age of 5 years, and a negative peanut challenge result at the age of 6 years. He then ate peanuts, pistachios, and almonds on multiple occasions without any reactions. At 7 years of age he ate a cookie containing small amounts of walnut and complained of throat itching. On another occasion he had raisins and chocolate candy from a trail mix containing walnuts. He developed urticaria on his neck and trunk, which resolved with diphenhydramine therapy. Results of skin testing were positive to Brazil nut (4×18 mm), cashew (3×20 mm), walnut (6×26 mm), hazelnut (5×27 mm), and pecan (6×22 mm).

DISCUSSION

We described 3 patients with a history of peanut sensitization but documented tolerance to peanut who were later diagnosed as having tree nut or sesame seed allergy. Patients with peanut allergy may be told to avoid tree nuts and sesame seed because they are considered to be at higher risk for these allergies. Once the 3 patients had negative peanut challenge results, 2 also stopped avoiding tree nuts, and the other was challenged to sesame because he had a positive sesame specific IgE reaction of

unclear clinical significance. In these patients, documentation of tolerance to peanut did not correlate with a decreased risk of tree nut and sesame seed allergies.

None of these 3 patients had a previous peanut challenge to establish the initial diagnosis of peanut allergy. Peanut specific IgE levels are also not available to compare levels at the time of diagnosis with those at the time of negative challenge results. Although the history in these patients is compelling, it is possible that the initial positive test reaction to peanut was a false positive. In this case, the positive test result may have been due to cross-reactivity to the implicated tree nut or sesame seed. These patients may have already been sensitized to tree nuts or sesame, but the clinical allergy was masked because they were avoiding these foods because of the peanut allergy. Therefore, a positive skin test result to peanut may be a marker of an unidentified tree nut or sesame seed allergy.

Most cases of tree nut allergy develop in early childhood.¹⁶ It has been suggested that delayed introduction may decrease the risk of allergy.¹⁷ In the 2 patients with tree nut allergy, introduction was delayed for many years, yet these patients still developed tree nut allergy. None of these patients were initially tested to tree nuts because avoidance was recommended regardless. It is, therefore, not known whether they were sensitized when younger or whether they became sensitized as their diet expanded when they no longer avoided peanut. Conversely, the patient with sesame allergy was clearly sensitized in early childhood, although until he was challenged it was not clear whether it was clinically relevant. In this case, he seemed to outgrow his peanut allergy but not his sesame allergy. He had unintentional ingestions of sesame, so sesame avoidance was not as strict as peanut avoidance and may be why he did not also outgrow the sesame allergy. Nevertheless, if his sesame allergy was related to cross-reactivity with peanut, it is interesting that once he outgrew the peanut allergy he did not, in turn, outgrow the cross-reacting allergy.

A positive skin test reaction to peanut in peanut-naïve patients has a 49% positive predictive value.¹⁸ In a study¹⁹ of a large population of peanut- and tree nut-allergic individuals, 46% of patients were sensitized to other tree nuts that they could tolerate. Given the limitations of testing, questions remain regarding the role of skin testing, in vitro testing, challenges, and epinephrine treatment in tree nut- or sesame-naïve patients who develop tolerance to peanut. Demonstration of tolerance to peanut may falsely reassure patients and physicians that they no longer need to avoid tree nuts or sesame. Tree nut and sesame allergy can exist or develop in patients despite the development of tolerance to peanut.

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