

Short communication

Cashew allergy: observations of 42 children without associated peanut allergy

Background: Cashew allergy seems to be increasingly frequent. The goal of the present study was to analyse the clinical features and results of investigations of 42 children with cashew allergy.

Methods: The clinical features and results of skin prick tests, specific IgE assays, and food challenges were analysed.

Results: The mean age at first allergic reaction was 2 years and the mean age at diagnosis of cashew allergy was 2.7 years. One in five children (12%) had a prior history of exposure to cashew nuts. Fifty-six per cent had skin symptoms, 25% had respiratory signs and 17% had digestive signs. Eighteen children had proven, associated food allergies (pistachio, seven; egg, five; mustard, three; shrimp, two; cow milk, one). The mean wheal diameter of the skin prick tests was 7 mm (3–16 mm) and the mean specific IgE level was 3.1 kUA/L (<0.35 – >100 kUA/L). Eight children had positive food challenges.

Conclusion: The increase in cashew allergy is worrying because it affects young children who may have a reaction without ever having been exposed to cashews. Almost one-third of children are allergic to pistachios, which belong to the same botanical family as cashews. Clinical history is generally and sufficiently suggestive to diagnose cashew allergy without recourse to food challenges.

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Changes in our eating habits have altered the distribution of food allergens. Cashews, in particular, are worrying because of their increasing importance as food allergens and the severity of the symptoms (1). Cashew trees (*Anacardium occidentale*) are indigenous to north-eastern Brazil and are members of the Anacardiaceae family, as are pistachios and mangoes. Very few cases of cashew allergy without associated peanut allergy have been reported. The goal of the present study was to analyse the clinical features and results of allergy investigations of 42 children with a clinical history of cashew allergy.

Material and methods

Study population

The children in the study population were under observation at four paediatric allergy centres in France. The cases were consecutive and involved 42 children with cashew allergy. The mean age at diagnosis was 2.7 years (1.5–11 years). The male/female sex ratio of the study population was 2.8 (31 boys and 11 girls). About 32 of the children's family had a history of atopic disease (76% of the study popula-

tion). Children with peanut allergy were excluded from the analysis (five subjects).

The diagnosis of cashew allergy was based on a clinical history suggestive of cashew allergy, and a positive skin prick test (SPT) and/or a positive specific IgE assay, and/or a positive food challenge.

Skin prick tests

Skin prick tests were performed using either a commercial extract (Allerbio[®], Varennes en Argonne; Stallergènes[®], Antony, France) or a native extract produced by crushing and diluting cashew nuts (1/10 w/v). The prick + prick technique was used for the native extracts (2). The following tree nuts were systematically tested: almond, hazelnut, walnut, pecan, Brazil nut, pistachio, and pine nut. The children were also tested for common aeroallergens: *Dermatophagoides pteronyssinus*, alternaria, cat dander, cockroach, orchard grass and timothy grass. The SPTs were considered positive when the wheal diameter was over 3 mm and 50% larger than the positive control, and the negative control remained negative (3). The possibility of dermatographism was eliminated by a negative reaction of the negative control.

Specific IgE assays

Serum samples were analysed for antigen-specific IgE antibodies using the CAP System FEIA[®] from Pharmacia (Guyancourt,

Abbreviations: LFC, labial food challenge; OFC, oral food challenge; SPT, skin prick test.

France). The detection limit for the kit is 0.35 kUA/L. Levels above 0.35 kUA/L were considered significant.

Food challenges

Open food challenges (OFCs) were performed at the hospitals using those described previously (4). Briefly, cashew nut extracts were given in gradually increasing doses, beginning with an initial dose of 5 mg. The doses were increased every 30 min up to a final dose of 20 g if no reaction was observed. The challenge was stopped with the appearance of cutaneous, respiratory, digestive, or cardiovascular symptoms. Grade 3 and that over labial food challenges (LFCs) (5) were considered positive (contiguous urticaria of the cheek or chin or a generalized reaction). LFCs were performed by depositing on the external face of the lower lip a small quantity of cashew nut that has been crushed and mixed in saline for 2 min. The reaction was scored 30 min later.

Results

Clinical features

The mean age at first allergic reaction was 2 years (11 months to 6 years of age). The ingestion of cashew nuts was responsible for 95% of the cases. Two children had a reaction on simple contact and five (12%) had been previously exposed to cashew nuts. Among the 112 clinical events, sometimes in association, the symptoms occurred during the first reaction included urticaria (31 cases, 26%), nonlaryngeal angio-oedema (36 cases, 32%), asthma (eight cases, 7%), rhinitis and rhinoconjunctivitis (nine cases, 8%), oral allergy syndrome (two cases, 2%), vomiting (15 cases, 13%), diarrhoea (one case, 0.8%) and asthenia (one case, 0.8%) (Table 1). No cardiovascular collapse was noted as systemic reactions appeared to have occurred.

The first allergic reaction occurred at home in 31 cases (74%), while four occurred at a friend's home, one at a grandparents' home, and three in the presence of a doctor at a hospital. The following treatments were administered: antihistamine alone (10 children), antihistamine plus corticosteroid (eight), antihistamine plus adrenaline (four), corticosteroid alone (four), adrenaline alone (three) and hospitalization (10). Five received no

Table 1. Clinical features of 42 children with cashew nut allergy and without peanut allergy

Reactions to cashew nuts (n = 42)	
Age at first allergic reaction (average)	2 years
Clinical signs at the first reaction	
Respiratory	28/112 (25%)
Cutaneous	63/112 (56%)
Digestive	19/112 (17%)
Anaphylactic shock	0
Other diagnosis	
Atopic dermatitis	25/42 (60%)
Asthma	22/42 (52%)
Allergic rhinitis	8/42 (19%)
Other food allergies	18/42 (43%)

treatment, while no treatment data are available for two others. Three children (7%) had several allergic reactions over time on ingesting cashew nuts. The clinical signs were identical to those noted at the initial reaction.

Sensitizations to aeroallergens were noted for 15 children (36%). Associated food allergies were documented for 18 children (43%): pistachio (seven), egg (five), mustard (five), shrimp (two), and cow milk (one).

Skin prick tests

All the children had positive cashew SPTs. The mean wheal diameter was 9 mm (3–16 mm). Twenty-nine children had positive SPTs for other tree nuts: pistachio (28 cases, 67%), almond (10 cases, 23.8%), hazelnut (6 cases, 14.3%), walnut (4 cases, 9.5%), pine nut (3 cases, 7%), pecan (2 cases, 4.8%) and Brazil nut (2 cases, 4.8%) (Fig. 1). Allergies to pistachio and almond were based on a clear clinical history of a reaction following the ingestion. We observed seven pistachio allergies and one almond allergy.

Specific IgE assays

The median value of the specific IgE assays using the CAP System FEIA was 3.1 kUA/L (< 0.35–> 100 kUA/L). The assay was negative for three (7%) children, one of whom had a clinical history of laryngeal oedema and two of whom had positive OFCs.

Food challenges

The diagnosis of cashew allergy was based on a clinical history suggestive of cashew allergy, as well as a positive SPT and/or a positive specific IgE assay and/or a positive food challenge. We first carried out SPTs and specific IgE assays for all the children. Food challenges are the gold standard for the diagnosis of food allergy, but were not carried out on the remaining children with a clear clinical history of a reaction following the isolated ingestion of cashew nuts and positive SPTs and/or specific IgE assays.

The main characteristics of the children with cashew nut allergy diagnosed by food challenges are presented in Table 2.

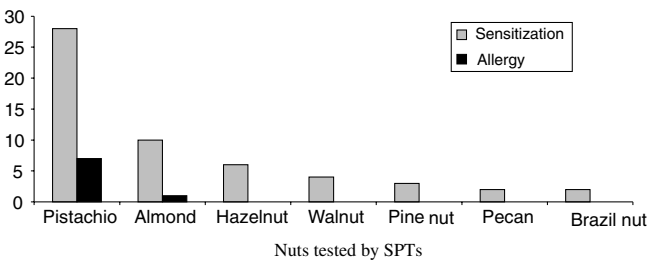


Figure 1. Number of sensitizations to other nuts in 42 children with cashew nut allergy (positive skin prick tests).

Table 2. Characteristics of children with cashew nut allergy diagnosed by food challenge

Sex	Age (years)	Clinical signs	SPT (mm)	s-IgE (kUA/L)	OFC	
					RCD (mg)	Signs
1 M	3.3	U, O	4	10.6	369	U
2 F	6.3	LO	6	0.72	66	LO
3 F	4.3	LO	4	1.59	869	O, A
4 F	4.3	U	11	<0.35	65	U
5 M	6.2	OAS, GIS	8	0.63	369	U, GIS
6 M	5.2	U, O	6	2.38	8765	U, O, Ap
7 F	3.1	U, A	21	7.28	LFC	
8 M	3.5	U	10	3.15	LFC	

RCD, reactive cumulative dose; U, urticaria; O, angioedema; LO, laryngeal oedema; A, asthma attack; OAS, oral allergy syndrome; GIS, gastrointestinal symptom; Ap, abdominal pain; OFC, oral food challenge; SPT, skin prick test; s-IgE, specific IgE.

The LFC triggered a grade 3 reaction (contiguous urticaria of the cheek and chin) in two other children. Two young children, 3.5 and 3.1 years of age had positive LFCs and both had positive test results (SPT and specific IgE). One developed asthma and the other developed urticaria after the ingestion of one cashew nut.

Discussion

Many more epidemiological studies of peanut allergy associated with tree nut allergies have been published rather than studies on isolated cashew allergy. In addition, cashew allergy studies generally involve cohorts of both adults and children. This makes our analysis of children with cashew allergy, all the more important. The large number of observations we present reflect the changes in our eating habits, especially peanut-based premeal snacks and the new social phenomenon of mixtures containing cashews and other tree nuts.

Sicherer et al. (6) estimated the prevalence of tree nut allergies with no associated peanut allergy at 0.7% among adults and 0.2% among children in the United States. These results are similar to those obtained by Tariq et al. (7), who conducted a structured review on the Isle of Wight of a cohort of 1218 children up to the age of 4 years. They reported a 0.2% prevalence of tree nut allergies and a 0.06% prevalence of cashew allergy. Sicherer et al. (6) estimated the prevalence of cashew allergy at 0.06% (eight of 12 032 individuals) and reported that among the 118 respondents with IgE-mediated reactions, eight were allergic to cashew nuts, i.e., 6.7% of those who were also allergic to peanut and/or tree nuts (6).

The severity of tree nut allergies is no longer in doubt (8–14). Cashew allergies have resulted in the deaths of children and adolescents (9). In a study of 32 fatal anaphylactic reactions caused by foods, Bock et al. (10) reported that nuts were responsible for 10 (31%) of the

deaths. In a study of 164 fatal anaphylactic reactions, Pumphrey (11) concluded that 25% were caused by foods and that tree nuts were the main culprits (15 cases). Sicherer et al. (12) used a questionnaire to gather 4159 responses from patients. The average age of the study group was 8.5 years, 67% were boys, 68% were allergic to peanut and 23% were allergic to tree nuts, including 11 patients who were allergic to cashews. The study reported that respiratory symptoms were frequently triggered by ingesting tree nuts (65% of cases) but did not specifically mention cashew allergy. No observations of anaphylactic reactions with hypotension and loss of consciousness were reported (12). MacDougall et al. (13) stated that seven severe reactions to cashew nuts were reported in the United Kingdom and Ireland from 1998 to 2000. Cases were considered severe if one or more of the following symptoms were noted: cardiorespiratory arrest, the need for inotropic support, the use of more than one dose of adrenaline, the use of more than one dose of nebulized bronchodilator. According to Clark and Ewan (14), allergic reactions caused by the ingestion of tree nuts are underestimated and their true prevalence is 7.3–11.6 per 100 000 children.

Based on a study of 29 adults and children, Hourihane et al. (1) reported that 48% of the patients developed wheezing and 38% had anaphylactic reactions with cardiovascular collapse, confirming that cashew allergy is at least as severe as peanut allergy. We observed no cardiovascular collapse in our paediatric population. Allergic reactions frequently occur with no prior exposure: 96% according to Hourihane et al. (1) and 88% in our population. Sensitization possibilities include the *in utero* route, breastfeeding and cross-reacting allergens. While we cannot put forward a specific mechanism, the average age of the children in our survey (2 years) points to very precocious sensitization, either *in utero* or by breastfeeding.

The study we have undertaken does have a number of limitations. A control group was not included. Challenge tests were not performed for all the cases. As with the study by Hourihane et al. (1), a clear clinical history together with positive SPTs and/or specific IgE assays were sufficient to make a diagnosis of cashew allergy in our study population. Only two of 29 patients in the study by Hourihane et al. (1) received an open OFC to confirm the diagnosis. The OFCs are the definitive test for confirming food allergy diagnoses in the event of unconvincing clinical histories and when allergic reactions occur following the ingestion of multiple foods (15).

Associated cashew and pistachio allergies were observed in seven of the children in our study, or 17% of the population. Ewan (16) estimated that 30% of patients who are allergic to at least one food in the nut group are allergic to several tree nuts. One of the major cashew nut allergens was recently identified as Ana o 1, a 50-kDa protein of the vicilin seed storage family (17). However, no cashew nut allergen identified to date shows

any similarity with Ara h 1, the peanut vicilin protein. This explains why no peanut/cashew co-sensitization was observed in our study. However, there is a strong *in vitro* cross-reactivity between cashew and pistachio, both of which belong to the same botanical family. A cashew nut allergic should avoid pistachios because of the cross-reactivity. Avoidance of other nuts would depend on the results of allergic tests and the clinical history.

As with peanut allergy, cashew allergy does not tend to disappear with time. However, because of a lack of follow-up, this cannot be confirmed with our study population. Reactions caused by accidental exposure appear less frequent than with peanut allergy. Hourihane et al. (1) reported a single allergic reaction among 72% of the patients studied (21/29). We observed more than one allergic reaction caused by accidental exposure in only 7% of our study population. The goal of eliminating cashews from the diet appears easy to achieve, especially given the cost of cashew nuts.

Conclusion

The apparent increase in the prevalence of cashew allergy is worrisome. The symptoms appear as severe as those of peanut allergy and more serious than those of other food allergies. Young children (average age of 2 years) are the most at risk. The reactions are triggered in three-quarters of cases at first exposure. It would be prudent to systematically test for associated pistachio allergy. A suggestive clinical history and a positive SPT and/or specific IgE assay for cashew nut were generally sufficient to make a diagnosis without the need for an OFC. Patients with cashew allergy should be referred for an allergy consultation to reduce the risk of accidental exposure (18). Measures to prevent the development of allergies in high-risk children, which usually include the delayed introduction of peanuts, must also incorporate the elimination of tree nuts such as cashews and pistachios from the diet (19).

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