BRIEF REPORT

Clinical presentation of cashew nut allergy in a paediatric cohort attending an allergy clinic in the West of Ireland

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Abstract

Background Cashew nut (CN) allergy appears to be increasing. Reactions are variable and may include anaphylaxis.
Aim To describe the clinical features of CN allergy in a group of children attending an allergy clinic with suspected peanut allergy and confirmed sensitisation to CN.
Methods Patients were identified retrospectively by reviewing the Immunology Database at University Hospital Galway over a 5-year period, Oct. 2010 to Sept. 2015. Patients confirmed sensitised to CN (specific IgE > 0.35 kUa/L, ImmunoCAP Assay) were selected and contacted.
Results Over the 5-year period, 115 children were identified; 102/115 were individually contacted. Of the 102 children, 55 had a history of prior CN exposure with confirmed clinical reaction, 43 had no prior CN exposure, and 4 were sensitised and tolerating CN. For those with clinical CN allergy ($N = 55$), 30 (55%) were male and median age of onset was 2 years (lower quartile 1.5, upper quartile 4.8). Severity of reaction was graded as mild for 13 children, moderate in 13 additional children, and severe in 29 children. Median CN serum IgE level was 3.2 kUa/L (range 0.36 to > 100) in the clinical reaction group, 2.91 kUa/L (range 0.36 to > 100) in the sensitised group, and 3.4 kUa/L (range 0.94 to 5.21) in those tolerating CN. IgE values were not significantly different between those with mild, moderate, or severe reaction to CN ($p = 0.346$).
Conclusion Children are ingesting CN at a young age with more than half of allergic reactions reportedly severe in nature. The specific CN IgE value was not helpful in predicting severity of reactions.

Keywords Anaphylaxis · Cashew nut · IgE-mediated allergy · Sensitisation · Tree nut allergy

Introduction

Cashew nuts (CN), which actually are seeds, are members of the *Anacardiaceae* family, as are pistachio nuts and mangoes; they are surrounded by a shell and a toxic oil layer requiring them to be roasted prior to consumption. There has been a tenfold increase in world production of CN over the last 50 years. The diagnosis of CN allergy appears to be increasing [1] with an approximate prevalence of 0.06–0.08% [2, 3]; currently, no Irish data are available. The Cork Baseline Cohort Study reported an incidence of 0.21% for tree nut allergy [4]. Clinical reaction to CN may be severe including anaphylaxis even in minute quantities; fatalities have been reported [5].

Aim

The aim of the study is to review the clinical features of CN allergy in a group of children with suspected peanut allergy attending an allergy clinic in the West of Ireland.

Methods

Patients were retrospectively identified via the Immunology Database, University Hospital Galway, Oct. 2011–Sept 2015. Individuals sensitised to CN (specific IgE > 0.35 kUa/L, ImmunoCAP (Thermo Fisher, Uppsala, Sweden) Assay) were identified. Phone interviews were conducted; relevant

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demographic and clinical information was collected. Severity of CN allergy was rated in line with current European Academy of Allergy and Clinical Immunology (EAACI) guidance [6]. A positive skin prick test (SPT) was defined as a mean wheal diameter in SPT at least 3 mm greater than the negative control. SPSS™ software package was used and chi-square test for associations between severity of reaction and IgE level.

Results

Over the 5-year period, 115 children were identified with raised specific CN IgE levels; 102 were individually contacted by telephone whilst 13 were uncontactable; 66 (65%) were male. Of the 102 children, 55 had a history of CN exposure with clinical reaction (13 mild, 13 moderate, 29 severe); Table 1 outlines the extent of clinical reaction. By definition of severe clinical allergy [6], more than half presented with anaphylaxis (53%), 44% reported use of intramuscular (IM) adrenaline. Of those contacted, 43 had never ingested CN (sensitised and unknown allergy); 4 were sensitised and tolerating CN. Median CN serum IgE level was 3.2 kUa/L (range 0.36 to > 100) in the clinical reaction group, 2.91 kUa/L

(range 0.36 to > 100) in the sensitised group, and 3.4 kUa/L (range 0.94 to 5.21) in those tolerating CN (see Table 2). IgE values were not significantly different between the patients with mild, moderate, or severe CN reaction ($p = 0.346$). SPTs were performed for 56 patients in total (27 CN allergy, 29 no prior CN exposure group). The mean wheal diameter of the positive SPTs was 7 mm (6 mm CN allergy, 7 mm no prior CN exposure) (range, 3–14 mm). Owing to patient preference and availability, oral food challenges (OFCs) have not yet been performed for those sensitised without CN exposure.

Additional food allergy was reported in 44/55 (23 egg, 12 milk, 8 hazelnut, 5 peanut, 3 pistachio); 22/55 had ingested mango, 3 (14%) reported mild oral symptoms. Among those with CN allergy, 56% were avoiding foods that "may contain nuts" and 29/55 (53%) were avoiding all nuts. Concerning atopic illness, 24/55 reported clinically significant asthma; 42/55 had a current or previous history of eczema and 36/55 had allergic rhinitis. Seven (7/55, 13%) in the clinical reaction group did not carry an adrenaline auto injector.

Discussion

Key points

CN allergy is an increasing issue among children likely due to increased consumption and recognition. There are a limited number of studies of CN allergy in children in comparison to peanut and other tree nuts. The median age of CN reaction was 2 years, similar to previous reports [1]. More than half of the children presented with anaphylaxis. There was no association between IgE level and severity of reaction. Eighty-two percent of children had a reaction after ingestion of 1 CN or less. Similar to peanut allergy, there was a strong correlation with other atopic diseases, notably eczema.

Clinical findings

CN allergy may be severe and is reportedly more so than peanut allergy [7]. Clark et al. report more bronchoconstriction and more cardiovascular symptoms in CN allergic compared to peanut-allergic patients [7]. More than half of the children with clinical reaction to CN in this study presented with anaphylaxis (53%) with 44% using adrenaline for their worst clinical reaction. Of those with anaphylaxis, 28/29 presented with at least skin and respiratory symptoms. However, there was one child who presented only with profuse vomiting and subsequent cardiovascular collapse in the absence of cutaneous features. Davoren et al. report CN anaphylaxis occurring in 3/20 without cutaneous features [5], 76% of children in the latter study presented with anaphylaxis. In our study, 82% had reaction after ingestion of 1 nut or less and 18% of children reacted after only cutaneous or mucosal exposure. Of those

Table 1 Clinical features of children with clinical reaction to cashew nut ($N = 55$)

Boys	30 (55%)
Median age at presentation (upper quartile, lower quartile)	2 years (1.5, 4.8)
Ethnicity (Irish)	94%
Type of CN exposure	
Pure CN	42 (77%)
Curry	4 (7%)
Pesto	4 (7%)
Bar/bread	5 (9%)
Quantity of CN ingested	
< 1 nut	20 (37%)
1 nut	25 (45%)
> 1 nut	6 (11%)
Unknown	4 (7%)
Type of CN exposure	
Skin	3 (5%)
Mucosal	7 (13%)
Oral ingestion	45 (82%)
Skin prick test (SPT) done	27/55 (49%)
Open food challenge (OFC)	0/55 (0%)
Adrenaline used in worst reaction	24 (44%)
Atopic illness	
Asthma	24 (44%)
Eczema	42 (76%)
Allergic rhinitis	36 (65%)

CN cashew nut

Table 2 Characterisation of clinical reactions to CN

Clinical reaction (N = 55)	Age (months) Mean (range)	CN IgE level (kUa/L)			Signs and symptoms (+/−)			
		Mean	Median	Range	Skin	GI	Resp	CVS
Mild (13)	50 (12–120)	10.69	6.17	0.36 to 75.1	13	0	0	0
Moderate (13)	47 (17–48)	12	1.44	0.4 to > 100	13	9	13	0
Severe (29)	49 (14–168)	6.9	1.6	0.43 to > 100	28	17	28	13
Sensitised (43)		14.7	2.19	0.36 to > 100				

CN cashew nut, *GI* gastrointestinal, *Resp* respiratory, *CVS* cardiovascular system

with only mucosal or cutaneous exposure, 3/10 had a severe reaction—which compares to 1/5 in Davoren's study.

Van der Valk reported 137 (76.5%) of their CN sensitised children had a positive double-blind placebo-controlled food challenge, with 46% (63) manifesting subjective symptoms to the lowest dose of 1 mg CN protein [8].

A significant proportion (26/55, 47%) of our cases had associated gastrointestinal symptoms. It has previously been reported that gastrointestinal symptoms are common with CN allergy [8] and more frequent in comparison to peanut and other tree nut allergies [9]. The breakdown of symptoms into mild (24%), moderate (24%), and severe (52%) was comparable to other studies [10]. Skin symptoms were the most common followed by respiratory symptoms, which corresponds to previous reports [7, 11]. In the mild reaction group, 2 had reactions after cutaneous contact and 2 after spitting the nut out. These cases could potentially have had a more severe reaction if the nut had actually been ingested and swallowed.

IgE levels and cross reactivity

In this study, the median value of CN-specific IgE for mild, moderate, and severe reactions was 6.17, 1.44, and 1.6 kUa/L respectively. Rance et al. report an overall median as 3.1 kUa/L [1]. IgE values were not significantly different between the patients with mild, moderate, or severe reaction to CN ($p = 0.346$). Ho et al. reported no difference in median IgE value between those who had positive and negative CN OFCs [12].

Three groups of allergenic proteins have been identified and characterised in cashew nut: Ana o 1 and Ana o 2 (cupin superfamily) and Ana o 3 (prolamin superfamily), all classified as major allergens [13] and each individually predictive for the outcome of food challenge tests in cashew-allergic children [14]. Component testing may be more predictive in the clinical setting to guide OFCs. Van der Valk recently published an internally validated diagnostic model for cashew nut sensitised children to identify children who have a > 97% chance of having a positive challenge test [15]. This model incorporates gender and results of SPT and component testing [15].

The majority (44/55, 80%) of children with CN allergy had clinically reacted to another food: 23 egg, 12 milk, 8 hazelnut, 5 peanut, and 3 pistachio; across the entire 102 children in this study, 73% had confirmed peanut allergy. It is probable that CN-specific IgE was performed as part of the workup in this group with suspected peanut allergy and likely accounts for why 43 of those tested had never consumed CN; CN specific IgE was performed to investigate for possible tree nut allergy. Ewan estimated that 30% of patients who are allergic to at least one food in the nut family are allergic to several tree nuts [16].

There is serological and clinical cross reactivity between CN and pistachio [9]; 100% of children with clinical CN allergy were appropriately avoiding pistachios in their diet. Mango is also botanically related to CN; 22/55 children had consumed mango and 3/22 (14%) reported a mild oral allergy symptom. Van der Walk and colleagues reported mango allergy among 7% of their CN-allergic children [8]. There is one case report of mango anaphylaxis in the literature, an adult who was also reported allergic to CN [17]. There is no clear advice at present concerning patients with CN allergy and consumption of mango.

Skin prick testing and oral food challenges

SPT was performed in 56 patients (27 in prior CN reaction, 29 no prior CN exposure). The mean wheal diameter of the positive SPTs was 7 mm (6 mm in CN reaction, 7 mm in no prior CN exposure groups) (range 3–14). Ho et al. report a SPT to CN of ≥ 8 mm predicted a positive food challenge with > 95% accuracy [12].

Cashew nut allergy and atopy

Comparable to peanut allergy, cashew nut allergy is associated with atopy [7]; 76% of those reacting to cashew nut had eczema (65% of those developing it in the first 6 months of life) and nearly half had asthma which is similar to previous reports [1]. CNs were most commonly ingested in a whole nut form (77%) and not incorporated into other foods. CNs are frequently and increasingly hidden in foods such as curries and pesto. Eating at restaurants or buying takeaway meals may be a common source of accidental exposure. It is very concerning that more than 10% of takeaway and restaurant managers and

staff believed that a person with a food allergy can safely consume a small amount of that allergen [18]. Parents should always check the ingredient list every time food is bought as the ingredients of the product may change over time. In Ireland, the Food Safety Authority dictates that all food labels must clearly state if allergens are present. Recent efforts to increase public awareness and strides made in labeling of food products are encouraging.

Of those with clinical reactions, 29 reported having a food allergy action plan. It is concerning that 13% of those with a previous clinical reaction did not have an in-date adrenaline auto injector at home. In studies reporting on fatal cases of anaphylaxis, adrenaline was used in treatment of only 62% of fatal reactions and before arrest in only 14% [19]. Education and training of parents and children on the use of adrenaline auto injectors is a central part of allergy care.

Conclusion

Children are ingesting CN in early childhood. In this study, most parents reported moderate to severe reactions with ingestion of one CN or less and more than half presented with anaphylaxis. Ingestion is most common in the nut form but is also hidden in other foods, e.g. pesto. Children with CN allergy are likely to be atopic with additional food allergies, most notably egg allergy. CN-specific IgE level and SPT wheal size did not predict severity of clinical reaction.

Compliance with ethical standards

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