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ORIGINAL ARTICLE

Pine nut allergy in Korean children: Clinical characteristics and diagnostic values of specific IgE against pine nuts

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Abstract
Background: Hypersensitivity reactions to pine nuts in children have been occasionally encountered recently, although reports on pine nut allergy cases are rare worldwide. The study aimed to feature clinical and laboratory findings pertaining to pine nut allergy in Korean children.
Methods: Forty-two subjects were enrolled through a retrospective review of medical records, from September 2010 to December 2015, at the Department of Pediatrics in Ajou University Hospital. The demographic profiles, clinical characteristics, and laboratory findings were evaluated.
Results: Twenty-four patients showed immediate-type reactions after exposure to pine nuts (the allergic group), while the remaining 18 were atopic controls, who exhibited no allergic symptoms (the tolerant group). The median age of the subjects in the allergic group was three years. More than half of the subjects in this group experienced allergic symptoms within 5 min, and seven of them experienced anaphylaxis. The median level of pine nut-specific immunoglobulin E (sIgE) in the allergic group (1.62 kU_A/L) was significantly higher ($p = 0.014$) than that in the tolerant group (0.11 kU_A/L), with an optimal cut-off level of 0.40 kU_A/L (sensitivity, 66.7% and specificity, 77.8%). The positive decision point of pine nut-sIgE (specificity, 100%) to distinguish the allergic and tolerant groups was 2.84 kU_A/L. However, there was no difference in pine nut-sIgE levels between the anaphylaxis and non-anaphylaxis cases.
Conclusion: About 30% of children with pine nut allergy experienced anaphylaxis. The optimal cut-off level of pine nut-sIgE to distinguish the allergic and tolerant groups was 0.40 kU_A/L and the positive decision point was 2.84 kU_A/L.

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Introduction

A food allergy is a common disease especially in children, with increasing prevalence and a relatively high risk of anaphylactic reactions.[1] Tree nuts, in particular, are a leading cause of severe allergic reactions and the prevalence of allergy to tree nuts is rapidly increasing.[2,3] In addition, allergic reactions to tree nut are often severe, and frequently associated with fatal reactions.[4]

Pine trees (genus *Pinus*) belong to the gymnosperm group and are among the most widely distributed and prominent trees in the world.[5] Pine nuts, the seeds of pine trees, are widely used for human consumption in Europe, America, and Asia. The most common pine nuts produced in Europe come from *Pinus pinea*, while in Korea, they are predominantly from *Pinus koraiensis*.[6] They are used in the preparation of pastries, soup, pasta, salads, and sauces.[7] In Korea, they are consumed either raw or are used as ingredients in a variety of traditional rice cakes, soup and cookies.[8]

Several case reports of hypersensitivity to pine nuts have been published. In most of these cases, severe anaphylactic reactions have been described.[9–13] Even small amounts of pine nuts have been reported to cause dangerous allergic reactions in sensitised patients.[14] The exact prevalence of allergic sensitisation to pine nuts is not known. In a recent study, pine nuts were found to be a cause of anaphylaxis, being responsible for 3% of child-related, food-induced anaphylaxis in Italy.[15] In Korean children and adolescents, pine nuts accounted for 2.3% of food-induced anaphylaxis between 2009 and 2013, as per a large-scale, multi-centre case study,[2] and were the third most common (7.1%) trigger among 126 anaphylactic cases caused by peanuts, tree nuts and seeds.[16]

Several major pine nut allergenic components were identified.[12,17,18] Pine nut allergy seems to be characterised by a high monosensitisation rate [12,14,19] and low immunoglobulin (Ig) E cross-reactivity with other commonly consumed nuts, although cross-reactivity between pine nut and almonds has been described.[10] A few studies have evaluated hypersensitivity to pine nut in patients with clinical symptoms and the level of pine nut-specific immunoglobulin E (pine nut-sIgE).[17,18] However, the relationship between pine nut-sIgE levels and clinical symptoms has not been substantially studied.

The aim of this study is to feature the clinical characteristics and to evaluate the diagnostic values of sIgE in Korean children who have a pine nut allergy.

Materials and methods

Forty-two subjects who underwent serum pine nut-sIgE assay, with a history of ingesting pine nuts, were enrolled through a retrospective review of medical records from September 2010 to December 2015, at the Department of Pediatrics in Ajou University Hospital, Suwon, South Korea. The allergic group ($n = 24$) comprised children with a convincing history of immediate hypersensitivity following the ingestion of pine nuts, recognised by an experienced paediatric allergist using a systematic case report form, while the tolerant group ($n = 18$) comprised children who were atopic controls and who exhibited no allergic reactions following the ingestion of pine nuts. Individual history was not confirmed by oral food challenges. The subjects in the allergic group were further classified into two sub-groups, based on their symptoms: pine nut allergy with anaphylaxis (anaphylaxis group) and pine nut allergy without anaphylaxis (non-anaphylaxis group). Anaphylaxis was diagnosed according to the clinical criteria proposed by the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network.[20] Demographic profiles, clinical symptoms and laboratory findings were recorded. The study was approved by the Institutional Review Board of Ajou University Hospital.

Measurement of the total IgE and sIgE antibody levels

The serum concentrations of total IgE and pine nut-sIgE for all the subjects were analysed by means of ImmunoCAP, following the manufacturer's instructions (Thermo Fisher Scientific, Uppsala, Sweden). The assay had a lower limit of pine nut-sIgE level of less than 0.05 kU_A/L and an upper limit of greater than 100 kU_A/L.

Statistical analysis

The Mann–Whitney *U* test was used for the analysis of continuous variables to compare characteristics and serologic parameters between study groups. A *p*-value of less than 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves were used to assess total IgE and pine nut-sIgE levels for diagnosing pine nut allergy. The area under the curve (AUC) was calculated to quantify the accuracy of the test.

Results

A total of 42 children, between the ages of zero and 15 years (mean age of four years), were enrolled in the study. The study population was highly atopic: 52% had atopic dermatitis and 85% had urticaria. Of the allergic group ($n = 24$), 58.3% were males between the ages of one and 11 years (median age at the time of presenting of symptoms was three years). The characteristics of the all the subjects pointed to a history of food allergy: 81% had a food allergy to other tree nuts and peanuts. These food allergies were confirmed through the convincing history of clinical symptoms with sIgE sensitisation (>0.1 kU_A/L) to other tree nuts and peanuts. The most common tree nut allergies among them were walnut (74%) and almond (57%) allergies, while 45% experienced allergic reactions to peanuts (Table 1).

As for the characteristics of the pine nut allergic reaction, 20 subjects (87%) in the allergic group experienced an allergic reaction on their very first exposure to pine nuts. Most subjects (83.3%) experienced symptoms only once because they strictly avoided pine nuts after experiencing symptoms. All the subjects had a reaction after oral ingestion; reactions have been reported after the consumption of raw pine nuts (75%) as well as in soups (17%), and sauces or cookies (12.5%). The amount of raw pine nuts ingested ranged from one to 15.

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