

Pinus halepensis (Aleppo pine) nuts induced anaphylaxis: a case series

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Pinus halepensis (Aleppo pine) nuts induced anaphylaxis: a case series

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Running title: Anaphylaxis to Aleppo pine nuts

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Main text

Pinus halepensis, commonly known as Aleppo pine, is an evergreen perennial tree distributed in the Northern hemisphere, especially in the Mediterranean area. This pine, which is a medicinal plant with numerous traditional applications, also produces seeds that can be used for culinary purposes¹. A fermented matrix, popularly known as “zgougou” and consisting of a watery mixture of ground Aleppo pine seeds, is traditionally consumed once a year during religious celebrations, particularly in Tunisia². *Pinus pinea*, a member of the same subfamily of pine as *Pinus halepensis* (both are in the Gymnosperms category) produces the pignoli nut, or white pine nut¹, an edible pine seed known for its various uses and commonly used in numerous countries. Allergic reactions to white pine nuts are well documented as mostly severe allergic reactions and high monosensitization rates^{3,4}. Surprisingly, allergy to Aleppo pine nuts, or zgougou, has never been

described, either in monosensitization or in cross-reactivity with white pine nuts. In this article, we present a case series of three Tunisian immigrant patients living in Québec (Canada) who presented anaphylaxis to Aleppo pine nuts.

Patient one is a five-year-old boy who developed rhinorrhea, angioedema, generalized urticaria, rapidly progressing respiratory difficulties and vomiting after his second spoonful of zgougou soup. He was treated with intramuscular epinephrine in an emergency department, leading to symptoms resolution within a few hours. All ingredients of the home-made soup, except for zgougou, and all nuts other than pine nuts were tolerated after this reaction. A year earlier, the last time the boy ate zgougou, he experienced swollen lips, conjunctival erythema, and urticaria. His symptoms were relieved with cetirizine alone. Skin prick-to-prick testing showed a positive response to pure zgougou paste and ground white pine nuts and serum-specific IgE for white pine nuts were also positive [Table 1]. The parents were almost certain their boy had tolerated white pine nuts between the two anaphylactic reactions to zgougou. Considering the discrepancy between the history and the positive skin test, an oral food challenge with white pine nuts was conducted and resulted in an anaphylactic reaction (urticaria, sneezing, nasal discharge, vomiting), which was treated with epinephrine.

Patient two is a 16-month-old girl who developed cough, dyspnea and vomiting within 10 minutes following ingestion of mixed nuts including white pine nuts. Minutes after, she developed swollen lips and urticaria. At the emergency department, she received two doses of epinephrine, diphenhydramine and prednisolone for recurrence of rash and dyspnea 30 minutes after the first dose of epinephrine. Two months later, she presented dyspnea and vomiting twice within 10 minutes of zgougou ingestion. Angioedema and urticaria occurred minutes later. She received one dose of epinephrine, which resulted in rapid resolution of symptoms. Skin prick and prick-to-prick testing [Table 1] showed a positive response to white pine nut extract, ground white pine nuts and pure zgougou paste. As well, skin prick testing showed a response of 4 mm for cashews extract, 2 mm for pistachios extract and negative for other nuts extracts (walnut, pecan, almond and hazelnut). Serum-specific IgE for white pine nuts were positive [Table 1]. Serum-specific IgE for almonds, hazelnuts, cashews, Brazil nuts, macadamia nuts, pecans, and pistachios were all negative. An oral food challenge with cashews was conducted and was well-tolerated, confirming an isolated allergy to white pine nuts.

Patient three is a four-year-old girl who developed swollen lips, peribuccal erythema, sneezing, vomiting, urticaria and dysphagia within minutes of ingestion of pesto (pistachio and white pine nuts). She was rapidly treated with diphenhydramine and her symptoms were resolved on arrival at the emergency room, except for persistent sneezing. She did not receive epinephrine. Two months later, she ate two spoonfuls of zgougou and presented cough, respiratory distress and dysphagia. She received a total of four doses of epinephrine, methylprednisolone, diphenhydramine and was observed overnight in the emergency room. Skin prick and prick-to-prick testing showed a positive response to white pine nut extract and pure zgougou paste and serum-specific IgE for white pine nuts were positive [Table 1].

These three cases involved IgE-mediated severe anaphylactic reaction to Aleppo pine nuts, which prompted an allergological assessment. All three children were Tunisian immigrants and presented with typical clinical manifestations of anaphylaxis and showed a positive skin test to the zgougou product. To our knowledge, no other cases of Aleppo pine nut allergy have been published. In addition, severe anaphylaxis reaction has been described in relation to other pine nuts from the same subfamily, namely *Pinus pinea* ^{3,4}.

Each patient also had an anaphylactic reaction to white pine nuts, with positive skin test, and positive serum-specific IgE for white pine nuts suggesting a cross-reactivity between Aleppo pine nuts and white pine nuts. We hypothesize that this immunological cross-reactivity is due to the substantial homology these two nuts share, being from the same pine subfamily. In fact, pine seed allergens have not been well described and, specifically, allergenic proteins from *Pinus halepensis* have never been studied. So far, only Pin p 1 from the white pine nut has been identified. This allergen is recognized by 75% of patients presenting with an allergic reaction to *Pinus pinea*, indicating that other proteins might be implicated⁵. In addition, cross-reactivity has been found between different pine nuts, namely, the Korean pine nut (*Pinus koraiensis*)⁶ and the Swiss stone pine nut (*Pinus cembra*)⁷. Of note, only 29% of the serum of patients allergic to white pine nuts recognizes the Korean pine vicilin, Pine k 2⁶. Cross-reaction with other tree nuts (angiosperms) is normally

low or absent, showing that pine nut allergy is characterized by a high degree of monosensitization. All three patients show monosensitization to pine nuts, which is consistent with the results presented in other publications^{3,4}.

In summary, this is the first report of IgE-mediated allergy to Aleppo pine nuts. Further studies to characterize pine nut allergens, especially Aleppo pine nut allergens, would be important to better understand cross-reactivity among the different pine nuts and their distinct clinical presentation. Allergists and patients must be aware that Aleppo pine nut allergy exists, and we believe that other pine nuts, if part of the local diet, should be tested to assess possible cross-reactivity. This article also stresses the importance for allergists to be sensitive to cultural differences in nutrition and to look for hidden allergens to counsel their patients. Finally, it would be interesting to compare the prevalence of this allergy among immigrant and local populations, to assess the impact of diet on the development of pine nut allergy.

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Impact statement

Our article presents the first cases of IgE-mediated allergy to Aleppo pine nuts with cross-reactivity with white pine nuts. We believe that this article should be of interest to both current and future generations of allergists, firstly to acknowledge the existence of this allergy and secondly to consider the cross-reactivity between Aleppo pine nuts and white pine nuts.

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Table

Table 1 Investigation of patients	Table 1 Investigation of patients	Table 1 Investigation of patients	Table 1 Investigation of patients	
Patient	One	Two	Three	Three
Skin prick-to-prick test, mm Zgougou paste Ground white pine nut	11 7	8 10	19 NA	19 NA
Skin prick test, mm White pine nut extract	NA	10	14	14
Total IgE, kUI/L N<60	157	587	581	581
White pine nut specific IgE, kUA/L N<0.35	1.73	1.07	49	49
<i>Skin test readings taken at 15 min were evaluated by comparing the wheal induced by the offending food and by a positive control of 10 mg/ml of histamine and a negative control of saline. A positive response was interpreted when the induced wheal was [?] 3 mm compared to the negative control. NA : not available</i>	<i>Skin test readings taken at 15 min were evaluated by comparing the wheal induced by the offending food and by a positive control of 10 mg/ml of histamine and a negative control of saline. A positive response was interpreted when the induced wheal was [?] 3 mm compared to the negative control. NA : not available</i>	<i>Skin test readings taken at 15 min were evaluated by comparing the wheal induced by the offending food and by a positive control of 10 mg/ml of histamine and a negative control of saline. A positive response was interpreted when the induced wheal was [?] 3 mm compared to the negative control. NA : not available</i>	<i>Skin test readings taken at 15 min were evaluated by comparing the wheal induced by the offending food and by a positive control of 10 mg/ml of histamine and a negative control of saline. A positive response was interpreted when the induced wheal was [?] 3 mm compared to the negative control. NA : not available</i>	