



Disponible en ligne sur

ScienceDirect
www.sciencedirect.com

Elsevier Masson France

EM|consulte
www.em-consulte.com



Case report

Is pine nut an emerging allergen? Clinical case and literature review

G. Dutau

9, rue Maurice Alet, 31000 Toulouse, France

ARTICLE INFO

Article history:

Received 18 December 2019

Accepted 12 January 2020

Available online xxx

Mots clés :

Allergie alimentaire

Anaphylaxie

Allergènes

Allergène émergent

Pignon de pin

ABSTRACT

Although the first reports of pine gable allergy are old, they total just over 50, despite the fact that a few series have been described, and despite the fact that pine nut consumption is common in southern Europe. The description of a new case in a 3-year-old girl, manifested by symptoms of anaphylaxis associated with gastrointestinal signs, prompted an exhaustive review of the literature. Pine nuts should be considered an emerging allergen requiring monitoring since it is present in many food preparations, particularly cakes, ice creams, confectionery and various sauces and seasonings.

© 2020 Elsevier Masson SAS. All rights reserved.

1. Introduction

The first case of food allergy to pine nuts was reported in 1958 by Santos and Unger [1] and the second (although often considered the first) was reported by Aaron Fine [2]. Although pine nuts are fairly common, especially in southern Europe, only 9 cases had been described in the literature up to 1998 [3]. For 20 years, the number of cases increased, and pine nuts may currently be considered as an emerging allergen [4].

2. Clinical case

Claudia T. is a 6-year-old Andorran girl. Since the age of 3 years, she has experienced recurrent episodes of wheezing associated with viral infections from October to January. Apart from these episodes, her respiratory status is excellent, especially during exercise in cold weather, since she enjoys skiing without any significant discomfort from January to February. Her parents reported three clinical events suggesting a food allergy.

At the age of 4 years, during the summer, while walking in a pine forest, her parents gathered pine cones lying on the ground in order to remove the pine nuts for consumption, which is a common cultural habit in the country. After eating one or two pine nuts, the girl developed edema of the lips and an itchy mouth, urticaria of the face, eye edema and respiratory discomfort. A few minutes later, she experienced nausea and vomiting, after which she was given epinephrine. All symptoms disappeared following

oral administration of anti-histamines and steroids. At that time, she did not receive epinephrine.

One year later, within a few minutes of eating a cake containing pine nuts, she again developed oral allergy syndrome (OAS) with pruritus of the lips, palate and uvula, respiratory discomfort and angioedema of the face. The symptoms disappeared once more after vomiting.

The last episode of anaphylaxis took place a year later, while she was staying at the house of a relative unaware of her allergy to pine nuts. After eating a dish seasoned with a sauce prepared using crushed pine nuts, according to a local recipe, Claudia developed the same symptoms as during the two previous episodes, and these again regressed after vomiting.

The family history showed biparental atopy (allergic rhinitis). The child's weight and height were in the normal range (20 kg for 114 cm). Her clinical examination was normal.

Since the child's skin reacted to codeine phosphate (4 mm × 20 mm) and histamine hydrochloride (4 mm × 20 mm), skin prick tests (SPTs) for common allergens were positive only for *Dactylis glomerata* and *Timothy grass* (3 mm × 15 mm) (results given according to papule/erythema area in mm). An SPT for pine pollen (*Pinus sylvestris*) was negative. SPTs for the usual foods were all negative, except for pine nut (15 mm × 35 mm), with pseudopodium and pruritus (Fig. 1). There was no cross-reactivity with legumes (peanut and lupin) or nuts such as almonds, walnuts, hazelnuts, Brazil nuts, cashews, pecan and pistachio.

The serum IgE (IgEs) assay confirmed the SPT results showing significant levels for *Dactylis* (2.80 IU/mL) and *Timothy grass* (2.24 IU/mL) pollen and, most importantly, high positivity for pine nuts (90.10 IU/mL). IgEs directed against mites, *Alternaria*, pine pollen and peanut were undetectable.

E-mail address: guy.dutau@wanadoo.fr

<https://doi.org/10.1016/j.reval.2020.01.004>

1877-0320/© 2020 Elsevier Masson SAS. All rights reserved.

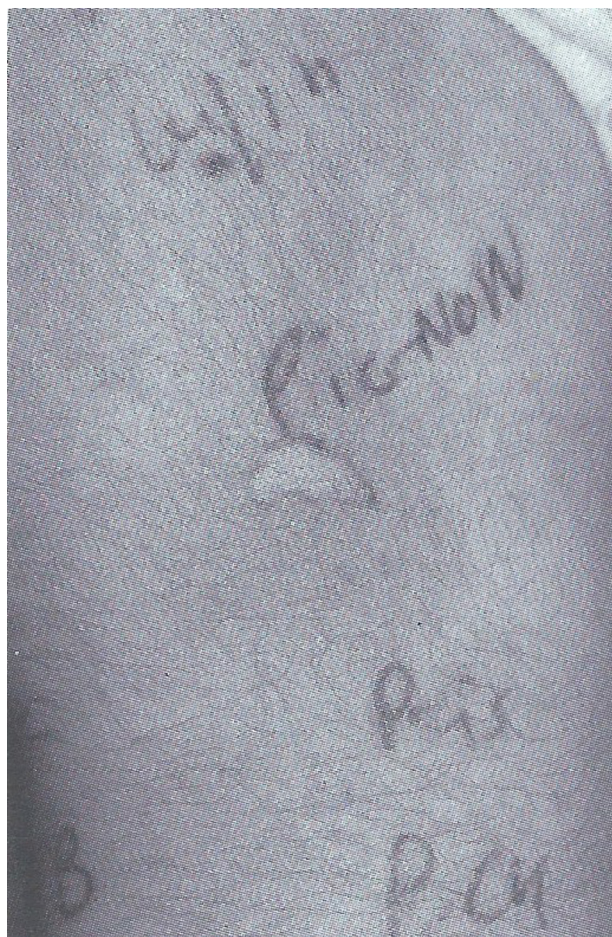


Fig. 1. Skin prick test to fresh pine nut: strong positivity (15 mm × 35 mm).

Respiratory function was slightly impaired, with a 20%–25% decrease in FEV₁ and PF vs. the expected values, but this was fully reversible after inhalation of 2 puffs of a short-acting bronchodilator.

In conclusion, this 6-year-old girl had a pine nut allergy associated with episodes of anaphylaxis, that occurred very quickly after ingestion of the offending nut. This clinical case was recorded before the consensus on anaphylaxis management proposed in the last 15 years and, at the time, should have prompted the prescription of intramuscular epinephrine. However, the presentation was unusual because of the gastrointestinal symptoms (nausea and vomiting), which in each case preceded rapid improvement of the systemic symptoms. Strict avoidance of pine nuts was advised. A kit containing corticosteroids and injectable epinephrine was prescribed, as well as a plan of action in the event of a further episode. There was no recurrence of allergy to pine nuts. In this case, as in those of the literature, there was no sensitization to pine pollen. In the presence of broncho-obstructive syndrome and respiratory symptoms in autumn and winter, given that asthma (or its equivalents) are risk factors for the severity of anaphylaxis, background treatment with inhaled corticosteroids was prescribed.

3. Discussion

The pine nut is the fruit of the pine, a member of the order of conifers. This order contains over hundred species growing in Europe, especially in the Mediterranean region, but also in Mexico and the United States. The main ones are *Pinus pinea* (Europe), *Pinus edulis* (United States), and *Pinus cembra* (Central Europe). The

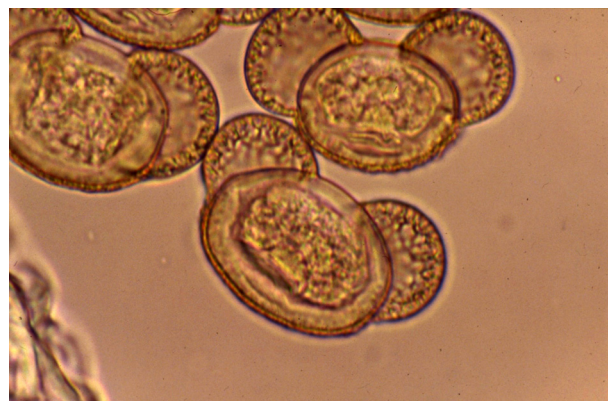


Fig. 2. Pine pollen (*Pinus sylvestris*). Typical aspect of this pollen with two lateral ornaments.

pollination period varies according to the different regions, usually from March to July. Pine pollen is a “heavy pollen”, measuring up to 200 microns or more (Fig. 2), and is thus unlikely to be airborne. A study carried out in the Bordeaux region, where the maritime pine (*Pinus pinaster*) is highly prevalent, has shown that sensitization to this pollen occurred in 1.9% of the study population (persons referred for pneumology-allergy consultations), especially (3%) in atopic subjects. Pine pollen sensitization has always been part of poly-sensitization programs in patients with asthma and/or rhinoconjunctivitis. These subjects had no particular phenotype, and mono-sensitization or mono-allergy to pine pollen has never been observed [5].

The cone-shaped fruit has woody scales with two seeds or pine nuts on their upper surface (Figs. 3 and 4). Each pine cone contains some 100 pine nuts. After breaking the bark, an oblong fruit is found, high in fat (60%), also containing protein (15% to 30%), carbohydrates (15% to 30%) and fibers. An oil can be obtained through pressing.

The first clinical cases were isolated [1,2] after which more and more case series were reported. Until 1996, it may be estimated (see 6) that fewer than 10 cases had been published [1,2,6–8]. After 1990, series of 3 to 5 or more cases were reported [6,8–12].

In 2012, the largest series was described by Moreigne and Bourrier [13]. They reported 10 clinical cases of food allergy to pine nuts reported over a period of 8 years in children aged from 18 months to 17 years. The diagnosis was based on an evocative clinical history, SPTs and positive serum IgE assays. The 10 children generally had their first symptoms between the ages of 5 and 8 years, with the youngest having developed angioedema at 18 months after sucking a pine nut. Eight of the 10 children had a personal and/or family history of atopy. The trigger food was raw pine nuts in 7 cases and in two cases pine-nut allergens were present in a pesto sauce. In this series, SPTs were strongly positive with a commercial extract (induration of 6 × 8 mm at 15 × 17 mm) as well as IgE assays (0.56 Ku/L at > 100 Ku/L) [13]. Two children were sensitized to several nuts. An oral challenge test (OCT), performed in patients with a history of multiple allergies, was positive for a cumulative dose of 1.941 grams [13]. Unlike many cases published in the literature where the symptoms are described as severe to very severe, they were less intense in this series and comprised urticaria, angioedema, abdominal pain and oral allergy syndrome (OAS). This difference may be explained by recruitment bias, homogeneous and rigorous semiological analysis, and/or possible overestimation of the symptoms of grade 2 anaphylaxis by certain authors. As in our case, gastrointestinal symptoms were seen and the clinical presentation improved after vomiting, with the allergen being present in the stomach prior to systemic passage. Perhaps it is also a particular phenotype of food allergy.



Fig. 3. *Pinus* (*Pinus edulis*): Detail of a pine branch (leaves and needles commonly inserted by couple) bearing pine nuts.

In 2014, Pralong et al. [14] reported 20 cases to the Allergo Vigilance Network of CICBAA (Center for Clinical and Biological Investigations in Food Allergology) between 2002 to 2013. These 20 subjects aged from 2 to 63 years (median: 20 years) had anaphylaxis, 10 were grade 3 (anaphylactic shock) and 10 were grade 2 (dyspnea with or without angioedema or urticaria). They were more often male (13 out of 20). Pine nuts were consumed 6 times in the raw form and 14 times within a dish (pastry, salad, pasta seasoning). This food allergy seems to chiefly affect young people since 14 patients were under 20 years old (mean: 11 years). Pralong et al. [14] also indicate that pine nut sensitization may be facilitated by pine pollen pollinosis, but this was not the case for our patient. The literature analysis shows, moreover, that pine pollen sensitization is extremely rare in patients with a food allergy to pine nuts.

In Spain, pine nut allergy is most often isolated, with 70% of cases corresponding to mono-sensitization, which causes severe symptoms in 80% of cases [12]. In the study by Cabanillas et al. [12] proteins of 6 kDa (albumin) and 50 kDa (vicillin) were purified and identified. In an anecdotal case, a patient with bird-egg syndrome became sensitized through nibbling the pine nuts with which she fed her parakeets [15].

Several studies are dedicated to “pine mouth syndrome” or “pine mouth”, which is characterized by the onset of ageusia marked by a bitter metallic taste a few hours after the consumption of American

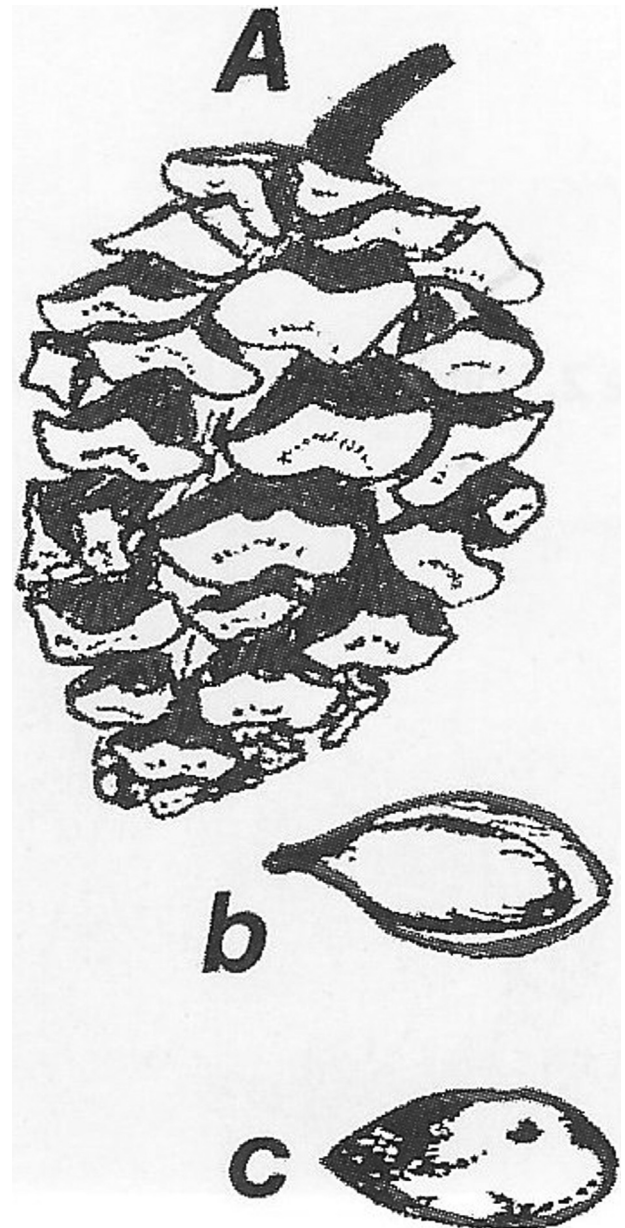


Fig. 4. Pin (*Pinus edulis*): pine nut or fruit presenting with conical-shaped shell (A). Each shell (b) holds two nuts on its upper side (c).

or Asian pine nuts which lasts for 8 to 15 days before disappearing without sequelae [16–19]. The pine nuts from these pines (in particular *Pinus armandii* and *Pinus massoniana*) are not edible. This form of cacoecia is known as metallogueusia (a sensation of metallic bitterness in the mouth), and is sometimes associated with abdominal pain, diarrhea [16], dry mouth and tonsillar swelling [18]. Flesch et al. [19] found reports in French poison control centers of 3111 cases of oral bitterness following ingestion of pine nuts between March 13, 2008 and January 31, 2010. In 2009, the frequency of this symptom increased from May, reaching a peak of 697 cases in August. Both raw and cooked pine nuts were involved. The toxin that found in inedible pine varieties has not been properly identified. In practice, it is essential to avoid eating pine nuts gathered in the wild.

4. Conclusion

Some 60 cases at least of pine nut food allergies have been published in the literature since the Santos and Fine index cases [1,2].

This food allergy is neither a new allergy, nor really an emerging allergy. However, as shown by several recent studies [1,13], the pine nut is an allergen that must be placed under surveillance since it can cause moderate to severe symptoms. The occurrence of severe symptoms while performing SPT is an argument for handling this allergen with great caution [20–22].

Disclosure of interest

The author declares that he has no competing interest.

References

- [1] Santos IM, Unger I. Severe allergic reaction to pignolia nut. *Ann Allergy* 1958;16(4):459–61.
- [2] Fine AJ. Hypersensitivity reaction to pine nuts (Pinon nuts, Pignola). *Ann Allergy* 1987;59(3):183–4.
- [3] Rubira N, Botey J, Eseverri JL, Marin A. Allergy to pine nuts in children. *Allerg Immunopathol (Madrid)* 1998;30(7):212–6.
- [4] Dutau G, Lavaud F. Le pignon de pin: allergène nouveau? Allergène émergent? *Rev Fr Allergol* 2014;54(2):41–3.
- [5] Nocent C, Raherison C, Portel L, et al. Étude de la sensibilisation au pollen de pin maritime (*Pinus pinaster*) dans la région bordelaise. *Rev Fr Allergol* 2005;45(4):298–302.
- [6] Pétrus M, Faucé J, Bouchet H, Dutau G. Allergie au pignon de pin: trois nouvelles observations et analyse de la littérature. In: Dutau G, editor. « Actualités en allergologie et en pneumologie pédiatrique ». Collection « Références en pédiatrie ». Paris: Elsevier Édition; 2002. p. 145–53.
- [7] Armentia A, Quintero A, Fernández-García A, et al. Allergy to pine pollen and pinon nuts: a review of three cases. *Ann Allergy* 1990;64(1):49–53.
- [8] Nielsen NH. Systemic allergic reaction to pine nuts. *Ann Allergy* 1990;64(2 Pt 1):132–3.
- [9] Roux N, Hogendijk S, Hauser C. Severe anaphylaxis to pine nuts. *Allergy* 1998;53(2):213–4.
- [10] Rubira N, Botey J, Eseverri JL, Marin A. Allergy to pine nuts in children. *Allerg Immunol* 1998;30(7):212–6.
- [11] Novembre E, Mori F, Barni S, Ferrante G, et al. Children monosensitized to pine nuts have similar patterns of sensitization. *Pediatr Allergy Immunol* 2012;23(8):762–5.
- [12] Cabanillas B, Cheng H, Grimm CC, et al. Pine nut allergy: clinical features and major allergens characterization. *Mol Nutr Food Res* 2012;56(12):1884–93.
- [13] Moreigne M, Bourrier T. Allergie au pignon de pin chez l'enfant. *Rev Fr Allergol* 2012;52(3):250.
- [14] Pralong P, Moneret-Vautrin DA, Pirson F, et al. Anaphylaxie au pignon de pin: à propos de vingt cas déclarés au Réseau Allergo Vigilance. *Rev Fr Allergol* 2014;54(2):61–5.
- [15] Jansen A, Vermeulen A, Dieges PH, van Toorenenbergen AW. Allergy to pine nuts in a bird fancier. *Allergy* 1996;51(10):741–4.
- [16] Munk MD. Pine mouth (pine nut) syndrome: description of the toxidrome, preliminary case definition, and best evidence regarding an apparent etiology. *Semin Neurol* 2012;32(5):525–7.
- [17] Hampton RL, Scully C, Gandhi S, Raber-Durlacher J. Cacogeusia following pine nut ingestion: a six patient case series. *Br J Oral Maxillofac Surg* 2013;51(1):e1–3.
- [18] Ballin NZ. A trial investigating the symptoms related to pine nut syndrome. *J Med Toxicol* 2012;8(3):278–80.
- [19] Flesch F, Rigaux-Barry F, Saviuc P, Garnier R, et al. Dysgeusia following consumption of pine nuts: more than 3000 cases in France. *Clin Toxicol (Phila)* 2011;49(7):668–70.
- [20] Van de Scheur MR, Bruynzeel DP. Acute anaphylaxis after pine nut skin testing. *Ann Allergy Asthma Immunol Off Publ Am Coll Allergy Asthma Immunol* 2004;92(1):93.
- [21] Tosca MA, Olcese R, Ciprandi G, Rossi GA. Acute anaphylactic reaction after prick-by-prick testing for pine nut in a child. *Allergol Immunopathol* 2012;41(1):67.
- [22] Bouvier M, Halpern SJ, Brunet JL, Berard F. Allergie sévère au pignon de pin chez l'adulte avec réaction systémique au prick-test. *Rev Fr Allergol* 2012;52(3):2–54.