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Allergic Reaction to Undeclared Lupin in a Chocolate

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Palabras clave: Alergia a lupino. Alérgenos ocultos. Alérgenos no declarados.

Although lupin (*Lupinus albus*) has been consumed as a snack for many years, it has only recently been introduced as a cereal substitute by the food industry. Its growing use has been accompanied by reports of allergic reactions, including respiratory symptoms after lupin inhalation and local or generalized reactions following ingestion [1]. Attempts to determine population threshold doses for lupin that elicit allergic reactions have been unsuccessful due to considerable interpatient variability [2]. Because of these difficulties and increasing reports of allergic reactions to lupin, the 2006 European Commission Directive included lupin in its mandatory labeling list, whereby lupin must always be listed as a food ingredient, irrespective of the amount present [3].

We report the case of a 30-year-old atopic woman who developed an itchy throat, cough, and shortness of breath shortly after eating a pepper and lemon chocolate. The symptoms disappeared in 2 hours with an oral antihistamine. The patient had never experienced oral pruritus after the ingestion of any food. One week before the reported reaction she developed mild urticaria affecting the arms and legs that subsided within 24 hours. She could not relate this reaction to the ingestion of any specific foods. The skin prick test was positive for cat dander (mean wheal diameter, 8 mm), dog dander (4 mm), grass pollen (6.5 mm), lupin (15 mm) and soybean (3.5 mm), and negative for milk, celery, egg, mustard, sesame, wheat, *Anisakis simplex*, latex, peach, tomato, tree nuts, peanut, legumes, mites, molds, and weed and tree pollens (Laboratorios Leti). The prick-prick test was positive for lupin (10 mm) and the pepper and lemon chocolate (5 mm). The serological study (ImmunoCAP, ThermoFisher Scientific Phadia) showed specific IgE (sIgE) for lupin (42.2 kU_A/L), chickpea (3.12 kU_A/L), vetch (0.90 kU_A/L), and carob (0.68 kU_A/L). sIgE levels were under 0.35 kUa/L for celery, sesame, pepper, Pru p 3, tree nuts, peanut, and other legumes. Total IgE and baseline tryptase levels were 85.9 and 2.22 kU_A/L, respectively.

The patient had eaten the pepper and lemon chocolate from a box of assorted chocolates. The labeled ingredients were cocoa, soy lecithin, milk, egg, sugar, sorbitol, honey, lemon essence, cayenne pepper, and unspecified flour. The

manufacturer denied the use of lupin in both the pepper and lemon chocolate and other foods processed nearby. Between the time of the reaction and her visit to our department, the patient had followed a normal diet and tolerated chocolate, lemon and other fruits, peanut, soybean, lentils, and sunflower seed. An open oral challenge excluded clinical reactivity to chickpea.

Lupin and the culprit chocolate were extracted as previously described [4] and SDS-PAGE was carried out under reducing conditions. Polyacrylamide concentrations of 14% (wt/vol) and 5% (wt/vol) were used for the separating and stacking gels, respectively. Twenty micrograms of protein extract was applied per lane and protein electrophoresis was performed for each extract. The separated proteins were transferred to nitrocellulose membranes for immunoblot analysis according to the method described by Benito et al [5]. The blocked membranes were washed and cut into strips for separate incubation with untreated patient serum, or serum previously incubated with either lupin or chocolate as previously described [6]. The strips were then washed and incubated with anti-human IgE antibody conjugated with horseradish peroxidase (SouthernBiotech). Finally, the presence of IgE-binding bands was visualized by enhanced chemiluminescence (GE Healthcare) following the instructions provided by the manufacturer. Serum binding to proteins exhibited a similar pattern in both extracts (Figure, A,B, lane 1). Serum preincubation with none of the extracts was able to inhibit the recognition of bands in both the lupin and chocolate extracts (Figure, lanes 4 and 5). Serum preincubation with bovine serum albumin did not affect band recognition in the lupin extract (Figure, lane 3), and serum from a negative control individual was not able to bind proteins in the lupin extract (Figure, lane 2).

Since the patient had experienced the reaction after the ingestion of an "unconventional" chocolate, and had previously developed mild self-limited urticaria, we decided to investigate clinical reactivity to lupin and explore its potential severity by means of a double-blind placebo-controlled food challenge (DBPCFC). Because of the risk of a reaction after the ingestion of, for instance, a lupin-containing spicy food that could induce confusing oral symptoms, we decided to skip the oropharyngeal mucosa by administering encapsulated lupin flour. This could trigger severe reactions, but also provides important information for risk management decisions. The patient was fully informed and provided written consent. The DBPCFC was performed by trained staff, with full equipment and medication readily available. An intravenous line was inserted. Lactose-filled capsules were prepared as placebo and increasing amounts of lupin flour were introduced into identical capsules for the up-dosing challenge protocol (0.5, 1, 3, 10, 30, 100 and 300 mg). The patient tolerated the placebo but developed epigastralgia, generalized urticaria, and conjunctivitis 20 minutes after the ingestion of the 300-mg lupin capsule (cumulative dose of 444.5 mg). The symptoms disappeared within 3 hours of the administration of intramuscular epinephrine plus intravenous antihistamines and corticosteroids. A significant increase in serum tryptase was observed, from 3.7 kU_A/L at the beginning of the reaction to 7.41 kU_A/L at 60 minutes and 16.0 kU_A/L at 120 minutes. The diagnosis of lupin allergy was established and a lupin-free diet was recommended. The patient was advised to read all food labels carefully and to carry rescue medication including self-injectable epinephrine. At the time of writing, the patient is still on a lupin-free diet and has had no further reactions.

According to the chocolate box label, flour was one of the ingredients. The use of lupin was denied by the manufacturer, without any further specifications. As the immunological study revealed full cross-reactivity of the patient's serum with both lupin and chocolate extracts, we think that this unspecified flour was lupin flour. The dose that elicited the reaction during the challenge was within the range previously reported for lupin [7]. In this case, lupin behaved as a hidden allergen [8]. This report reveals that despite current regulation, it appears that there are still manufacturers that do not report the presence of lupin as an ingredient and also emphasizes the need for adequate control of food production, manipulation, and labeling processes.

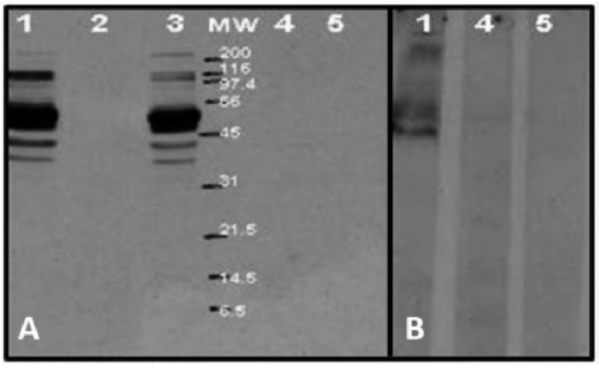

Figure. Immunoblot analysis of lupin (panel A) and chocolate (panel B) extracts. Lanes 1, Patient's serum (noninhibited). Lane 2, Negative control. Lane 3, Patient's serum inhibited with BSA. MW, Molecular weight markers (kDa). Lanes 4, Patient's serum inhibited with lupin extract. Lanes 5, Patient's serum inhibited with chocolate extract.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Anaphylaxis in a Child After Ingestion of Persimmon

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Palabras clave: Alergia alimentaria. Proteína de transferencia de lípidos. Caqui. Saroni.

Persimmon is a tropical fruit belonging to the Ebenaceae family. It is thought to have antioxidant properties owing to its high content in flavonoids and vitamins A, C, and E. The different varieties of persimmon are classified according to whether they are astringent or not. The nonastringent variety includes Sharon fruit (*Diospyros kaki*). Allergy to this fruit is extremely rare.

We present the case of an 8-year-old boy who was referred to our clinic in December 2011 because he had experienced pruritus, generalized itching, urticaria, labial and palpebral edema, dyspnea, and wheeze while eating Sharon fruit. He had not developed gastrointestinal symptoms or hypotension. He required emergency treatment (inhaled salbutamol, intramuscular adrenaline, dexchlorpheniramine, and intravenous prednisone), which led to resolution of symptoms.

Until then he had eaten persimmon without problems and tolerated banana, avocado, kiwi, chestnut, and peach, as well as other fruits and nuts. He also tolerated contact with latex.

The patient had had rhinoconjunctivitis due to pollen sensitization since the age of 3 years that was being treated with oral antihistamines on demand. He had never received pollen-specific immunotherapy and was not exposed to animals at home.

Skin prick testing was performed with commercial extracts of the most common local pollens, profilin, standardized peach lipid transfer protein (LTP) (ALK-Abelló), fruits, nuts (Leti), and latex. The results were positive for grasses, cypress, plane tree, *Plantago, Artemisia, Chenopodium*, cat dander, standardized peach LTP, avocado, and chestnut. Prick-prick testing with persimmon was positive with both the peel (10 mm) and the flesh (22 mm).

Total IgE was 517 kU_A/L. Specific IgE testing (sIgE) (CAP System, Phadia Thermo Fisher) was performed with the following allergens: plane tree (5.30 kU_A/L), avocado (2.52 kU_A/L), kiwi (3.91 kU_A/L), chestnut (10.00 kU_A/L), and latex (0.48 kU_A/L). sIgE results for recombinant allergens of *Phleum pratense* were as follows: rPhl p 1, 20.70 kU_A/L and rPhl p 5, rPhl p 7 (polcalcin), and Phl p 12 (*Phleum pratense* profilin), <0.35 kU_A/L. sIgE for peach LTP (Pru p 3) was 53.40 kU_A/L.

A persimmon extract was obtained in order to investigate the allergens recognized by the patient. The peel was separated from the flesh and each sample was lyophilized separately.