Anaphylaxis to Sunflower Seed With Tolerance to Other Nuts: The Role of Lipophilic Allergens

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Sunflower (*Helianthus annuus*) belongs to the genus of the Asteraceae plant family (Compositae). Sunflower seeds are consumed throughout the world, and patients who are allergic to other nuts usually tolerate them.

Sunflower seed allergy is rare. Very few cases of anaphylaxis after ingestion have been described [1-5], with most involving an occupational origin in exposed workers [2,4].

Several allergenic proteins have been identified in sunflower seeds [1,3,4,6] and are documented by the World Health Organization/International Union of Immunological Studies Allergen Nomenclature Sub-Committee [www.allergen.org], as follows: Hel a 1 (34 kDa, a major inhaled allergen with no specific protein family described to date); Hel a 2 (a 14.7-kDa profilin); Hel a 3 (a 9-kDa lipid transfer protein [LTP], food allergen); and Hel a 6 (a 42-kDa pectate lyase, inhaled allergen). Others, such as Hel a 2S albumin (16 kDa), a 12-kDa storage protein that appears to be the mature form of Hel a 2S albumin, and a 13-kDa LTP, have also been described as potential allergens in other publications [1,5,6].

We present a case of anaphylaxis after ingestion of sunflower seeds in a patient sensitized to other nuts, all of which he tolerated.

A 35-year-old man with a personal history of atopy (egg allergy in childhood that resolved and seasonal rhinoconjunctivitis) experienced lingual and palmoplantar pruritus, generalized hives, facial angioedema, conjunctival injection, dyspnea, and intense cough 5 minutes after eating a handful of roasted sunflower seeds (previously well tolerated). He went to the emergency department (blood pressure 128/65 mmHg and baseline $SatO_2$ of 95%) and was treated with intravenous antihistamines and corticosteroids. His condition gradually improved within the following hour. No cofactors were identified.

A series of complementary tests were carried out.

Commercial skin prick tests (ALK-Abelló) were performed with peanut, walnut, pistachio, almond, hazelnut, chestnut, sunflower seed, peach LTP, profilin, mustard, and mugwort. The results were positive only for sunflower seed (12 mm).

Prick-prick test with hazelnut, walnut, peanut, almond, and pistachio. The results were positive only for hazelnut (9 mm) and walnut (7 mm). Sunflower seed was not tested owing to the 12-mm skin prick test result and a moderate initial reaction.

ImmunoCAP (ThermoFisher) revealed the following: total Immunoglobulin E (IgE), 124 IU/mL; specific IgE against sunflower seed, 3.18 kU_A/L; almond, 0.11 kU_A/L; cashew, 0.06 kU_A/L; hazelnut, 0.27 kU_A/L; peanut, 0.14 kU_A/L; walnut, 0.27 kU_A/L; pistachio, 0.18 kU_A/L; and rPru p 3 (peach LTP), 0.01 kU_A/L.

ImmunoCAP ISAC 112 (ThermoFisher) revealed the following: moderate-to-high levels of cypress allergen (Cup a 1), 10.30 ISU; group 1 timothy grass pollen allergens, 2.76 ISU; and *Alternaria* (Alt a 1), 4.90 ISU.

The results were negative for all nut proteins included.

Open oral challenges with roasted hazelnuts and walnut were negative.

The patient tolerated peanuts, almonds, pistachios, and cashews.

Proteins from hydrosoluble and liposoluble fractions of peanut, hazelnut, walnut, and sunflower seed extracts were obtained using SDS-PAGE following the method described by Barbarroja-Escudero et al [7]. After the homogenization and extract centrifugation processes, the liposoluble fraction was separated from the hydrosoluble fraction, and each was treated independently to obtain the aqueous and oil-body extracts [7]. SDS-PAGE of the extracts revealed proteins ranging from 10

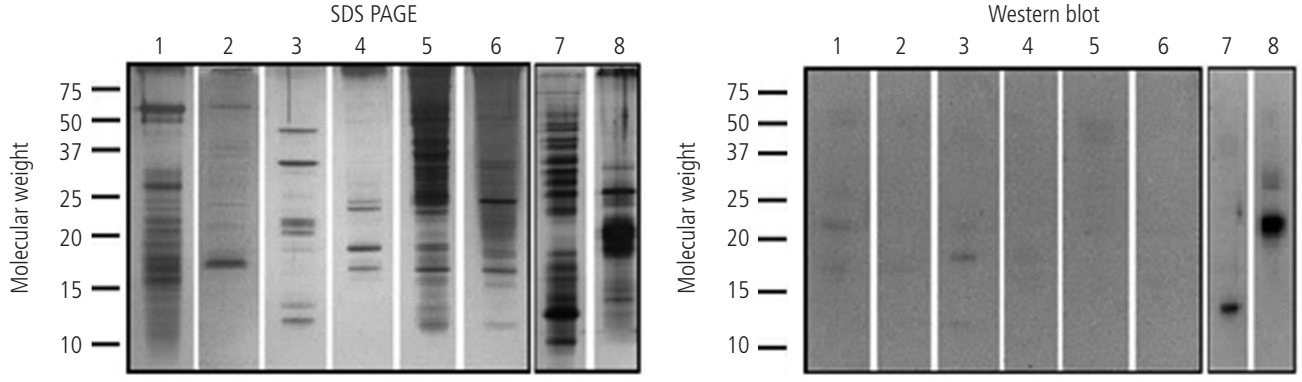

Figure. SDS PAGE and Western blot. 1, peanut hydrophilic fraction; 2, peanut lipophilic fraction; 3, hazelnut hydrophilic fraction; 4, hazelnut lipophilic fraction; 5, walnut hydrophilic fraction; 6, walnut lipophilic fraction; 7, sunflower seed hydrophilic fraction; 8, sunflower lipophilic fraction.

to 50 kDa in the hydrosoluble fraction and from 13 to 75 kDa in the liposoluble fraction.

Immunoblotting with the patient's sera was performed according to the Laemmli method [1,3]. The patient's sera recognized 2 protein bands with an estimated molecular mass of 12-14 kDa in the hydrosoluble fraction and 21-23 kDa in the liposoluble fraction of the sunflower seed extract. These bands were not recognized in other nut extracts.

Allergy to sunflower seeds with tolerance to other nuts is rare. Some allergenic proteins have been thought to cause reactions.

According to previous publications, the 12- to 14-kDa hydrosoluble protein band identified could correspond to a 12-kDa storage protein [1,6], a 13-kDa LTP [5], or a 14.7-kDa profilin (Hel a 2) [3,4,6]. Despite identification of a similar protein band in the hydrosoluble fraction after electrophoresis of peanut, hazelnut, and walnut extracts, which might correspond to profilins [8] (Ara h 5, 14 kDa; Cor a 2, 14 kDa; and Jug r 7, 13 kDa), the severity of the reaction means that Hel a 2 is less likely to be responsible, although this possibility cannot be ruled out. Additionally, the ImmunoCAP ISAC test was negative for all storage proteins, LTPs, PR-10, and profilins of those nuts included. Therefore, primary sensitization to a sunflower seed protein only is unlikely.

Because lipophilic allergens tend to elude standard protein purification procedures, they are not included in aqueous diagnostic extracts [9,10]. Consequently, more hydrosoluble allergens than lipophilic allergens have been identified [3,9]. Both fractions were analyzed in all extracts for a more precise diagnosis regarding the high lipid content reported in nuts and seeds [9,10].

Compared with other nuts analyzed by electrophoresis, significantly more lipoproteins were observed in sunflower seed extract. The few lipoproteins described include oleosins, which are structural proteins that stabilize oil bodies in seeds and nuts [7,9] and have been associated with severe allergic symptoms [3,9,10], such as those presented by the patient.

A protein band with an estimated molecular mass of 21-23 kDa was identified in the liposoluble fraction. This was only recognized in sunflower seed extract during immunoblotting with the patient's sera. This lipoprotein could also be an oleosin responsible for the patient's anaphylactic reaction.

After electrophoresis, all extracts analyzed (peanut, hazelnut, walnut, and sunflower seed) recognized a protein band of 16-17 kDa in the liposoluble fraction. This band might correspond to previously described oleosins such as Cor a 12 (17 kDa), Cor a 13 (14-16 kDa), Ara h 10 (16 kDa), Ara h 14 (17.5 kDa), and Ara h 15 (17 kDa) [8,9]. Although lipoproteins have been postulated as a possible cause of cross-reactivity [9], the patient we report tolerates other nuts, despite the probable presence of oleosins.

These findings support the hypothesis of Barbarroja-Escudero et al [3], which points to the possible involvement of lipoproteins ranging from 17 to 23.5 kDa being potentially responsible for anaphylaxis in patients monosensitized to sunflower seeds. Therefore, we propose that the implication of lipoproteins in cases of allergy to sunflower seeds is probably related to a higher lipid content than for other nuts studied by electrophoresis.

To our knowledge, this is the third report of a monoallergic patient experiencing an anaphylactic reaction after ingestion of sunflower seeds. The probable cause was sensitization to lipoproteins, specifically a 21- to 23-kDa oleosin. As oleosins seem to be a relevant cause of severe allergic reactions to nuts and seeds, we emphasize the need to incorporate lipophilic allergens into routine diagnostics in order to improve risk assessment.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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