

Letter to the Editor

Anaphylaxis caused by hidden soybean allergens in pillows

To the Editor:

Pillow stuffing can contain polyester, feathers, down, or, more recently, soy-based materials. Component-resolved diagnosis and microarray technology might be useful in patients with food-sensitized allergies or anaphylaxis caused by hidden allergens.

We report 4 patients with repeated anaphylaxis, which was defined as a decrease in blood pressure and possibly life-threatening adverse reactions¹ during sleep at home but not in other places. Patient 1 was a 64-year-old woman with previous nocturnal rhinitis who began to experience anaphylaxis during sleep. Patient 2 was a 58-year-old man with progressive rhinitis, asthma, and anaphylaxis after changing his bedroom furniture and bed linen. Patient 3 was a 64-year-old woman with previous sensitization to *Anisakis simplex* and nocturnal pharyngeal angioedema unrelated to eating fish or other sources of *A simplex* who experienced severe anaphylaxis during sleep. Patient 4 was a 69-year-old woman with nocturnal anaphylaxis for 1 year before diagnosis.

All patients had food-related rhinitis and asthma, although the sources were not clear.

Patient 4 also had severe anaphylaxis after eating soy sauce in a Japanese restaurant, which led to our initial suspicion. All patients had negative skin prick test (SPT) responses and IgE determination (ImmunoCAP Assay; Phadia, Uppsala, Sweden) to conventional aeroallergens and foods, including soybean.

The only common finding among these patients was the purchase of a viscoelastic pillow before symptom onset. Information was obtained on the soy oil composition of the pillow matrices, and an allergy study focusing on obtaining the proteins contained within the oil bodies of soybean seeds was performed. Symptoms disappeared after the pillows were removed.

After informed consent, new SPTs with soybean nut, hull, and oil were performed. Specific IgE levels were analyzed by using IgE microarrays (ISAC) and immunoblots with proteins extracted from plant lipid storage bodies (most allergens are obtained through hydrosoluble methods, which remove the lipid derivatives from the allergenic extract) and proteins extracted from the pillow core.

All SPT responses to different nut extracts were negative. Only SPT responses to soybean oil were positive, with a mean wheal major diameter for soy oil of $8 \times 8 \pm 3$ mm. The mean wheal diameter for histamine was 5×5 mm.

Microarray-based IgE detection assay (ISAC) revealed hypersensitivity to β -conglycinin (nGly m 5) in all patients.

Western blot experiments detected serum-specific IgE to several proteins, with molecular masses compatible with the allergens Gly m 5, Gly m 6, and oleosins, and dot blots confirmed these IgE bindings. Sera from all 4 patients showed a positive response to the aqueous fraction and lipoprotein fraction extracts of soybean seeds and the core extract of the pillows. Sera from nonatopic control subjects did not react to any product tested (Fig 1).

Sensitization to soy and soy oil have been described.² Exposure to soy antigens has been associated with asthma in community and workplace outbreaks. Recent evaluation of 135 Tennessee

soy flake-processing workers for immune reactivity to soy showed that allergic sensitization to soy was common and 5 times more prevalent than in control health care workers with no known soy exposure. Nano high-performance liquid chromatography mass spectrometry analysis showed the high-molecular-weight soybean storage proteins β -conglycinin (Gly m 5) and glycinin (Gly m 6) were the proteins that bound soy flake-processing worker IgE.³

Gly m 5 and Gly m 6 might be respiratory sensitizers in occupationally and nonoccupationally exposed workers. Soy protein has shown great potential for use in biobased adhesives. β -Conglycinin, a major component of soy protein, accounts for 30% of the total storage protein in soybean seeds. β -Conglycinin was isolated and purified, and the physicochemical and adhesive properties of its subunits (β and α') were characterized.³ Soy is also used in pharmaceutical products as soymorphins⁴ or drug excipients.²

The diagnostic workup for suspected soy allergy includes food allergy screening tests, responses to an elimination diet, and an oral food challenge. No screening test, alone or in combination, can definitively diagnose or exclude soy allergy. A wider panel of proteins extracted from plant lipid storage bodies called oil bodies^{5,6} in combination with diagnostic microarray methods, including those that focus on immune responses to specific food proteins or protein epitopes, are being studied.

Oral allergy syndrome to soy milk is classified as a phenotype of pollen-food allergy syndrome (PFAS). Gly m 4 (Bet v 1 homolog, 17 kDa) and oleosin (23 kDa) are reported as causative antigens. Recently, 2 cases of PFAS to soy milk have been reported,⁷ with positive reactions to soy milk in SPTs and to Gly m 4 in specific serum IgE antibody assays. Microarray analysis of specific serum IgE antibodies of soy-related proteins showed a positive reaction to Bet v 1 in both cases, and this was diagnosed as PFAS to Gly m 4.

In our patients protein microarray analysis was useful as a screening test for immediate allergy, such as PFAS. The reason for the negative SPT responses and IgE assay results to soy in our patients might be due, in part, to the localization of oleosins (and other as yet uncharacterized proteins) in oil bodies because they are underrepresented or denatured in most diagnostic extracts of nuts and seeds that are usually extensively defatted. The absence or presence of denatured (during defatting) oleosins might provoke a false-negative *in vitro* diagnosis of some nut and seed allergies.⁸ Acidic subunits of glycinin and β -conglycinin, major soybean storage proteins, might be absent or present in much reduced amounts in these techniques. Immunoblotting with sera from patients with soy allergy indicates alteration, reduction, or loss of IgE binding in the commercial extracts compared with extracts of soy flour. Preparation methods appear to be partially responsible for the variable allergen content in commercial soybean SPT extract.⁹

The major limitation of this study was the lack of specific oral challenge with soybean. However, the severity of the anaphylaxis precluded these tests.

In summary, soy is recognized as a common food allergen. IgE antibodies from soybean-sensitive patients recognize more than 15 soybean proteins,⁹ some of which can be found as hidden allergens in pillows. Sensitization to the soybean allergens Gly m 5,

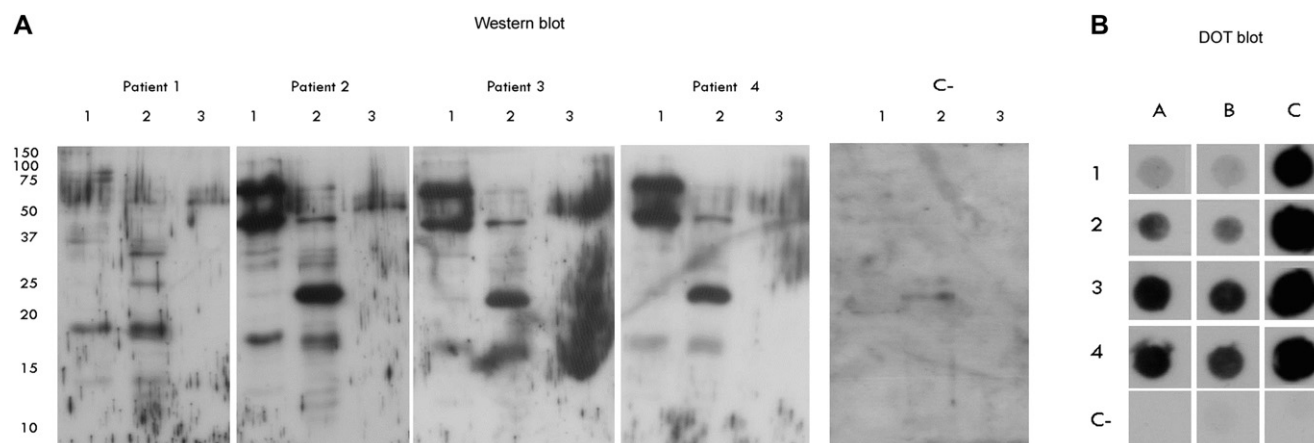


FIG 1. IgE immunoblotting after exposure to soybean seed extracts. **A**, Responses of sera from patients 1 to 4 and a negative control subject (C-). Lane 1, Aqueous fraction of soybean seeds; lane 2, lipid fraction of soybean seeds; lane 3, protein extract from the pillow core. **B**, Responses of sera from patients 1 to 4 to the aqueous fraction (A), lipoprotein fraction (B), and pillow core (C).

Gly m 6, and oleosins is potentially indicative of severe allergic reactions to soy, as in our patients.¹⁰

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