

Fixed drug eruption caused by dimenhydrinate

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Key words: dimenhydrinate; fixed drug eruption; oral challenge; patch test.

• DIMENHYDRINATE is the diphenhydramine salt of 8-chlorotheophylline, and belongs to the ethanolamine group of H₁ antihistamines. It is used in various disorders such as vertigo, motion sickness, nausea, vomiting, and cold symptoms. In view of the frequency of administration, side-effects are rare, sedation being the most frequent one.

We report a fixed drug eruption (FDE) associated with

A case with positive oral challenge and patch test.

dimenhydrinate, in a nonprescription motion sickness medicine, confirmed by positive oral challenge test and patch testing in previously affected skin.

A 66-year-old man had presented erythematous macular lesions on the right subarmpit area, 12 h after he had taken a tablet (50 mg) of dimenhydrinate to prevent motion sickness. The lesions resolved in approximately 20 days.

After written informed consent had been obtained, the patient underwent a single-blind, placebo-controlled oral challenge with dimenhydrinate. He developed two intensely erythematous pruritic lesions, 6 h after taking dimenhydrinate (62.5 mg); one on the right subarmpit area and the other on the right side, below the other lesion.

Two months later, the epicutaneous patch tests were performed on unaffected and affected skin with different H₁ antihistamines. The drugs were prepared at 10% concentration, and the vehicles utilized were petrolatum and dimethylsulfoxide (DMSO). We used dimenhydrinate, doxylamine, ebastine, loratadine, cetirizine, mizolastine, terfenadine, hydroxyzine, and chlorpheniramine. The topical provocation with dimenhydrinate was positive (25×6 mm) on affected areas; all the other H₁ antihistamines tested in both areas gave negative reactions.

Thus, we have documented by oral drug challenge and epicutaneous patch test one of the few case reports of FDE caused by a drug belonging to the ethanolamine group of H₁-receptor antagonists, dimenhydrinate (1-4).

On the basis of the patch test results, we suggest that cross-reactivity does not seem to exist among antihistamines belonging to the same ethanolamine group (for example, doxylamine) and other, chemically unrelated antihistamines.

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Allergenic cross-reactivity in the Liliaceae family

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Key words: asparagus allergy; garlic; Liliaceae; onion; RAST inhibition.

• THE Liliaceae family is divided into two subfamilies: Aliolideae (garlic, onion, chives, and leek) and Asparagoideae (asparagus). Few publications have identified them as causative agents of allergic disorders.

We present two patients with IgE-mediated contact urticaria caused by canned asparagus and investigate the possible cross-reactivity among garlic, onion, and asparagus.

We have studied two patients with an established diagnosis of IgE-mediated contact urticaria caused by cooked white asparagus, as demonstrated by rub test, prick test, and specific IgE. They had a clinical history of rhinoconjunctivitis and asthma due to sensitivity to grass pollens.

Allergenic similarity among asparagus, onion, and garlic is individually recognized.

Patient 1 was a 26-year-old housewife, and patient 2 a 29-year-old woman employed in asparagus canning and production. The patients reported immediate cutaneous symptoms only on handling asparagus, and they tolerated its ingestion. No symptoms related to contact or ingestion of onion and garlic were reported.

The onion and garlic prick-prick tests were done with native material. Fifteen atopic patients without history of allergy to the Liliaceae family were additionally tested by the same procedure.

Allergen-specific antibodies in serum were measured with Pharmacia RAST.

RAST inhibition was done according to Yman et al., as described in Jiménez et al. (1). The solid-phase antigen was obtained by coupling the extract solution (10 mg/ml, 2 mg/disk) to the 6-mm-diameter CNBr-activated paper disks by the method of Ceska and Lundqvist. A volume of 50 µl of serum from patients plus 50 µl of four dilutions (0.01–10 mg/ml) of inhibitor extracts (asparagus, onion, garlic) were added to solid-phase antigen.

In patient 1, prick by prick tests with fresh onion (15 mm) and garlic (13 mm) were positive. The patient's serum contained a high level of garlic- and onion-specific IgE (5.46 and 12.7 kU/l, respectively). Patient 2

showed a positive result in the prick-prick test with native onion (8 mm) and garlic (10 mm) as well as specific IgE (7.28 kU/l for garlic and 12.5 kU/l for onion). All the control subjects presented negative results to garlic and onion by prick-prick test. Table 1 shows the maximal inhibition, in both patients, to onion and asparagus proteins.

Since Henson (2) described the first case of asthma caused by garlic, a number of reports on allergic illnesses induced by garlic (3), onion (4), and asparagus (5, 6) have been published.

Lybarger et al. (3) described a case of occupational asthma caused by inhalation and ingestion of garlic. Through garlic RAST inhibition, they demonstrated cross-reactivity among garlic, onion, and asparagus. Other authors (5) have published two cases of respiratory allergy caused by inhalation of fresh asparagus and through CAP inhibition showed no immunologic cross-reactivity among asparagus, onion, and garlic. These differences can be explained by the different extracts inhibited in the solid phase – garlic as opposed to the rest of the vegetables (3) – whereas Eng et al. (5) presented the asparagus extract in the solid phase as opposed to the rest of the allergens. However, using identical

techniques with both patients, we have also observed different results. Thus, while asparagus RAST presented only a self-inhibiting capacity in patient 1, in patient 2 it also inhibited onion by 55%.

Onion RAST was significantly inhibited by asparagus in patient 1 (86%), and rather less so in patient 2 (70%), but asparagus RAST was not inhibited by onion in patient 1 and was inhibited by only 50% in patient 2. Therefore, it seems that there are common epitopes, but a much smaller allergenic content in onion than in asparagus. Alternatively, onion can induce only specific antibodies, while the immunologic response to asparagus may be due to the induction of antibodies against common epitopes both for onion and for asparagus.

Unlike Eng et al.'s results (5), our patients reported cutaneous symptoms with cooked asparagus and showed a positive response in both *in vivo* and *in vitro* tests also with cooked asparagus extract. Moreover, we think that the allergenic fraction to which our patients were sensitized is thermostable. Nevertheless, it may be denatured by a digestion process, and this fact can explain the well-tolerated ingestion.

In conclusion, we believe that the level of cross-reactivity among the different Liliaceae vegetables varies among individuals. Nevertheless, we need to carry out further investigations in order to determine the clinical relevance of the cross-reactivity of this food family.

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Table 1. RAST-inhibition studies of serum with onion and asparagus extracts

	Patient 1		Patient 2	
	Concentration of inhibiting extract	Inhibition (%)	Concentration of inhibiting extract	Inhibition (%)
Onion RAST				
Control	0 mg/ml	0	0 mg/ml	0
Onion	1 mg/ml	71	10 mg/ml	91
Garlic	10 mg/ml	64	100 mg/ml	95
Asparagus	100 mg/ml	86	10 mg/ml	70
Asparagus RAST				
Control	0 mg/ml	0	0 mg/ml	0
Onion	100 mg/ml	0	100 mg/ml	55
Garlic	100 mg/ml	0	100 mg/ml	0
Asparagus	10 mg/ml	84	10 mg/ml	90

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Fern allergy

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Key words: fern allergy; rhinitis; Western blot.

● A 54-year-old woman was referred to the allergy clinic. Two years before, she had begun to suffer persistent sneezing and rhinorrhea outside the pollen season. Symptoms were pronounced at home.

Treatment with

cetirizine led to the resolution of symptoms.

Anamnesis revealed that she kept a big fern (*Nephrolepis* sp.) in her living room. Skin testing and immunoblot investigations demonstrated the presence of fern-specific IgE antibodies. After removal of the plant, the patient remained symptom-free. The skin prick test included

A case of IgE-mediated rhinitis to a fern.

pollens, mites, animal danders, and molds (Soluprick, ALK, Denmark). Total and specific IgE was assessed by Pharmacia UniCAP (Pharmacia, Uppsala, Sweden). Skin prick testing with fern was performed with an aqueous leaf extract. Specific IgE to fern proteins was investigated by Western blot. Briefly, a fern leaf was ground and extracted in PBS, and the supernatant was dialyzed. An amount of 200 µg protein was separated by SDS-PAGE and blotted. Nitrocellulose strips were incubated with serum of the patient as well as with control sera. Bound IgE was detected with ¹²⁵I-labeled rabbit antihuman IgE. Prick testing with the fern extract produced a wheal of 14 mm in the patient. Five healthy controls remained negative. Routine prick testing was positive to birch, hazel, mixed grasses, dog, and horse. CAP was positive for birch, mixed grasses, and cat. Total IgE was 198 kU/l.

Immunoblotting showed distinct binding of the patient's serum to two proteins of 35 and 40 kDa and weak binding around 28, 50, and 60 kDa (Fig. 1). IgE-binding obtained with all sera at 20 and below 7 kDa was considered nonspecific. Among the

panel of indoor allergens causing inhalative symptoms, fern allergen seems to be very rare. Only some anecdotal reports on fern allergy have been published in recent years. Fern spores, released under optimal conditions of humidity and temperature from the sporangia on the bottom sides of the leaves, have been reported to represent the third most common airborne spora in the Bangkok (Thailand) atmosphere (1). In a study in 36 atopics exposed to ferns, 50% had at least one positive skin test reaction to spore extracts from seven common ferns, but none of eight nonatopic controls reacted positively (2).

In our patient, skin testing with fern was strongly positive. Likewise, specific IgE binding in the immunoblot was obtained. It seems likely that sensitization to fern allergens in our patient occurred via inhalation of spores. There is increasing evidence that IgE-mediated reactions to potted plants, including contact urticaria, conjunctivitis, and asthma, may be elicited by a number of other plant species of many different plant families (3–5). Nonflowering ornamental plants, including ferns, represent an underestimated source of indoor allergens.

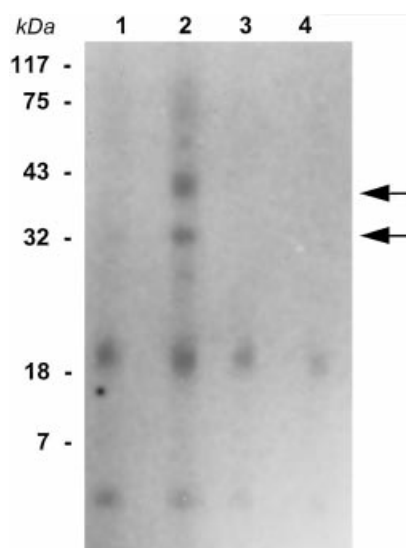


Figure 1. Immunoblot IgE reactivity with leaf extracts from fern *Nephrolepis* sp. of patient (lane 2), grass-pollen-allergic subject (lane 1), *Ficus benjamina*-allergic subject (lane 3), and nonatopic control (lane 4).