

Case report

Occupational type I allergy to Christmas cactus (*Schlumbergera*)

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The study aimed to determine whether occupational contact urticaria and symptoms of mucous membranes, reported by five workers in a cactus nursery, were due to IgE-mediated allergy to *Schlumbergera* cacti. The five persons had positive skin prick tests to the plants as is and positive histamine-release tests, and in three of them specific IgE to the cacti could be demonstrated by Maxisorp RAST and immunoblotting. Four of the patients were atopic, and the fifth had a positive skin prick test to cat dander, indicating latent atopy. Skin prick tests with cacti were negative in most atopic volunteers, and all had negative histamine-release tests. The results suggest a true IgE-mediated allergy to the cacti, and both genetic predisposition and close contact with the plants at work seem to be important factors in the emergence of this new occupational allergy.

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Schlumbergera hybrids, originating from the genera *Schlumbergera* and *Zygocactus* of the cactus family (Cactaceae), are popular pot plants under the colloquial name "Christmas cactus" (1). In connection with an investigation of occupational eczema and allergy among gardeners, several persons have reported symptoms of skin and mucous membranes, suggestive of type I allergy, when handling these cactus hybrids.

The present study aimed to determine whether the symptoms could be caused by an IgE-mediated allergy to these plants.

Material and methods

Clinical tests

Five persons working in the same cactus nursery and 10 control persons were skin-prick-tested with 10 common inhalant allergens and *Pityrosporum ovale*. Type I allergy to the cacti was tested by passing the lancet through a "leaf" (actually a flat shoot) into the epidermis. The cultivars 'Madisto' (Fig. 1) and 'Eva' were brought from the nursery, whereas 'Sonja' came from a private home where it had been cultivated for years. Reactions where

the largest diameter was 3 mm or more were considered positive. Histamine hydrochloride 10 mg/ml was used as a positive control.

Laboratory investigations

Preparation of cactus extracts used for in vitro experiments. One leaf of each of the cacti was extracted in 1 ml of Pipes buffer overnight at 4°C. The supernatant was decanted and used as stock solution. Each extract was used for histamine-release experiments in the following dilutions of stock solution: 1:30, 1:100, and 1:300 v/v. For Maxisorp RAST, SDS-PAGE, and IgE immunoblotting, stock solutions of extracts were used. Since the *in vitro* investigations were performed up to 13 months after the first skin prick tests, new and freshly prepared extracts had to be used for the former.

Determination of allergen-specific IgE by RAST. IgE was measured by an immunoradiometric assay, Maxisorp RAST, according to Poulsen et al. (2). In short, 300 µl of allergen extract (stock solution) was incubated overnight in polystyrene test tubes (Maxisorp, NUNC, Roskilde, Denmark). After



Fig. 1. *Schlumbergera* hybrid 'Madisto'.

washing with PBS-Tween 0.1%, tubes were incubated with serum (diluted 1 : 10 in PBS-Tween 0.1%) overnight. The bound IgE was detected with ^{125}I -labeled anti-IgE (Phadebas RAST, Pharmacia, Sweden, 25 000 cpm per tube). All serum samples from each individual patient were tested in duplicate. The results were expressed in cpm. Positive results were defined as those having cpm of 400 or more, whereas serum from a negative control person and serum from a patient with allergy to grass showed less than 100 cpm.

SDS-PAGE. SDS-PAGE was performed in a vertical slab gel apparatus (Hoefer Scientific Instruments, San Francisco, CA, USA), by the method of Laemmli (3) with a 16% separating gel and a 5% stacking gel in a discontinuous buffer system (0.0025 M Tris, 0.2 M glycine, and 0.1% SDS [w/v]). The extracts were boiled for 5 min in sample buffer containing 2% 2-mercaptoethanol and 2% SDS. A volume of 100 μl of allergen extracts (stock solutions) per 0.5 cm gel was loaded. The molecular weights were determined with prestained standards (Amersham International, Buckinghamshire, UK). After electrophoresis, gels were stained with Coomassie brilliant blue or subjected to immunoblotting.

IgE immunoblotting. The protein components of cacti were transferred onto nitrocellulose membrane 0.45 μm pore size (Scheicher and Schuell, Dassel, Germany). Blotting was performed with a semidry electroblotter (JKA Biotech, Copenhagen, Denmark), according to the manufacturer's instructions. After blocking with TBS/T (50 mM Tris and 150 mM NaCl, 0.5% Tween, pH 7.4) containing 3% of powdered milk, the blots were cut into strips and incubated with 10 μl serum each in 1 ml of blocking buffer overnight at room temperature. The bound IgE was detected with ^{125}I -labeled

rabbit-antihuman-IgE (Pharmacia, Sweden). Per strip, 100 000 cpm was applied overnight. Autoradiography was performed by exposing immunoblots to radiographic film (Amersham) for 10 days. Control experiments performed with serum from nonatopic donors demonstrated no binding to cactus proteins in the blots.

Histamine release (HR). The histamine release was analyzed in a glass fiber-based histamine-release test (HR-Test, Reference Laboratory, Copenhagen, Denmark) according to Nolte et al. (4). In short, 25 μl of cactus extract in the following dilutions of stock solution was added to the glass fiber-coated microtiter plates: 1 : 10, 1 : 30, and 1 : 300. The plates were incubated for 1 h at 37°C with 25 μl of heparinized blood. After incubation, the blood was washed away, and the glass fiber-bound histamine was determined in a spectrofluorometer (Gilson, USA) after coupling to *o*-phthaldialdehyde (Fluka, Chemie AG, Buchs, Switzerland). The released histamine was measured in ng/ml. A histamine release >15 ng/ml was considered positive.

Removal of surface IgE from patient basophils (HR[strip]). To demonstrate a cactus-specific, IgE-dependent release in the patients, experiments were performed with cells deprived of IgE. This is done by a short exposure of the cells to a low pH (5). Histamine release was then performed as described above.

Refixation of specific IgE to patient basophils (HR[refix]). To substantiate cactus IgE-dependent release in the patients, experiments were performed to refix specific IgE to IgE-deprived cells (5). Refixation was performed with a patient's own serum. After refixation, histamine release was performed as described earlier.

Case reports

Case 1

Our first case was that of a 26-year-old female gardener with hay fever who had worked in the nursery for about 7 years. Within the first year, she noticed urticarial lesions on the back of her hands and volar aspects of forearms after contact with *Schlumbergera* and the closely related *Rhipsalidopsis* hybrids. She had never had urticaria before. The contact with the cacti was especially close in the work of propagating the plants, during which the top shoots were broken off manually. Within the first year, the patient also developed persistent sneezing, itching of the eyes, periorbital edema, and once asthmatic dyspnea when engaged in this work. These symptoms gradually worsened, finally including severe itching of the palate, pharynx, and ears, and making medication with antihistamines and nasal corticosteroid spray necessary.

Skin prick tests were positive to birch and timothy pollen, but negative to food allergens. Skin prick tests with the cultivars 'Sonja' and 'Madisto' were positive, with 3- and 8-mm reactions, respectively.

Case 2

Our second case was that of a 25-year-old female greenhouse worker with no family or personal history of atopy. She had worked in the nursery for 4 years, and from the first day she had noticed that certain *Schlumbergera* and *Rhipsalidopsis* hybrids elicited gradually worsening urticaria on the volar aspect of her forearms. She had had urticaria only once before as an adult. At first, she occasionally had symptoms at work of the mucous membranes, such as sneezing, but later she developed more persistent itching of the eyes.

Skin prick tests showed positive reactions to cat dander and 5-, 9-, and 9-mm positive reactions to, respectively, 'Sonja', 'Eva', and 'Madisto'.

Case 3

Our third case was that of a 33-year-old female gardener with asthma from infancy who had worked with *Schlumbergera* and *Rhipsalidopsis* cacti for 9 years. After 4 years, she developed urticaria on the volar aspect of her forearms, face, backs of hands and fingers, and finger webs when she touched the cacti, especially during propagation and potting. She had had urticaria only once before when she was younger. After 6 years, she noticed occasional sneezing when working with the plants. Skin prick tests were positive to birch,

timothy, and mugwort pollen; cat and dog dander; house-dust mites; and 'Sonja', 'Eva', and 'Madisto', the three last-mentioned with 5-, 13-, and 3-mm reactions, respectively.

Case 4

Our fourth case was that of a 26-year-old female gardener with hay fever who had worked in the nursery for about 8 years. After 5 years, she developed gradually worsening urticarial lesions on the flexor aspect of her forearms when handling *Schlumbergera* cacti, especially during propagation and potting. The patient had had an urticarial drug eruption once before due to penicillin. Apart from slight irritation, she had no occupational symptoms of the mucous membranes. Skin prick tests showed positive reactions to birch pollen, 'Sonja' (4 mm), and 'Madisto' (6 mm).

Case 5

Our fifth case was that of a 39-year-old female gardener with a personal history of hay fever for a few years who had worked in the nursery for 5 years. Unlike the four others, she had only once had urticaria on her forearms at work, and she had never noticed symptoms of the mucous membranes when handling the cactus plants. The skin prick test with 'Sonja' was negative (2 mm), whereas the prick test with 'Madisto' (6 mm) and birch pollen was positive.

Results

The results of clinical and laboratory investigations in the patients are summarized in Table 1. Histamine release was positive in all five patients, whereas control experiments using basophils from healthy volunteers showed no release to the tested cultivars.

Removal of surface IgE from basophils reduced or completely eliminated the histamine release to the tested cultivars in all five patients; in three patients, to levels below 10 ng/ml, and in two patients, to levels higher than this. Fig. 2 shows representative examples of the two kinds of reactions. Basophils from nonallergic persons did not respond to the extract in the selected concentration range.

When refixation of IgE, using the patients' own sera, was performed on the IgE-deprived cells, the histamine-release responses to the tested cultivars were regained. Control experiments using refixation with serum from nonatopic subjects showed no histamine-release response.

The presence of specific IgE to the three cultivars could be demonstrated in patients 1, 2, and 3 by Maxisorp RAST and by immunoblotting.

Table 1. Summary of occupational symptoms, clinical tests, and laboratory investigations in five patients

Case	Occupational symptoms	SPT cactus			HR			HR (strip)			HR (refix)			RAST			IB		
		S	E	M	S	E	M	S	E	M	S	E	M	S	E	M	S	E	M
1	CU, MS	+	NT	+	+	NT	+	(+)	NT	(+)	+	+	+	+	+	+	+	+	+
2	CU, MS	+	+	+	+	+	+	(+)	(+)	(+)	+	+	+	+	+	+	+	+	+
3	CU, MS	+	+	+	+	+	+	(+)	(+)	(+)	+	+	+	+	+	+	+	+	+
4	CU (MS)	+	NT	+	+	NT	+	(+)	NT	(+)	+	+	+	-	-	-	-	-	-
5	CU	-	NT	+	+	NT	+	(+)	NT	(+)	+	+	+	-	-	-	-	-	-

SPT = skin prick test; HR = histamine release from basophils; HR(strip) = histamine release from basophils deprived of IgE; HR(refix) = histamine release from heterologous basophils with patient IgE on surface; RAST = specific IgE measured by Maxisorp technique; IB = immunoblotting; S = cultivar 'Sonja'; E = cultivar 'Eva'; M = cultivar 'Madisto'; CU = contact urticaria; MS = mucosal symptoms; + = positive reaction; - = negative reaction; NT = not tested; (+) = significant reduction (shift to right) in histamine release.

Skin prick tests with 'Sonja', 'Eva', and 'Madisto' were negative in 10 volunteers (one atopic and nine nonatopic subjects). In a recent study, skin prick tests with 'Madisto' were positive in 2/8 atopic volunteers, but all of them had negative histamine-release tests (personal communication, Flemming Andersen).

Discussion

The occupational symptoms of the five patients and the results of clinical and laboratory investigations

indicate a true IgE-mediated allergy to these cacti. The results in Fig. 2 are not at variance with this, since the IgE removal in some cases was not complete, as also demonstrated by a remaining weak histamine release to anti-IgE. The release was not due to a histamine-liberating effect of the crude extract, since basophils from nonallergic persons did not respond to the extract in the selected concentration range. The negative results of immunoblotting and RAST in patients 4 and 5 may be due to failure of the test to detect low IgE levels. Alternatively, they may reflect a low-grade

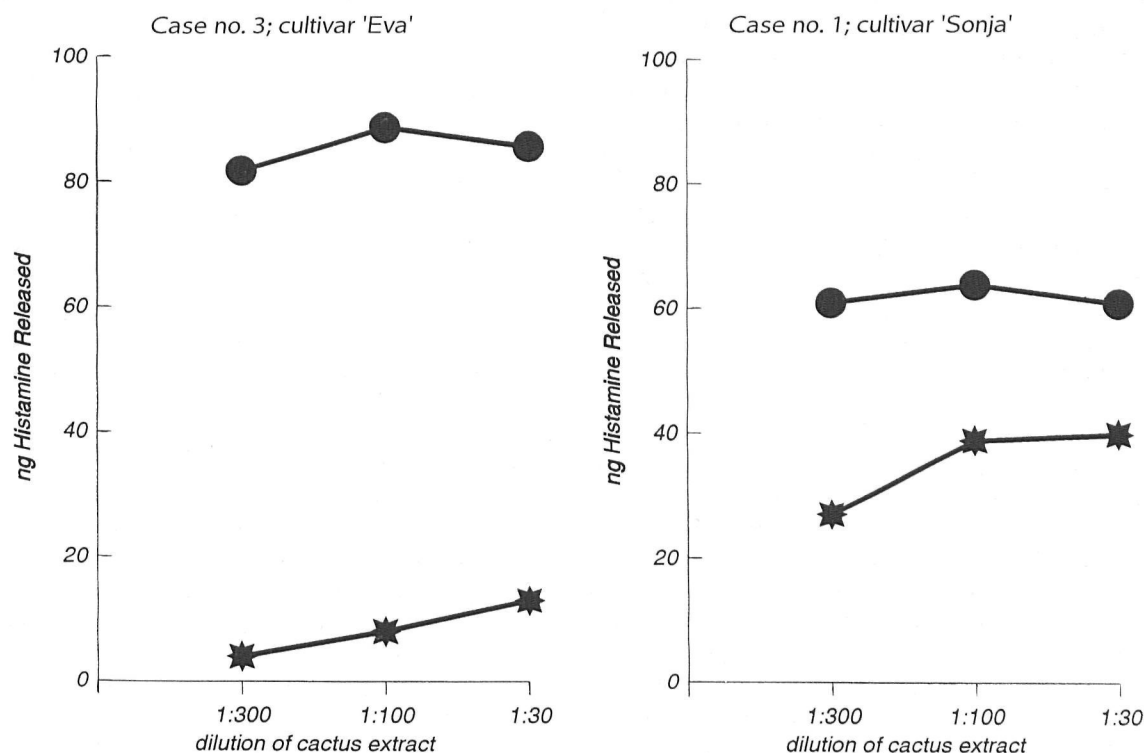


Fig. 2. Elimination or reduction of histamine release from basophils after removal of surface IgE. ●=before removal; *=after removal.

sensitivity in the two women who had contact urticaria as the only or main symptom.

The mode of sensitization is unknown. However, close contact with the cacti when breaking off the top shoots may release minute amounts of sap, whose entrance into the skin may be facilitated by microscopic punctures by the spines. Patient 1, who had the most severe mucosal symptoms, was additionally exposed to the pollens of several thousand flowering cactus plants, as she worked in a research department of the nursery. Nevertheless, the symptoms from the mucous membranes appeared every time she broke off top shoots, indicating that the aerosol of released sap may be important.

Contact urticaria caused by plants is considered to be fairly common (6). Immunologic contact urticaria caused by ornamental plants such as *Iris* spp., tulips, and chrysanthemum cultivars has been described; likewise, though rarely, it has been reported in pot plants such as *Monstera deliciosa*, *Bougainvillea*, and *Ficus benjamina* (7, 8). However, contact urticaria and other symptoms of type I allergy caused by cactus of the *Schlumbergera* genus have never been described before. An allergic mechanism has been suspected in cactus granulomas due to spines, but that was a combination of immediate and delayed-type hypersensitivity to a different genus (9). It is established that atopic subjects are at a higher risk of developing new IgE-mediated allergies, and this, in connection with prolonged and close contact with the cacti, was probably an important factor in the appearance of the allergy.

Further investigations are needed to determine the prevalence of these reactions among nursery

workers and to elucidate the possibility of cross-reacting allergens and/or the presence of environmental allergens, such as molds, as an alternative explanation of the respiratory symptoms. Such investigations are now in progress.

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