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CONTACT DERMATITIS

Airborne contact dermatitis due to Japanese cedar pollen

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Contact dermatitis caused by airborne antigen is a well-recognized problem. Previously, airborne contact dermatitis after contact with Japanese cedar pollen [Japanese cedar pollen dermatitis (JCPD)] has been reported in Japan. However, there is still no diagnostic test to evaluate contact dermatitis due to Japanese cedar pollen. Skin tests with Japanese cedar pollen have been used to investigate these patients. A histological analysis was also conducted to clarify the mechanism of JCPD. We performed a scratch-patch test, scratch test and assays for total immunoglobulin E (IgE) and specific IgE in 13 patients suspected to have skin symptoms from Japanese cedar pollen, 5 patients with Japanese cedar pollinosis and 15 control normal subjects. All subjects were tested with Japanese cedar pollen allergen extract. A skin biopsy was performed from a Japanese cedar pollen-scratch-patch-test positive in patients with JCPD. The result after 48 hr of scratch-patch test was compared with the patient's history and the findings of corresponding scratch test and specific IgE. 100% of the 13 patients with JCPD showed a positive scratch-patch-test reaction to Japanese cedar pollen extract. However, 20% of the patients with the Japanese cedar pollinosis without any eruptions showed a positive scratch-patch-test reaction. The percentage of positive results for specific IgE and the scratch test did not differ substantially between Japanese cedar pollionosis patients with a history of chronic erythema after contact with Japanese cedar pollen and those without such a history. No side-effects were observed regarding the scratch-patch test. Control subjects showed 7% positive reaction. Histological examination showed that eczematous change (spongiosis, intracellular oedema and acanthosis), and infiltration of lymphocytes and eosinophils were all observed at the scratch-patch-test–positive sites. We therefore concluded that the use of the scratch-patch test with Japanese cedar pollen extract was useful for accurately diagnosing JCPD.

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Contact dermatitis caused by airborne antigen is a well-recognized problem in which there is chronic persistent erythema, induration and intense pruritus that mainly involves exposed skin, particularly the face and hands. When there is no occupational exposure to an antigen known to cause airborne contact dermatitis, this condition may be misdiagnosed as atopic dermatitis, photo-induced dermatitis or neurodermatitis (1). Previouly, exposure to airborne Japanese cedar pollen has been reported to cause contact dermatitis in Japan (2–4). Due to the increase in Japanese cedar pollionosis, more attention has been paid to these patients in the last decade in Japan (5, 6). Horiguchi et al. (5) reported, for the first time, the existence of patients suffering from Japanese cedar pollinosis in 1964. Airborne Japanese cedar pollen has been further increasing with yearly variations, leading to a marked increase in the number of patients with Japanese cedar pollinosis (6). Japanese cedar pollen is globe-shaped with a short papilla, measuring 30 μm in diameter, which ruptures in water, thus resulting in the escape of the intragrain plasma to the outside of the pollen particle. 2 allergenic substances, Cryptomeia japonica (Cry j) 1 and 2, have been extracted and purified from Japanese cedar pollen, and their amino acid sequences have recently been clarified (7, 8).

Previously, airborne contact dermatitis due to Japanese cedar pollen [Japanese cedar pollen dermatitis (JCPD)] during the Japanese cedar pollen season (January to April) has been reported (2–4). However, it is not clear whether Japanese

cedar pollen causes airborne contact dermatitis or not. According to several authors, patch testing with airborne allergens known to elicit a skin reaction can be used to elicit eczematous skin lesions (9, 10).

On the other hand, exacerbations of atopic dermatitis lesions have been described in patients after contact with airborne antigens: animal dander, house-dust mites or pollen (11, 12). It is well known that an atopy patch test is a useful technique and is well investigated (13, 14). However, it is still not clear which technique is useful in patients with JCPD, who do not suffer from atopic dermatitis. Furthermore, scratch-patch test is an interesting alternative to patch tests, as they do not elicit a greater irritant response than patch tests but can be evaluated earlier (15, 16). To examine whether Japanese cedar pollen elicits a skin reaction, a scratch-patch test using Japanese cedar pollen and histological analysis of airborne-allergen-elicited skin sites was conducted.

Patients and Methods

Patient and control subjects

13 patients (all females) with a mean age of 29.5 years (from 15 years old to 45 years old), with moderate to severe skin symptoms from Japanese cedar pollen, were included in this study. All patients claimed to have persistent erythema with pruritus or eczematous skin lesions on their face or arms during the previous Japanese cedar pollen spring season every year, while patients with other skin diseases involving the face, such as contact dermatitis, atopic dermatitis, seborrhoeic dermatitis, acne, systemic lupus erythematosus and photosensitive dermatitis were excluded based on their history and a clinical examination. All patients were suspected of having skin symptoms from Japanese cedar pollen and allergic rhinoconjunctivitis (Japanese cedar pollinosis), but not atopic dermatitis. The control groups consisted of 5 patients with Japanese cedar pollinosis without any previous acute skin change and 15 healthy non-atopic volunteers with no history of allergic rhinoconjunctivitis, bronchial asthma or atopic dermatitis. The total and specific immunoglobulin E (IgE) to common aeroallergens were normal for the healthy control subjects. All healthy volunteers were free of the skin stigmata associated with atopy.

The patients with JCPD were all in a stable phase of partial or complete remission. Most had a few remaining eczematous skin lesions on parts of their face but not on their back. Informed consent was obtained from each patient or from his/her parents.

Test material

Scratch-patch test. The Scratch-patch test was performed using a commercial crude Japanese cedar pollen extract (Cry j 1; Torii Comp., Tokyo, Japan; 37.6 PNU/ml) and petrolatum as a negative control. After antihistamines and systemic and topical corticoids (test area) had been discontinued for at least 7 days, 20 μl of each scratch-patch test substances were applied for 48 hr in Finn chambers® (8 mm; Epitest Ltd, Tuusula, Finland) on the back of the subjects to clinically uninvolved skin, as previously described (11). The skin was given mechanical injury to remove the corneal layer by scratching the skin (11). The test reactions were read after 24–48 hr. The method of grading a positive scratch-patch test was similar to that used for conventional patch testing. ? represented a doubtful reaction, i.e. only erythema; + erythema, infiltration, none or few papules; ++ erythema, intensive infiltration, many papules and occasionally vesicles and +++ densely aggregated papules and vesicles. In control areas, vesicle without allergen was tested.

Scratch test, IgE and statistics. Scratch test with commercial crude Japanese cedar pollen extract (Torii Comp.) was performed in each subject on his/her forearms. 20 μl of the substance was applied after scratching. The tests were evaluated after 15 min, and the reaction was graded as the mean diameter of the wheal. A reaction with a mean diameter of 3 mm or more was considered to be positive. The serum levels of total IgE were determined, and Japanese cedar pollen-specific IgE was measured using Pharmacia CAP system-specific IgE RIA (Uppsala, Sweden). The serum samples were taken before the scratch-patch test from each patient and the control subjects.

Statistical analysis was performed using χ^2 test to compare the positivity rate to Japanese cedar pollen in different groups.

Histological examination. Skin biopsies were taken from positive scratch-patch-test reaction sites of the patients with JCPD. A biopsy was fixed in formalin, and 2 μm sections were stained with haematoxylin and eosin.

Results

Scratch-patch-test reaction

Figure 1 showed the typical clinical feature of JCPD. As shown in Table 1, all 13 patients with JCPD [a suggestive history, i.e. an exacerbation of contact dermatitis during the Japanese cedar pollen spring (from February to May) and/or pruritus after contact with Japanese cedar pollen]

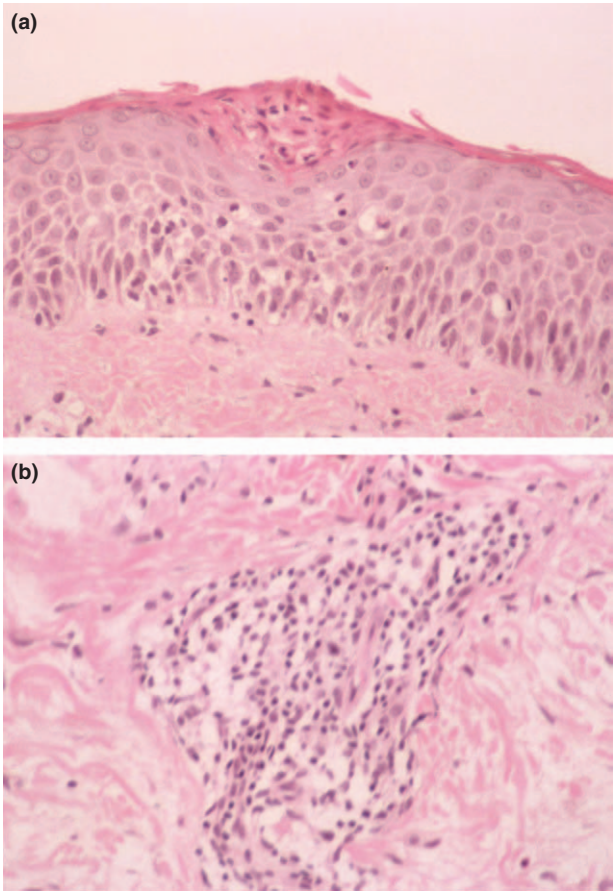

Fig. 1. Clinical features of a patient with Japanese cedar pollen dermatitis (JCPD). (a) Oedematous erythema seen on the face. (b) Erythema with lichenification seen on the neck.

showed 1 or more clear-cut positive scratch-patch-test reactions to Japanese cedar pollen extract after 24 hr and 48 hr. On the other hand, only 20% of the 5 patients with Japanese cedar pollinosis without JCPD showed such a reaction. 7% of the control healthy subjects showed a positive reaction. The positive rate of the scratch-patch test to the Japanese cedar test of patients with a suggestive history was significantly higher than that of the other group (Table 1).

Results of scratch test and the serum level of IgE

As shown in Table 1, the serum levels of IgE (radioimmunosorbent; geometrical mean values) in the JCPD patients with a suggestive history, i.e. an exacerbation of dermatitis during the Japanese cedar pollen spring season, was 393 IU/ml, those in Japanese cedar pollinosis without a suggestive history being 305 IU/ml.

Phamacia CAP system-specific IgE RIA of Japanese cedar pollen

All patients with JCPD showed a score of 2 or more. The average score for Japanese cedar pollen-specific IgE in JCPD patients with a suggestive history was 38.9 UA/ml, and that with Japanese cedar pollinosis without eruption was 40.2 UA/ml.

Scratch test

100% of the JCPD patients were positive to the scratch test. However, 80% of the Japanese cedar pollinosis patients without suggestive dermatitis were also positive (Table 1).

Histological examination of scratch-patch-test–positive sites

Figure 2 shows the typical histological findings of the scratch-patch-test sites. Histological examination of the scratch-patch-test–positive sites demonstrated that 0% spongiosis, 50% acanthosis, 100% exocytosis, 100% lymphocyte infiltration and 25% eosinophilic infiltration to be observed at the scratch-patch-test–positive reaction sites in JCPD patients.

Discussion

We report here that an airborne contact dermatitis was observed, which induced a chronic persistent oedematous erythema after contact with Japanese cedar pollen in the spring season. The JCPD rash has a characteristic appearance: it is well-circumscribed and maximally affects the

Table 1. Results of skin tests

	Group of subjects (*n*)	Total IgE (IU/ml)	CAP (UA/ml)	Scratch test	Scratch-patch test (48 hr)
JCPD	13	393	38.9	13/13 (100%)	13/13 (100%*)
Japanese cedar pollinosis without JCPD	5	305	40.2	4/5 (80%)	1/5 (20%)
Normal control	15	ND	ND	0/15 (0%)	1/15 (7%)

CAP = CAP system-specific IgE RIA; IgE = immunoglobulin E; JCPD = Japanese cedar pollen dermatitis; ND = not determined.
*$P < 0.05$.

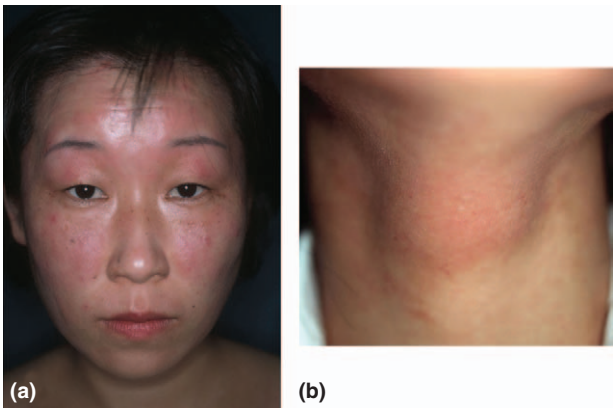

Fig. 2. Histological findings of a scratch-patch-test site in a patient with Japanese cedar pollen dermatitis (JCPD). Lymphocytic infiltration was observed in the epidermis (a) and mononuclear cells and eosinophils infiltrated in the dermis (b).

face, especially periorbitally or on the cheeks, and arms and is similar to an urticarial erythema eruption without papules (Fig. 1a). Sometimes, it has a non-specific appearance: erythema with seropapules (acute eczematous appearance) or lichenification (chronic eczematous lesion) (Fig. 1b) (2–4). It is difficult to diagnose JCPD clinically, because there are many factors, which may induce airborne contact dermatitis or photocontact dermatitis in the spring season, including sunlight, other pollens and house dust (7–9). Although the atopy patch test has been carefully investigated regarding its ability to evaluate airborne exacerbating factors of atopic dermatitis (13, 14), the optimal technique to diagnose airborne contact dermatitis patients who do not suffer from atopic dermatitis remains to be elucidated. We therefore investigated the scratch-patch test to diagnose JCPD, because the scratch-patch test is known to be a useful test for testing and detecting protein antigen (15, 16). The results of these studies showed the Scratch-patch test with cedar pollen to be very useful for diagnosing patients with JCPD and a history of cedar pollen-induced persistent, urticarial erythema on the face, arms or hands. On the other hand, there was no difference in the results regarding total IgE level, cedar pollen-specific IgE level or scratch test findings between patients with JCPD and Japanese cedar pollinosis without eruptions. Most of cedar pollen scratch-patch-test–positive patients also had a positive scratch test or an elevated specific serum IgE to cedar pollen. In the control subjects, 7% of the Scratch-patch-test reactions were positive, while 20% of the subjects with Japanese cedar pollinosis showed positive scratch-patch test to Japanese cedar pollen. However, the specificity of the atopy patch test was much higher (13, 14). Because these results may be explained by the fact that Japanese cedar pollen extract may function as an irritant in patients, we need to modify this Scratch-patch-test method in the future. There was a significant correlation in positive scratch-patch test to Japanese cedar pollen extract and patient's history suggesting Japanese cedar pollen-induced persistent oedematous erythema. As a result, we could thus calculate the preliminary values for the sensitivity and specificity for the Scratch-patch test, which allows us to conclude that this reasonable test may identify JCPD patients who have eczema exacerbation by Japanese cedar pollen. Our data are consistent with a recent report, which concluded that the Scratch-patch test was an interesting alternative to the patch test, as it can evaluate protein antigen earlier (16).

Table 2. Histological features

	Subject with JCPD			
Histological feature (%)	1	2	3	4
Spongiosis (0)	–	–	–	–
Acanthosis (50)	–	+	–	+
Exocytosis (100)	+	++	+	++
Lymphocytic infiltration (100)	+	+++	++	++

JCPD = Japanese cedar pollen dermatitis.

Furthermore, we conducted a histological examination (Table 2) to clarify the mechanism of allergic contact dermatitis due to Japanese cedar pollen. Histological examination revealed 0% spongiosis, 50% acanthosis, 100% exocytosis, 100% lymphocytic infiltration and 25% eosinophils infiltration at the Japanese cedar pollen scratch-patch-test–positive reaction sites. These data indicated that the late phase but not delayed-type hypersensitivity caused by Japanese cedar pollen may be a major mechanism in the induction of JCPD, because spongiosis and intracellular oedema were not detected at the scratch-patch-test site (7, 8). Although Bruynzeel-Koomen et al. (17) demonstrated that eosinophils play an important role in the patch test reaction to inhalant allergens in patients with atopic dermatitis, few eosinophils infiltrated into the dermis but not epidermis in scratch-patch-test lesions in patients with JCPD (Fig. 2). The rash of the airborne contact dermatitis usually has a characteristic appearance, and it mainly affects the face and hands. This eruption frequently has a sharp demarcation at the mid-biceps level and the upper sternal V line, reminiscent of photo-induced dermatitis. Unlike photo-induced dermatitis, airborne contact dermatitis does not spare the submental area or

postauricular sites. The skin manifestation of JCPD is very similar to the rash of airborne contact dermatitis due to other airborne pollens. The most common airborne contact dermatitis is one due to Ragweeds. Ragweed has long been known to cause eczematous allergic contact dermatitis by both direct contact of the plant with the skin and by airborne dissemination of ragweed pollen. However, airborne contact dermatitis due to pollen other than ragweed pollen is rare. Recently, airborne contact dermatitis due to Japanese cedar pollen has been reported as a skin manifestation of Japanese cedar pollinosis and as JCPD, although an accurate diagnostic test for JCPD has yet to be established. In this paper, the scratch-patch test using Japanese cedar pollen was shown to be useful for diagnosing JCPD.

The higher prevalence of a positive scratch-patch-test reaction to Japanese cedar pollen in patients with a distribution of oedematous erythema in air-exposed areas also points to the clinical relevance of these findings. It is important to consider the possible relevance of other aeroallergens, e.g. house-dust mite, in this group. The phenomenon of spring eruption of airborne contact dermatitis due to pollen is well known (18, 19). Our results indicate that none of these cases were due to an exacerbation caused by ultraviolet radiation. However, the exact proportion reactive to Japanese cedar pollen remains to be determined. Further studies utilizing specific provocation and elimination procedures, therefore, need to be performed before the scratch-patch test can be recommended for the routine clinical diagnosis of exacerbation due to Japanese cedar pollen.

The ability to utilize the scratch-patch test with Japanese cedar pollen, and then combine the results with the patient's history and other parameters for IgE-mediated hypersensitivity, provides an effective method to investigate the interaction of Japanese cedar pollen and the skin in patients with JCPD.

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