

Clinical and immunologic features of systemic contact dermatitis from ingestion of *Rhus* (*Toxicodendron*)

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Oral or parenteral exposure to certain contact allergens may elicit an eczematous skin reaction in sensitized individuals. This phenomenon has been called systemic contact dermatitis (SCD) and is relatively rare when compared with classical contact dermatitis. We reviewed and analysed the clinical and immunologic features of 42 patients with SCD caused by ingestion of *Rhus* (*Toxicodendron*), 24 males and 18 females, average age 44 years (range 24–72). Several of such patients (33%) had a known history of allergy to lacquer. The patients developed skin lesions such as generalized maculopapular eruptions (50%), erythroderma (29%), vesiculobullous lesions (14%) and erythema multiform (EM)-like lesions (7%). Many patients (57%) developed leucocytosis with neutrophilia (74%). In some patients (5%), abnormalities of liver function developed. We also analysed lymphocyte subsets in the peripheral blood of 12 patients. The lymphocyte subsets studied were T cells (CD3), B cells (CD19), natural killer (NK) cells (CD3⁺CD16⁺/CD56⁺), helper/inducer cells (CD4), cytotoxic/suppressor cells (CD8) and helper/suppressor ratio (CD4/CD8). The lymphocyte subsets of all 12 patients studied were within the normal range. Moreover, there were no differences between patients with a history of allergy to lacquer and those without a history of allergy to lacquer. Therefore, rather than an immunologic response, the skin eruption seems to be caused by a toxic reaction because of *Rhus*.

Key words: clinical and immunologic features; lymphocyte subsets, *Rhus*; systemic contact dermatitis. © Blackwell Munksgaard, 2003.

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Allergic contact dermatitis is elicited ordinarily by external exposure of the skin to an allergen. Occasionally, however, in sensitized individuals, a systemically administered allergen may reach the skin through the circulatory system and provoke a systemic contact dermatitis (SCD) (1). There is no consensus about the role of various types of pathogenic immune reactions associated with SCD, whether it is Type I (immunoglobulin (Ig)-E mediated) or Type IV (cellular delayed-type hypersensitivity) or some other kind of allergic reaction (2). Therefore, we performed this study to evaluate immunologic features in SCD caused by ingestion of *Rhus* (*Toxicodendron*), which has traditionally been used as a folk medicine in Korea. Also, we reviewed and analysed the clinical and routine laboratory findings in 42 patients with SCD after *Rhus* ingestion.

Patients and Methods

42 patients with SCD caused by ingestion of *Rhus* treated in the Department of Dermatology at Kyunghee University Hospital from February 1995 to February 2001 were involved in this study. The study involved the taking of a history to determine whether or not patients had previously experienced allergic reactions following contact with lacquer. SCD was categorized according to the nature of the skin eruption. We also analysed lymphocyte subsets in the peripheral blood from 12 of the 42 patients. The lymphocyte subsets were analysed on a FACScan (Becton Dickinson Immunocytometry Systems, San Jose, CA, USA) flow cytometer. Routine laboratory examinations including full blood count, liver function test and renal function test were also conducted on most patients.

Results

Characteristics of patients studied

The total of 42 patients involved in this study included 24 men and 18 women with a male/female ratio of 1.3:1. Ages ranged from 24 to 72 years with a mean age of 44 ± 8 years. In 14 (33%) of the 42 patients, there was a known previous history of allergy to *Rhus* (Table 1).

Time to onset of symptoms after *Rhus* ingestion

We reviewed time to onset of symptoms after ingestion of *Rhus*; within 24 h (17 patients, 40%), between 24 and 48 h (18 patients, 43%), between 48 and 72 h (3 patients, 7%), between 72 and 96 h (1 patient, 2%), between 96 and 120 h (2 patients, 5%) and between 120 and 144 h (1 patient, 2%). Symptoms occurred in most patients within 48 h of ingestion of *Rhus* (Table 2).

Types of clinical reaction

The skin manifestations of SCD following ingestion of *Rhus* were 4 in total: 1st, generalized erythematous maculopapular eruptions in 21 patients (50%), the most common type of eruption; 2nd, generalized erythroderma in 12 patients (29%); 3rd, vesiculobullous lesions in 6 patients (14%) and 4th, erythema multiform (EM)-like lesions in 3 patients (7%) (Table 3).

Routine laboratory examinations

Leucocytosis ($>10 \times 10^9/L$) was detected in 57% (24/42 patients). 17 (74%) of 23 patients who had leucocytosis also had neutrophilia ($>70\%$). 2 patients showed raised liver enzyme levels. One patient had an abnormality of renal function test.

Lymphocyte subsets in peripheral blood

The lymphocyte subsets analysed were T cells (CD3, reference range 59–85%), B cells (CD19, reference range 6–23%), natural killer (NK) cells (CD3⁺CD16⁺/CD56⁺, reference range 6–31%), helper/inducer cells (CD4, reference range 28.5–60.5%), cytotoxic/suppressor cells (CD8, reference range 11–38%) and helper/suppressor ratio (CD4/CD8, reference range 1–4). Our results were as follows: T cells ($65 \pm 8\%$), B cells ($19 \pm 5\%$), NK cells ($15 \pm 7\%$), helper/inducer

Table 2. Time to onset of symptoms after *Rhus* ingestion

Time (h)	No. (%)
<24	17 (40)
24–48	18 (43)
48–72	3 (7)
72–96	1 (2)
96–120	2 (5)
120–144	1 (2)

cells ($42 \pm 7\%$), cytotoxic/suppressor cells ($21 \pm 5\%$) and helper/suppressor ratio (2 ± 1) (all figures quoted to nearest whole number). All lymphocyte subsets of 12 patients studied were within the normal range. No differences in the numbers of lymphocyte subsets were observed between allergic history patients and non-allergic history patients to *Rhus* (Table 4).

Discussion

The lacquer tree is widely distributed over subtropical and warm temperate regions. There are over 150 species in the genus *Rhus* (*Toxicodendron*), 5 of which, *Toxicodendron vernicifluum* Kuntze (Japanese lacquer tree), *T. succedaneum* Kuntze, *T. sylvestris* (Sieb. et Zucc.), *T. trichocarpum* Kuntze and *T. semialatum* Kuntze are found in Korea (3). The lacquer is obtained by tapping the trees by making incisions in the bark. The raw sap (oleoresin) flowing from the incised trees contains 50–80% urushiol, which consists of a catechol nucleus with a C15 lipophilic tail, containing 2 or 3 unsaturated bonds (4). The conjugation of urushiol to cell membranes is believed to involve an initial lipophilic interaction of the cell membrane with the tail, followed by the formation of a covalent bond between the catechol nucleus and cell-surface proteins through a quinone intermediate (5). Apart from the quinone hypothesis, suggesting that quinone acts as the haptenic species of urushiols, the free radical hypothesis, in which the local levels of endogenous reducing equivalents, such as nicotinamide adenine dinucleotide (NADH) and glutathione, are reduced in the skin following urushiol exposure, resulting in the formation of free radical species which in turn act as haptens, has been proposed (6). In contact with air, urushiol

Table 1. Profile of patients with systemic contact dermatitis

	No. of patients	Mean age (y) at onset	Positive history of Allergy to <i>Rhus</i>
Male	24	41.5	7
Female	18	47.6	7

Table 3. Types of clinical reaction

Clinical forms	No. of patients (%)
Generalized maculopapular eruption	21 (50)
Generalized erythroderma	12 (29)
Vesiculobullous	6 (14)
EM-like	3 (7)

Table 4. Lymphocyte subsets in peripheral blood

Lymphocyte subsets history patients to <i>Rhus</i> (n = 7)	Allergic history patients to <i>Rhus</i> (n = 5)	Non-allergic
T cells (reference range 59–85)	63 ± 6%*	67 ± 7%
B cells (reference range 6–23)	18 ± 6%	21 ± 7%
Natural killer (NK) cells (reference range 6–31)	16 ± 7%	14 ± 6%
Helper/inducer cells (reference range 28.5–60.5)	45 ± 6%	39 ± 7%
Cytotoxic/suppressor cells reference range (11–38)	20 ± 8%	24 ± 5%
Helper/suppressor ratio (reference range 1–4)	2 ± 1	2 ± 3

*Figures all quoted to nearest whole number.

becomes a black oleoresin by the action of an oxidative enzyme called laccase (7–9). Urushiol is found in the stems, canals and skin of the fruits of these plants. Urushiol has not been found in the flowers or pollen. The use of lacquer for the decoration or protection of furniture, floors, tea-pots, canes and ornaments is widespread in East Asia (Korea, Japan and China) and is part of its cultural heritage.

According to Oriental medicine, the ingestion of lacquer is thought to be an effective remedy for gastrointestinal disorders and a health supplement. However, no commercially available preparation is used, and extracts are made from the leaves, roots and bark by boiling with the extracts subsequently ingested by themselves or as an additive when cooking chicken in specialized restaurants or at home. The tree itself may be dried and used as an ingredient in Oriental medicinal preparations. Oriental herb vendors, who also deal in lacquer tree parts, classify the genus *Rhus* according to the morphological and anatomical characteristics of the inflorescence, fruits and seeds. Raw sap from lacquer trees (*T. vernicifluum*, *T. trichocarpum* and *T. semialatum*) has been used as a herbal medicine (3). *T. sylvestris* and *T. semialatum* are known to be less frequent causes of contact dermatitis than *T. vernicifluum* and *T. succedaneum* (10).

From the epidemiological point of view, in our study, SCD caused by the ingestion of lacquer was only slightly more common in men. Most of our patients were between 30 and 50 years old, indicating that young people also favour traditional folk medicine.

Only 14 (33%) of the patients who took part in our study were known to be allergic to *Rhus*; this finding is very similar to that of Park et al. (13), who have reported that only 10 of the 31 patients examined (32%) for systemic reaction to *Rhus* had a history of previous contact allergy to *Rhus*. In addition, the possibility remains that many of the patients examined were previously exposed and sensitized to *Rhus* and yet had not experienced a second exposure episode and thus were found to have no history of contact allergy

to *Rhus*; this notion is strongly supported by the study of Park et al. (11) in which 12% of the patients who had no previous history of *Rhus*-induced contact dermatitis showed positive patch-test results. This means that, if ingested, lacquer can cause SCD in a patient without a known history of allergy.

After a susceptible person comes into contact with the oleoresin, the eruption usually appears within 2 days, and delay in onset rarely exceeds 10 days. In a few cases, the skin reaction may occur within 8 h of exposure. Such temporal differences are probably because of the degree of exposure, individual susceptibility and regional variation in cutaneous reactivity (12). Most patients developed the eruption within 48 h of ingestion of *Rhus* in our study.

The generally reported cutaneous manifestations of SCD are eczema, pompholyx, symmetrical maculopapular rash, urticaria, EM and rarely vasculitis or fixed drug eruption. Park et al. classified the major skin eruptions into 3 types: (1) A localized or generalized maculopapular rash, (2) EM and (3) Generalized erythroderma (13). In our study, however, we observed vesiculobullous lesions more than EM.

To evaluate the cell-mediated immunity in SCD from ingestion of *Rhus*, we quantified peripheral blood T cells and their subsets. However, we could not find any immunologic abnormalities. Also, in only 14 (33%) of the 42 patients, there was a known history of allergy to *Rhus*. Moreover, no differences in the numbers of lymphocyte subsets were observed between allergic history patients and non-allergic history patients to *Rhus*. Therefore, we suggest that SCD from ingestion of *Rhus* may be a toxic reaction rather than an allergic reaction.

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