

Immediate and Delayed-type Reactions in Caterpillar Dermatitis

Masaru Natsuaki

Abstract

The mechanism of dermatitis induced by *Euproctis* caterpillars has not been fully clarified, although mechanical stimulation by the spicules as well as chemical irritation by venomous components from spicules have been suggested to be involved. In this study, skin tests using venomous spicules and the venomous extract from the caterpillar of *E. pseudoconspersa* were carried out on a subject. The test site developed both immediate and delayed-type reactions. Next, the crude extract was separated into 8 fractions (No. 1-8) using gel filtration HPLC, and a skin test using each fraction was performed in the same subject. The result showed that only fraction No. 3 caused reactions similar to those in crude venom extract. Then skin tests using the crude venom and fraction No. 3 were performed in 10 healthy volunteers. The skin reaction caused by crude venom was similar to that caused by fraction No. 3 in each subject. Two volunteers showed neither immediate nor delayed-type reactions, 4 volunteers showed a delayed-type reaction, and the other 4 showed both immediate and delayed-type reactions. These results indicate that allergic reactions against venom released by the spicules play a role in the induction of dermatitis by *E. pseudoconspersa* caterpillars. Variations in the clinical course of individual patients may be attributable to differences in the state of sensitization to the venomous components.

Key words: caterpillar dermatitis; *Euproctis pseudoconspersa*; venom; immediate reaction; delayed-type reaction

Introduction

The tea tussock moth, *Euproctis pseudoconspersa* (Strand) belongs to the genus *Euproctis* (Lymantriidae) and is widely distributed in Japan. The larva of this moth is covered by fine venomous hairs, called "venomous spicules", which are 0.1 to 0.2 mm long. Contact with these spicules can cause dermatitis. The larva feeds on the leaves of camellia plants, and because these are often grown in yards and parks, infestations with *E. pseudoconspersa* can occur in urban areas.

Accordingly, dermatitis due to contact with the caterpillar of this moth often occurs in housing estates and is a very common problem in the ambulatory practice of dermatologists in Japan.

Clinically, patients with caterpillar dermatitis show wheals in the early stage and/or erythematous papules in the late stage after contact with the spicules.

Regarding the mechanism of dermatitis caused by contact with the venomous spicules of the *E. pseudoconspersa* caterpillar, mechanical stimulation by the spicules as well as chemical irritation by venomous components released from the spicules have been suggested to be involved (1, 2), but the details have not been fully clarified so far. It is known that immediate and/or delayed-type skin reactions develop in mosquito bites and the variation of reactivity is associated with the state of sensitization to anti-

Received February 7, 2002; accepted for publication May 28, 2002.

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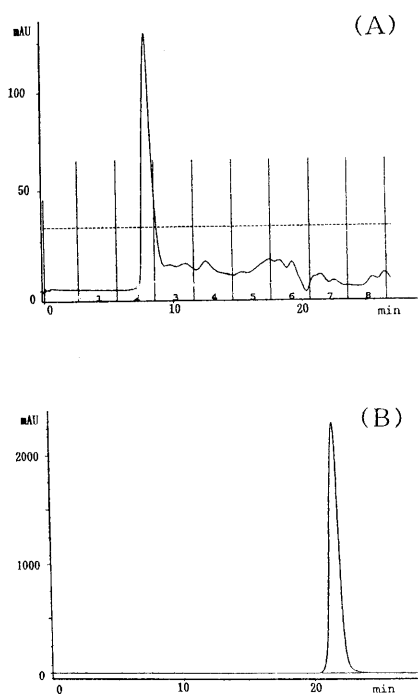


Fig. 1. HPLC analysis of the crude venom extract (A) and histamine (B).

The crude venom extract was fractionated from No. 1 to No. 8.

gens in the salivary glands (3, 4).

In this study, skin tests with venomous spicules or extracted venom from the *E. pseudoconspersa* caterpillar were performed in healthy volunteers to determine whether allergic reactions to venomous components play a role in the development of caterpillar dermatitis.

Subjects and Methods

1. The larvae of *E. pseudoconspersa*

Caterpillars of the moth were collected at Amagasaki in Hyogo Prefecture for use in the study.

2. Subjects

Induction of dermatitis by the spicules and

skin tests using venomous extracts were carried out on the author himself (a 42-year-old male). The author had a history of several episodes of dermatitis caused by contact with caterpillars of *E. pseudoconspersa*.

Skin tests using crude venom and fractionated venomous extract were performed in 10 healthy volunteers (5 men and 5 women aged 22 to 31 years) who gave informed consent to participation in the study.

3. Extraction of the spicule venom

Venomous spicules from one *E. pseudoconspersa* caterpillar in the final larval stage (about 300,000 spicules) were placed in 10 ml of PBS and stirred for 1 minute, after which the mixture was left at 4°C overnight. The supernatant ("crude venom extract") was passed through a 0.45 µm filter and stored at -70°C.

4. Analysis and fractionation of the venom

SRL Incorporated determined histamine and serotonin levels by using high-performance liquid chromatography (HPLC) and bradykinin level by radioimmunoassay in crude venom extract.

A Superdex 75 HR 10/30 column (Amersham Pharmacia Biotech, Sweden) was used for gel filtration of the crude venom extract, and an AKTA explorer 10S (Amersham Pharmacia Biotech, Sweden) was employed for fractionation of the extract into fractions No. 1 to No. 8. Each fraction was stored at -70°C.

Results

1. Induction of dermatitis by venomous spicules

A caterpillar in the last larval stage was brought into contact with the anterior thigh of the subject. Mild pruritus developed immediately after contact with the caterpillar, and wheals appeared 10 minutes later. Thirty minutes after contact, the wheals were accompanied by erythema. This erythema began to disappear after 3 hours, but it expanded again after 6 hours, and the pruritus worsened gradually. After 24 to 48 hours, the infiltrated erythema reached its maximum extent, being accompanied by local heat and severe pruritus. After 72 hours, the erythema began to gradually fade and there

was almost complete recovery after 10 days with only slight pigmentation remaining.

2. Histamine, serotonin and bradykinin contents of crude venom

The crude venom extract contained 57 ng/ml of histamine, *i.e.*, about 570 ng per caterpillar in the final larval stage. In contrast, serotonin and bradykinin were below the detection limit (1 ng/ml and 2 pg/ml, respectively), indicating that there were almost no serotonin and bradykinin present in the venomous spicules of the caterpillars.

3. Chromatography of crude venom extract

When the crude venom extract was analyzed and fractionated by HPLC using a gel filtration column, there was a distinct single peak in fraction No. 2, and fractions No. 3 to No. 8 showed some smaller peaks (Fig. 1A). For comparison, 1% histamine solution was analyzed by HPLC under the same conditions, yielding a single peak (Fig. 1B). The chromatogram of the crude venom extract did not show any peak that corre-

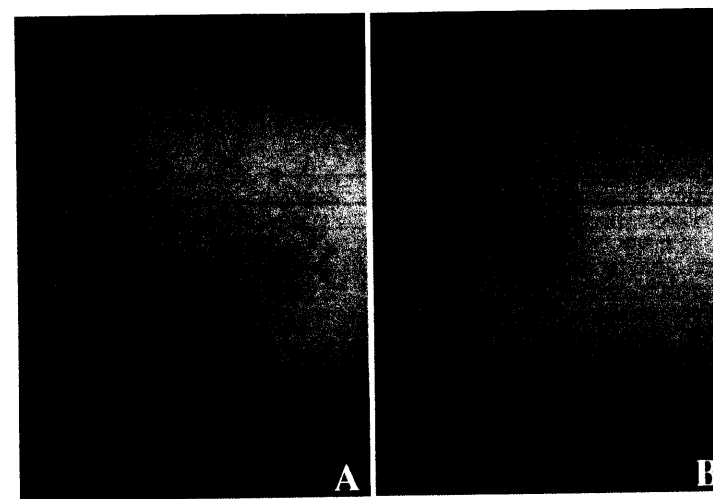


Fig. 2. Immediate and delayed-type reactions in skin testing.

When the venom extract (Fraction No. 3) was injected intradermally, an immediate reaction (A) and/or a delayed-type reaction (B) were recognized.

sponded to the peak of histamine.

4. Intradermal testing using the crude venom extract and fractions No. 1 to No. 8

Crude venom extract was injected intradermally into the subject's forearm at a dose of 0.02 ml, and the response was followed. Pruritus and erythema developed immediately after injection and wheals developed after 15 to 30 minutes. After 2 hours, the pruritus and wheals disappeared, but then the area of erythema expanded. After 24 to 48 hours, the infiltrated erythema reached its maximum extent and was accompanied by marked pruritus. After 72 hours, the skin lesions began to subside, and there was almost complete resolution after 7 days.

Next, 0.02 ml each of the fractions No. 1 to No. 8 was injected intradermally into the subject's forearm. Fraction No. 3 caused wheals and erythema after 15 to 30 minutes (Fig. 2A). The rash then disappeared, but infiltrated erythema developed after 24 to 48 hours (Fig. 2B). The early response is designated as the "immediate reaction", and

Table 1. Results of intradermal testing using crude venom extract and venom extract (fraction 3) in 10 healthy volunteers and the author

Subject	Age	Sex	Crude venom extract		Venom extract (fraction 3)		Past history of caterpillar dermatitis
			Immediate reaction	Delayed-type reaction	Immediate reaction	Delayed-type reaction	
1	31	Male	—	—	—	—	—
2	24	Male	—	—	—	—	—
3	29	Female	—	+	—	+	—
4	22	Male	—	+	—	+	Unknown
5	23	Female	—	+	—	+	—
6	22	Female	—	+	—	+	Unknown
7	30	Male	+	+	+	+	+
8	30	Female	+	+	+	+	+
9	22	Male	+	+	+	+	+
10	22	Female	+	+	+	+	Unknown
Author	42	Male	+	+	+	+	+

the late response is called "delayed-type reaction" hereafter.

5. Intradermal testing using crude venom extract and fraction 3 in volunteers

Crude venom extract and fraction 3 were injected intradermally into the forearms of healthy volunteers at a dose of 0.02 ml to examine the immediate and delayed-type reactions. If a wheal >5 mm in diameter developed by 30 minutes after injection, this was judged as an immediate reaction. If erythema >10 mm in diameter was present at 48 hours after injection, this was judged to be a delayed-type reaction. All the volunteers were subjected to skin prick testing with 1% histamine solution, and all of them developed wheals >10 mm in diameter.

As shown in Table 1, the volunteers (10 subjects) were classified into 3 groups according to the reactions detected: neither immediate nor delayed-type reactions (No. 1 and No. 2), a delayed-type reaction only (No. 3 to No. 6), and both immediate and delayed-type reactions (No. 7 to No. 10). Interestingly, in each subject, the skin reaction caused by crude venom extract was similar to that caused by fraction 3. In these volunteers, there was no definite relationship between a history of caterpillar dermatitis and the results of skin testing. However, the two

subjects (No. 1 and No. 2) who showed neither immediate nor delayed-type reactions had no history of caterpillar dermatitis.

Discussion

A variety of caterpillars are capable of causing dermatitis in man (5). In Japan, caterpillar dermatitis caused by the larvae of *E. pseudoconspersa* is a common disease in dermatological practice. Clinically, it is characterized by wheals in the early stage and multiple, isolated, red papules centering on the site of contact with the caterpillar in the late stage. Since about 80% of patients with this type of dermatitis cannot recall having touched a caterpillar (6), it is thought that there are individual differences in the severity of the skin reaction and the time of onset after contact with the venomous spicules.

The development of dermatitis caused by the spicules of *Euproctis* caterpillars has been attributed to mechanical stimulation, chemical stimulation, and an allergic response. De Jong et al. (7, 8) extracted venom from the venomous spicules of the caterpillar of the Brown-tail moth, *Euproctis chrysorrhoea* and confirmed that the venom had various enzymatic activities (including esterases, proteases, and phospholipase A2). They reported that dermatitis caused by this moth

was probably due to mechanical stimulation by the spicules plus chemical stimulation by venomous components. Kawamoto et al. (1) found proteinase activity and intestinal contraction activity in a component extracted from the venomous spicules of *Euproctis subflava* caterpillars and concluded that the main cause of dermatitis was the chemical action of the venom in the venomous spicules. Kubo et al. (2) induced dermatitis due to the spicules of *E. subflava* and reported that it was probably caused by both mechanical and chemical stimulation after contact with the spicules. None of these authors found any role for an allergic reaction.

In the case of the urticarial reaction that occurs after contact with the pine processionary caterpillars, however, it has been suggested that IgE against venomous components of the caterpillar spicules may be involved in the reaction and that some of the components act as allergens (9–11).

In the present study, skin responses that were classified as immediate and delayed-type reactions were observed after contact with the venomous spicules. Histological examination of biopsy specimens taken from the author's skin at 48 hours after contact with the spicules revealed a dense infiltration of inflammatory cells, mainly T lymphocytes, around the skin vessels (the author's unpublished data). This suggests the possibility that not only chemical stimulation but also a delayed-type allergic reaction is involved in the development of caterpillar dermatitis. In fact, some reports have suggested that a mechanism of delayed hypersensitivity is involved in the dermatitis caused by the gypsy moth caterpillar (12, 13) and the saddleback caterpillar (14).

Analysis of the venom revealed a small amount of histamine in the venomous spicules of the *E. pseudoconspersa* caterpillar. It is possible that, when the spicules enter the skin, histamine is released and stimulates a response. However, the concentration (57 ng/ml) is too little to induce an immediate skin reaction. Intradermal testing with fraction 3 (which did not contain hista-

mine) caused an immediate reaction in the author and in some of the volunteers, indicating that a type I allergic reaction against venomous components from the spicules occurred in these individuals. Fraction 3 also caused a delayed-type reaction in the author and some of the volunteers, suggesting that type IV allergy may also be caused by the venomous components. Since a delayed-type reaction was also observed in volunteers with no known history of caterpillar dermatitis, sensitization may occur without the person being aware of it.

Further analysis of fraction 3 is underway at present, and the molecular weight of the compounds is estimated to be 20,000 to 40,000. The results of the present study do not exclude the involvement of mechanical stimulation by the spicules, chemical stimulation or effect of lipid-soluble materials in venomous components. However, the findings suggest that a substance in fraction 3 is likely to be an allergen that contributes to dermatitis due to *E. pseudoconspersa* caterpillars. Variations in the clinical course of individual patients may be attributable to difference in the state of sensitization.

Acknowledgment

The author acknowledges the technical assistance of Yoshiharu Sato, Central Research Laboratory in Hyogo College of Medicine.

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Clinical Manifestations of Hand Eczema Compared by Etiologic Classification and Irritation Reactivity to SLS

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Abstract

Hand eczema is a common skin disease. Because of its variable etiologies and clinical manifestations, it is difficult to determine the etiology from the clinical manifestation. Among the contact allergens, nickel is the most common. Patients with hand eczema and a nickel allergy have a poorer prognosis than patients without a nickel allergy. The reason is still uncertain; suggestions include persistent exposure to nickel or a weak skin barrier. The purpose of our study was to identify the characteristic clinical manifestations by etiology and to compare the skin barrier state between patients with nickel allergies and those without them. Ninety-three patients were classified into 4 types; irritation contact type, allergic contact type, atopic type and mixed type. After the sodium lauryl sulfate (SLS) test to compare the skin barrier state, visual score and transepidermal water loss (TEWL) were measured and analyzed statistically. From this study, it was not possible to ascertain a statistical difference, however a few characteristic clinical manifestations according to etiology can be stated. There was no difference in the visual scoring system or the TEWL after the SLS irritation test between the nickel-allergy group and the non-allergy group. Therefore, we believe that the poor prognosis of hand eczema with nickel allergy may be due to the nickel allergy itself rather than skin barrier state.

Key words: hand eczema; SLS; skin barrier; transepidermal water loss

Introduction

Hand eczema includes allergic contact dermatitis, irritation contact dermatitis, atopic dermatitis, nummular eczema, pompholyx and unclassified eczema (1). It occurs in approximately 9-11% of the population (2). The causes are mainly soap, detergent, oil, water, and various other allergens.

The classifications of hand eczema according to clinical manifestation and etiology are diverse and complex. Thus, it is difficult for physicians to choose the appropriate

treatment and prevention plan based on the clinical manifestation alone. Although there have been attempts to develop a classification system based on the clinical manifestations of hand eczema (3, 4), we could not find any research reports supporting the linkage of causes and clinical characteristics. We studied the clinical manifestation of hand eczema according to etiology. We found some characteristic differences among the different groups and used these clinical differences to identify the causes of hand eczema.

The nickel positive rate of the standard patch test in hand eczema patients has varied from 8% to 58%, but it has been more common than that of other allergens (5-7). Therefore, nickel is suspected as a cause of hand eczema. Furthermore, patients with a nickel allergy are known to have a worse prognosis than non-allergic patients (8). Al-

Received July 30, 2001; accepted for publication May 28, 2002.

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