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Heat Contact Urticaria
-A case report-

Hae-Shin Chung, Kwang Hoon Lee, and Jai Youl Ro*

Heat contact urticaria is very rare and it is characterized by the development of wheal limited to the areas of heat contact. We report a case of heat contact urticaria in a 65-year-old women. The wheal was induced by hot bathing, washing in hot water or leaning on hot radiators. Symptoms started within 5 minutes of exposure and lasted 30 to 60 minutes. She had no systemic symptoms. The clinical diagnosis of localized heat urticaria was confirmed by experimental induction of localized wheals.

Our investigation showed that the threshold temperature needed for induction of the heat urticaria was 39℃. We tried to investigate the plasma levels of prostaglandin D_2 and blood histamine before and after heat challenge. The patient showed marked improvement after a combination treatment of desensitizing by repeated exposure to heat and indomethacine.

Key Words: Urticaria, heat, contact, desensitization, prostaglandin D_2

There are two ways in which urticaria may be produced by heat. First is the generalized form, or cholinergic urticaria, which may follow exercise or generalized body heating and which may also be induced by emotional stress. Second is heat contact urticaria produced only by direct contact of the skin with heat and not by exercise or emotional stress (Wise *et al.* 1978). Localized heat urticaria which was first described by Duke (1924) is characterized by the development of urticarial lesions within minutes of heat exposure. These lesions are sharply localized to the area of contact with heat. Mucosal involvement has been reported in some cases, and systemic symptoms can occur if large areas of skin are exposed (Greaves *et al.* 1981). The natural history of this condition is uncertain, but some cases have lasted for several years. The mechanism of localized heat urticaria is not known and the responses to treatment variable (Illig, 1973).

We report a case of heat contact urticaria in whom we obtained symptomatic relief by producing tachyphylaxis to heat and performed an assay for plasma levels of PGD_2 and histamine, before and after heat challenge and the clinical response after inhibition of PGD_2 synthesis.

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Departments of Dermatology & Department of Pharmacology*, Yonsei University College of Medicine, Seoul, Korea
Address reprint request to Dr. K.H. Lee, Department of Dermatology, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul, 120-752, Korea

CASE REPORT

Case

A 65-year-old woman presented with a 1-year history of recurrent redness, itching, swelling of the skin localized to areas exposed to increased temperature. The wheal was in-

duced by bathing, washing in hot water, leaning on hot radiators, and by direct or indirect exposure to warm sunlight. The patient did not have swelling of the oral mucosal surfaces upon drinking or eating hot foods. Symptoms started within 5 minutes of exposure and usually lasted from 30 to 60 minutes. She had no other systemic symptoms. Although the patient tried to avoid triggering stimuli, she remained with urticarial symptoms. General physical examination was unremarkable. A provocation of running hot tap water (temperature undetermined) over the arm produced the lesion seen in the photograph (Fig. 1). A skin biopsy of the arm taken after provocation showed mild perivascular lymphocytic infiltration (Fig. 2). Dermographism was absent. The clinical diagnosis of localized heat urticaria was confirmed by experimental induction of localized wheals. A water-filled glass beaker (6.5 cm diameter) at 39℃ and at 42℃ were applied to the skin of the back for 4 minutes. Clinical signs of erythema and wheal were assessed. Using this method, the erythema was induced within 4 minutes at 39℃

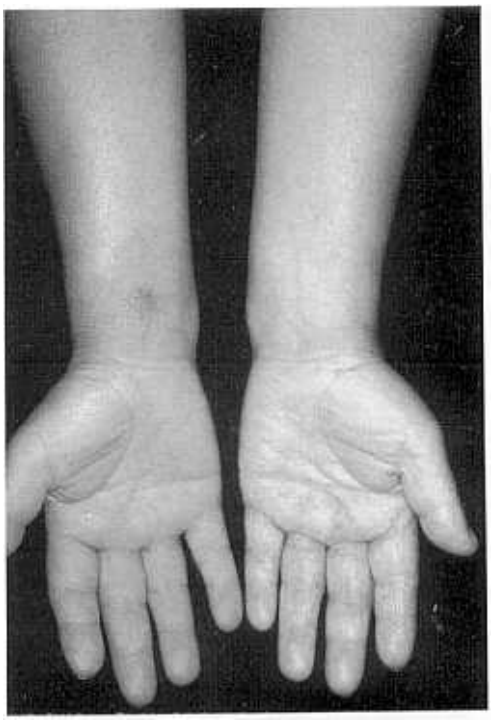

Fig. 1. *Lesion induced on the forearm of the patient by running hot tap water.*

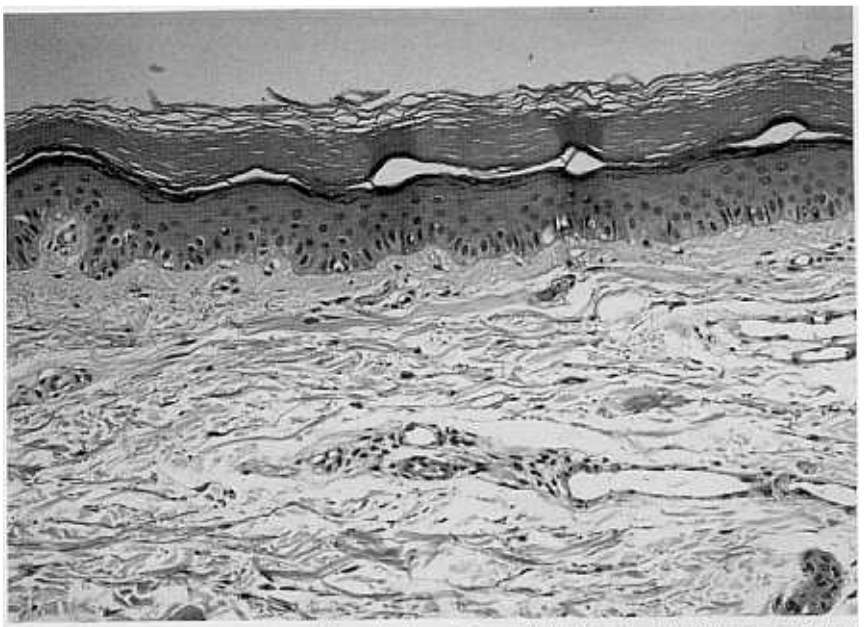

Fig. 2. *Skin biopsy taken at provocation site showing mild perivascular lymphocytic infiltration.*

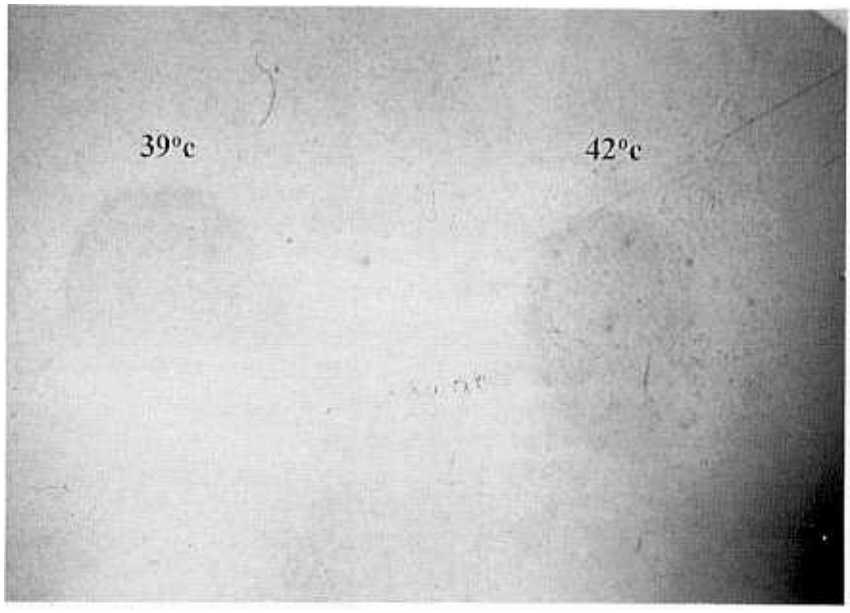

Fig. 3. *Itching and erythema was evoked at 4 minutes at a threshold temperature of 39℃.*

(Fig. 3). Erythema persisted for between 60 and 90 minutes. Full blood count, ESR, antinuclear antibody, serum IgE level, C3 and C4 levels, VDRL were normal or within normal limits.

PGD_2 radioimmunoassay and histamine assay

Blood samples (10 ml) from the antecubital vein of the patient's right forearm were collected for PGD_2 and histamine analysis before, during, and after heat challenge with a water-filled glass beaker (6.5 cm diameter) at 39℃ and at 42℃ on the back of the patient for 4 minutes. The samples were centrifuged at 1,400 g for 10 minutes and the plasma removed and stored at −70℃ until analyzed. Five subjects with no known clinical disorder were used as control.

Blood PGD_2 levels were measured by Biotrak® prostaglandin D_2[^{3}H] assay system (Amersham, Arlington Heights, IL, USA). A 1 ml aliquot of plasma was diluted with an equal volume of ethanol: water (1 : 4 v : v) and acidified with 0.01 ml acetic acid. The mixture was allowed to equilibrate for 5 min and was then centrifuged at 10,000 g in a microcentrifuge for 5 minutes. The supernatant was applied to an extraction column which had been previously equilibrated with ethanol and then ethanol: water (1 : 9 v : v). The extraction column was then washed with 5 ml water followed by 3 ml hexane. PGD_2 was eluted 1.5 ml ethyl acetate. The ethyl acetate in the sample was removed by evaporation under a stream of nitrogen. The PGD_2 in the lipid extract was measured by radioimmunoassay (RIA) using a rabbit antiserum specific to PGD_2-11-methyloximate. Briefly, the plasma lipid extract was redissolved in 0.1 ml of methloximating solution (450 ml 1 M sodium acetate, 5 g methoxyamine hydrochloride and ethanol to a final volume of 500 ml, pH 5.7) and then diluted with an equal volume of assay buffer (0.1 M tris-HCl buffer, pH 7.4, containing 0.336 g/l EDTA, 0.5 g/l sodium azide and 5 g/l bovine γ-globulin). Samples were heated to 60℃ for 30 minutes to give PGD_2-ethyloximate and diluted with a further 0.2 ml assay buffer before RIA. Each RIA assay tube contained 0.1 ml of serially diluted sample or standard PGD_2-methyloximate, 7,000 dpm [^{3}H] PGD_2-methyloximate in 0.1 ml RIA buffer and 0.1 ml of a 1 : 16,000 dilution of antiserum to PGD_2-methyloximate. The tubes were equilibrated

at 4℃ overnight and the bound tracer precipitated with 0.8 ml 25% (w/v) polyethylene glycol and centrifuged at 1,400 g for 30 minutes. The supernatant was aspirated and the pellet resuspended in 1.2 ml Pico-Fluor 30 and the radioactivity determined by liquid scintillation counting.

Blood histamine levels were assayed by the fluorometric analyzer according to Siragamian (1974) method.

Results for PGD_2 and histamine are shown in Table 1. There were no changes in the values of PGD_2 concentration before and after challenge or treatment. The control subjects had blood PGD_2 level of 11.2 ± 0.7 (pg/ml).

Table 1. Plasma PGD_2 level and histamine level after heat challenge

	Blood PGD_2(pg/ml)	Blood Histamine(ng/ml)
Controls(n=5)	11.2±0.7*	1.4±0.6*
Pretreatment		
Pre-challenge	10.2	1.2
After challenge	11.2	1.3
Posttreatment		
Pre-challenge	11.4	1.4
After challenge	10.0	1.2

*: mean±S.D.

Plasma PGD_2 and histamine levels measured in patients before and after treatment, and in control subjects not sensitive to heat. Blood histamine levels in the patient before treatment are also given.

Blood histamine levels were below the limit of detection of the bioassay. (<2.5 ng/ml) in the patient before and after heat challenge and in the control subjects (1.4±0.6 ng/ml) at all times.

Treatment

The patient was given three forms of treatment. The first approach was to suppress the effects of released histamine by means of H1 receptor inhibitor. The second approach was to desensitize the patient, a method reported to have been effective in two other cases. Initial tests demonstrated localized heat tolerance at supra-threshold and slightly less at sub-threshold temperatures after repeated hot water beaker. Warm water baths, each of 4 minute duration, were given daily with the water temperature starting sub-threshold at 39℃ and increasing 0.5℃ every bath with an hour interval for 10 times a day starting with the lower legs (Table 2). Each day more of the body was exposed until on day 4 the entire body except the head was immersed and the number of baths taken was reduced to 5. On subsequent days, the starting bath temperature was slowly increased and the number of baths taken reduced until on day 8 one bath at 41℃ was taken. There was no wheal, only slight itch and no systemic effects during the 3 week course of desensitization. After desensitization, the threshold had increased to 45℃ in a 4 minute beaker test (Fig. 4). The

Table 2. Schedule for induction of tolerance to heat

Day	Site exposed	Time interval	Temperature, initial(℃)	Temperature increment(℃)	Number exposed
1	Lower legs	hourly	39	0.5	10
2	Legs	hourly	39	0.5	10
3	Trunk & legs	hourly	39	0.5	10
4	Total body	2 hours	39	0.5	5
5	Total body	2 hours	40	0.5	5
6	Total body	3 hours	40.5	0.5	4
7	Total body	3 hours	40.5	0.5	4
8~10	Total body	6 hours	41	1	2
11~20	Total body	6 hours	41.5	1	2
21~	Total body	6 hours	42	0	2

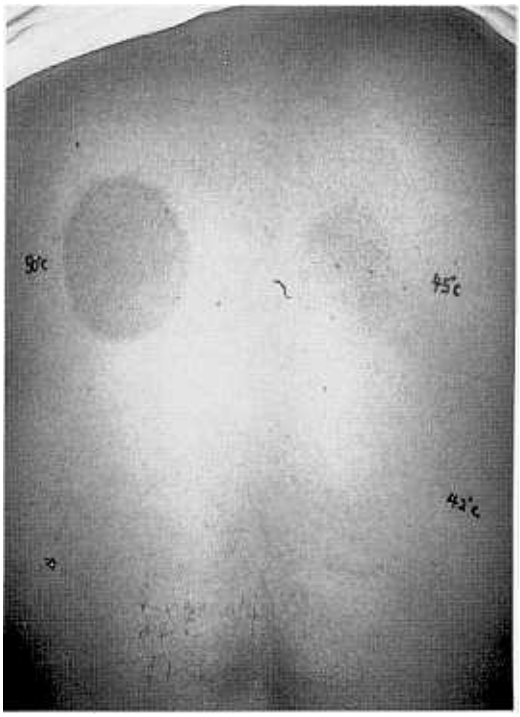

Fig. 4. *The whealing threshold was increased to 45℃ after a desensitization and indomethacine therapy.*

patient had a slower response, less itch and wheal and was able to take baths at a higher temperature. Indomethacin 25 mg four times a day was added to the tolerance program.

DISCUSSION

The mechanism of heat contact urticaria is unknown and because the condition is extremely rare no single investigator has been able to study a group of affected patients (Tatnall *et al.* 1984). Although it is a form of physical urticaria induced by heat, it produces the urticarial lesion on the heat contact site only (Daman *et al.* 1978). Therefore, a vascular change due to localized factors can be assumed to be involved in the pathogenesis of heat contact urticaria.

In heat contact urticaria it may be difficult to exclude cholinergic, aquagenic or solar urticaria. Cholinergic urticaria can be precipitated by emotion and exercise, unlike localized heat urticaria, and experimentally reproduced by injection of various cholinomimetics. A positive result is indicated by the development of satellite wheals. However, exercise and hot bathing are the diagnostic methods of choice. Aquagenic urticaria may be excluded by challenge with cool water. Heat contact urticaria may also be confused with solar urticaria but a formal testing to heat and light can distinguish between these conditions. Another diagnosis which might be considered is factitious urticaria caused by towel friction following a bath, shower or swimming.

In our patient, we have tried to demonstrate the generation of PGD_2, an arachidonic acid metabolite, which can be considered a specific indicator of mast cell activation (Lewis *et al.* 1982). The time course of PGD_2 release into the plasma was approximately the same as for histamine and coincide with the appearance of the clinical signs and symptoms after challenge. The activation of mast cells leading the release of preformed inflammatory mediators and the concomitant generation of newly formed mediators is clearly implicated in the pathogenesis of heat contact urticaria in several cases, although the specific nature of the stimulus which activates the mast cells is not yet known (Holgate *et al.* 1984). In previous studies, there has been reports in changes in the concentration of PGD_2 and histamine levels after indomethacine treatment. In our patient we have failed to support any changes in the level of PGD_2 and histamine. Since the patient did not have any systemic symptoms after local challenge, this may not be a sufficient method of challenge for any changes to occur in the concentration of PGD_2 and histamine levels.

Treatment of heat contact urticaria remains difficult and avoidance is impractical. Desensitization by the induction of physical tolerance has been reported to be successful in other cases (Leigh and Ramsay, 1975). In our patient, addition of indomethacine to the desensitization treatment did not result in complete suppression of PGD_2 and histamine release to the blood, but there was much im-

provement of the symptoms. As in other physical urticaria, a method of desensitization may relieve the symptoms of urticaria, however, further studies are needed for the evaluation on the mechanism of desensitization treatment.

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