

Delayed-type hypersensitivity to contact allergens in psoriasis

A clinical evaluation

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The possibility for patch testing procedures to detect contact allergy was examined in 85 hospitalized patients with forms of psoriasis. Exclusion criteria were active lesions on the back, the use of strong topical corticosteroids, methotrexate, cyclosporin and UV therapy. After screening, a group of 47 patients with different forms of psoriasis were selected for patch testing. Personal history, including topical treatment, occupation and domestic circumstances, were reasons to extend the standard series of allergens. Tars, nickel sulfate, perfume and balsam of Peru scored high. The overall positive rate was 68%. This is higher than that observed in earlier studies. The unexpected results are discussed in the light of the possible mechanism of action.

Key words: psoriasis; delayed-type hypersensitivity; contact allergy; patch testing; coal tar; nickel; fragrance. © Munksgaard, 1998.

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Psoriasis can be triggered by many endogenous or exogenous factors. The clinical picture (location of lesions) and course (therapy resistance) in certain psoriatic patients may suggest involvement of local triggering factors and contact allergy. Therefore, the question as to what extent exogenously triggered delayed-type hypersensitivity (DTH) to contact allergens played an additional etiological rôle in the development of the clinical picture of psoriasis, was addressed. Only a few reports are available on the rôle of contact allergy in palmo-plantar psoriasis (1, 2) and in forms with mixed locations (3). Moreover, in psoriasis, some attention has been focussed in psoriasis on topical drugs such as tar and dithranol with respect to their allergenicity (4, 5).

In the present study, 85 hospitalized patients with psoriasis (period 1992–1996) were evaluated for the possibility of contact allergy by means of patch testing with European standard series and extended series. An unexpectedly high score (68%) of positive patch tests was observed in the group of 47 patients who were tested.

Patients and Methods

85 hospitalized patients with different forms of psoriasis were evaluated to establish contact al-

lergy. Out of the original group ($n=85$), a cohort of 47 patients remained to be tested, after exclusions (38) were made because of the existence of active lesions on the back, the use of strong topical corticosteroids, methotrexate, cyclosporin and UV-therapy. They were treated along the lines of good clinical practice either topically, systemically or with a combination therapy. Clinical parameters that were considered were age, sex, clinical diagnosis and location of the lesions. In the original group of 85 hospitalized patients, 3 sub-groups were noted: psoriasis vulgaris (PV, $n=69$), other forms of psoriasis like pustular, erythrodermal, inverse, etc. (OF, $n=6$), and the seborrhoeic type of psoriasis (SP, $n=10$).

Patients treated with strong topical corticosteroids, systemic therapies such as cyclosporin, methotrexate, or UV light (PUVA/UVB) were not patch tested. Patch tests were carried out as soon as the overall disease activity had decreased and the area of the upper back was free from active lesions. The test area was weaned from topical treatment for at least 3 days before testing; only emollients were allowed there. Antihistamines were stopped 1 week prior to testing.

When the upper back was free of active lesions, the area was cleaned with alcohol and patch tests

were performed. A single remaining psoriatic spot was marked with a waterproof ink.

The following series were used: the European standard series, a Rotterdam extended series and a topical treatment series, including a corticosteroid series. If the history in the individual patient indicated the possible relevance of particular substances, such as topical drugs including homeopathic remedies, cosmetics or substances used in occupational duties or hobbies, such substances were also tested. Curatest®, the tape used for the tests was obtained from Lohmann, Almere, The Netherlands. Plastic chambers and standard series of allergens were obtained from Van der Bend (Trolab) Brielle, The Netherlands. Other products were prepared by the hospital pharmacy or tested "as is". All test results were read after 2 and 3 days and corticosteroid series were read again after 5 days. Scores of the tests were: +redness; ++redness and papules; +++ redness, papules and vesicles; ++++ reaction with eczema beyond the boundary of the test area.

Results

Out of the original group of 85 patients with psoriasis, a cohort of 47 patients was tested (18 males, 29 females), 38 others not being tested according to the exclusion criteria. The mean age of the 47 patients was 49 years (range 10–82), 44 years for the males (24–67) and 51 years for the females (20–82). The cohort of 47 patients was divided into sub-groups based on the clinical pattern. The sub-group of patients with PV consisted of 35 cases (14 male, 21 female) and in this sub-group 23 patients (10 male, 13 female) had 1 or more positive patch tests. The sub-group of patients with OF comprised 5 cases (1 male, 4 female), all patients being positive to 1 or more allergens tested. The 3rd sub-group of patients with SP consisted of 7 cases (3 male, 4 female). In this last sub-group, 4 patients (1 male, 3 female) were observed to have positive patch tests. Overall, 12 (66.7%) out of the 18 males were positive and 20 (68.3%) out of the 29 females, representing a total of 32 patients (68.0%) who were positive out of the 47 patients (Table 1). Detailed analysis of the 7 patients with hand and/or

foot involvement showed that 5 cases (2 PV, 3 SP) were positive and 2 cases (1 PV, 1 SP) were negative.

A summary of the allergens that were positive in patch tests is shown in Table 2. Considering these results, a preference for some allergens can be noted: tars (14×), nickel sulfate (5×), perfume and balsam of Peru (both 4×, each). At the concentrations used we did not see any irritant reactions. In cases of doubt the rest of the group served as controls.

In a number of cases, there was a clear relation between a positive patch test and the lesion's location. This is shown in Table 3.

Discussion

Clinically and histopathologically, psoriasis may present as different variants (6, 7). Location, course and duration of lesions, itching or therapeutic resistance may suggest the involvement of an underlying trigger in the form of an irritant or a contact allergen such as tars or dithranol (4, 5, 8–10). A thorough history of the patient must be taken regarding these possible factors and a relationship to particular past and current topical treatment, occupational or hobby activities responsible for cell-mediated (delayed-type) allergic immune response (DTH) must be considered. In-depth reports on the role of DTH in psoriasis are scarce and the publications available are case reports (9–13). In studies on larger groups focussing on allergic contact dermatitis, mention is made of only a few psoriasis patients with contact allergy. The incidence of contact allergy in psoriasis has been particularly investigated in the sub-group of palmo-plantar psoriasis. The % of patients who are positive to patch tests in this form of psoriasis has ranged from 41.7 (3) to about 20 (1, 2), whereas these authors observed positive patch tests in only 6.6% of patients with other forms of psoriasis. In our study, 5 out of 7 patients with palmo-plantar lesions were positive to one or more of the test allergens that were used. These aforementioned data show that particularly psoriasis of palms and soles is suspect for contact allergy. Our study, which was conducted in patients with differ-

Table 1. Results of patch tests and DTH in 3 groups of psoriasis patients

	PV m	PV f	OF m	OF f	SP m	SP f	Total
no. of patch tested patients	14	21	1	4	3	4	47
% of total patch tested patients	29.8%	44.7%	2.1%	8.5%	6.4%	8.5%	100%
DTH pos. patients	10	13	1	4	1	3	32
% DTH pos. patients per diagnosis group	71.4%	61.9%	100%	100%	33.3%	75%	68%

PV: psoriasis vulgaris; OF: other forms of psoriasis; SP: seborrhoeic psoriasis; m: male; f: female.

Table 2. The allergens that showed 77 positive patch tests on 3 groups of psoriasis patients ($n=32$), arranged in groups, absolute frequencies of positive tests

Group/substance	PV m	PV f	SP m	SP f	OF m	OF f	Total	Conc %	In
<i>Tars</i>	7	2	0	3	0	3	15	—	—
coal tar sol.	2	2		1		1	6	5	pet.
wood tar mix	5			2		2	9	12	pet.
<i>Steroids</i>	2	0	0	0	0	0	2	—	—
hydrocortisone butyrate	1						1	1	alc.
tixocortol-21-pivalate	1						1	1	vas.
<i>Other local medication</i>	11	5	1	0	0	1	18	—	—
sorbic acid	1						1	2	vas.
Phenergan® cream	1						1	as is	as is
lanolin wax	1	1					2	as is	as is
Hansaplast® plaster	1	1					2	as is	as is
Axungia	1						1	as is	as is
cetomacrogol cream	1						1	as is	as is
dithranol	1						1	0.1/0.2	vas.
Daktakort®	1						1	as is	as is
Eucerin cream	1						1	as is	as is
Flamazine®						1	1	as is	as is
povidone-iodine ointment		1					1	as is	as is
salicylic acid		1					1	1	vas.
vioform	1						1	3	pet.
thimerosal		1	1				2	0.1	vas.
wool alcohols	1						1	30	vas.
<i>Cosmetics</i>	1	2	0	1	0	4	8	—	—
perfume mix	1	1		1		4	7	8	vas.
eye cream		1					1	as is	as is
<i>Detergents</i>	2	2	0	0	0	0	4	—	—
Basonal® shampoo	1						1	1	aq.
liquid soap		1					1	1	aq.
Lyorthol		1					1	1	aq.
sodium lauryl sulfate	1						1	1	aq.
<i>Other allergens</i>	6	21	0	1	0	2	30	—	—
nickel sulfate		5					5	5	vas.
balsam of Peru	2	1				1	4	25	vas.
para-aminobenzene		3					3	10	vas.
para-phenylenediamine		3					3	0.25	vas.
potassium dichromate	1	1					2	0.5	vas.
formaldehyde		1		1			2	1	aq.
isoeugenol		1				1	2	1	vas.
benzocaine		1					1	5	vas.
cobalt chloride	1						1	1	vas.
epoxy resin	1						1	1	vas.
ethylenediamine		1					1	1	vas.
organic dye		1					1	1	vas.
panty		1					1	as is	as is
propylene glycol	1						1	5	aq.
rubber mix		1					1	0.10	vas.
thiuram mix		1					1	1	vas.

ent forms of psoriasis, with both local and diffuse patterns, stresses the impact of these other forms of psoriasis. The evaluation with extended test series based on patients' histories and previous experience of topical treatment is also relevant, as this approach detected more patients with DTH than could be expected from the literature. It cannot be stated that the high incidence of positive results in this study is due to misinterpretation of the clinical status of the patients, because in only 7 of the 47 patients that were tested was the clinical

pattern of seborrhoeic psoriasis partly resembling that of eczema (sub-group with SP) observed. In this sub-group, a positive patch test was noted in 4 patients (57.0%), but in the sub-group of patients with clinically typical PV, a positive patch test was also observed in 23 (65.7%) out of 35 patients.

Psoriasis apparently triggered by contact allergens shows a T-cell dependent pathophysiological mechanism (14). It is not clear whether the psoriatic skin lesions are more prone to react to a certain antigen after repeated applications (and ensu-

Table 3. Relation of allergen and location

No. observations	Allergen	Location	Form of psoriasis
1	panty hose	legs	PV
1	Basonal® shampoo	head	PV
1	steering wheel	hands	PV
2	para-phenylenediamine	trunk and extremities	PV
1	para-aminoazobenzene	trunk and extremities	PV
1	organic dye	trunk and extremities	PV
1	balsam of Peru	on application site	PV
1	hydrocortisone-butyrate	on application site	OF
1	tixocortol-21-pivalate	on application site	OF
1	Daktacort®	on application site	OF
1	LCD	on application site	OF
1	thiuram mix	contact places of bra and skin	PV
1	wool alcohols	on application site	OF
1	thimerosal	palms of hands and feet	SP
1	benzocaine	on application site	PV

ing sensitization) with a sustained inflammatory response of mixed eczematous and psoriatic character than non-involved skin of psoriatics. In this respect, the observation of Grolnick (cited in ref. (15)) is worth mentioning. He demonstrated that the skin at the site of eczema is more reactive than normal skin; he challenged subjects with an antigen to which they were previously allergic. 1 to 2 months later when the challenge site was completely healed, the same subjects were patch tested with an allergen to which they were not allergic. He showed that subjects gave a positive reaction at the previous eczema site but not on the control site. This may also be true for healed sites of psoriatic skin. The triggered immune system in lupus erythematosus similarly leads to a significantly increased prevalence of skin allergies (16). Eventually, decreased thickness of the epidermis overlying elongated dermal papillae might enhance penetration of possible antigens in combination with keratolytics.

In psoriasis, antigen-presenting cells play an important rôle in "spontaneous" activation by up-regulation of self-antigen receptors on T lymphocytes. This phenomenon is possibly due to the inductive rôle of the (auto)antigens in the epidermis (17). Moreover, in psoriasis, specific interleukins (IL), such as IL-4, IL-6 and IL-8, are produced in large quantities, whereas the amount of IL-1 is lowered (17). These data suggest a triggerability of the immune system. It is to be considered that an allergen can more easily penetrate the skin because of the damaged barrier, as in eczematous lesions, thus causing a contact allergy. In several of our patients, a strongly positive eczematous patch area evolved after several days into a spot that was similar to psoriasis, thus supporting the significance in vivo of the mechanism of Köbner phenomenon, although poorly understood (6). A positive patch test with a patient's own substance eventually, in

combination with a positive outcome of a patch test with its corresponding ingredients (from standard testseries), supports the (clinical) relevance of this test (7).

In conclusion, the overall result of 68% of the patients who were observed to be positive in patch tests points to DTH to contact allergens as a possibly relevant factor in the presentation or course of psoriasis and should be evaluated accordingly. It is possible that avoiding selected antigens may alleviate chronic, recalcitrant psoriasis.

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