

FREQUENCY OF DELAYED-TYPE HYPERSENSITIVITY TO CONTACT ALLERGENS IN PALMO-PLANTAR PSORIASIS

**Nina Caca-Biljanovska, Marija V'ickova-Laskoska,
Margareta Balabanova-Stefanova, Vesna Grivceva-Panovska**

*Dermatovenerology Clinic, Faculty of Medicine, University of Skopje,
R. Macedonia*

Abstract: Psoriasis is a common, chronic, genetically determined, T-cell-mediated inflammatory dermatosis. The *aim* of this study is to determine the frequency of delayed-type hypersensitivity to contact allergens in palmo-plantar psoriasis and their importance in provoking and/or perpetuating the same.

Materials and methods: 101 patients with different clinical forms of psoriasis were included in our study. The patients were divided into two groups, on the base of the clinical aspects and localizations of the lesions. The first group consisted of 38 patients with palmo-plantar psoriasis. The second, control, group of patients with psoriasis vulgaris but without lesions on palms and soles included 63 cases. The patch-tests were performed on all 101 patients.

Results: In the first group of patients with palmo-plantar psoriasis, the patch-tests were positive in 15 patients (39.5%). Only 8 patients (12.7%) had positive results of patch-testing in the control group (psoriasis without palmoplantar involvement). The study showed a highly statistically significant difference in the frequency of positive patch-tests between the two investigative groups ($p < 0.01$). In the first group of patients with palmo-plantar psoriasis there was noted a statistically significant greater number of positive patch-tests.

Conclusion: The results of our study showed a statistically significant bigger number of positive patch-tests in patients with palmo-plantar psoriasis, which confirmed the role of contact allergens in the triggering and/or perpetuating of the lesions. Therefore, it is necessary for patch-testing to be included as a diagnostic procedure in patients with psoriasis unresponsive to conventional topical treatment. It is possible that avoiding selected antigens may alleviate chronic, recalcitrant psoriasis.

Key words: palmar-plantar psoriasis, delayed-type hypersensitivity, patch-test.

Introduction

Today, psoriasis is definitely recognized as a T-cell-mediated inflammatory disease [1]. Psoriasis occurs in 0.1–3% of the world's population with significant variants in different regions. [2]. Clinical presentations vary in individuals from presenting only a few salmon-pink papules and/or plaques with silvery-white scales or with generalized skin involvement [3]. The forming of the psoriatic plaque, an inflammatory reaction, is triggered by environmental factors; many exogenous and endogenous provocations may precipitate a transition of clinical latent genetic psoriasis into clinically manifest psoriasis. In addition to genetic predisposition and environmental factors, immunological mechanisms are also involved in the pathogenesis of psoriasis. Disproportionate levels of pro-inflammatory cytokines and growth factors in psoriatic lesions determine the three key events: epidermal keratinocyte hyperproliferation without proper differentiation, vascular proliferation and associated inflammation [2, 4]. It is suggested that systemic lymphocyte activation is followed by the local accumulation of specific CD4+ T-cells and subsequently by the activation of intradermal CD8+ T-cells [1]. Thus T-cells are responsible for the initiation and maintenance of psoriasis. The psoriatic process is a dynamic process that includes interaction between Th1 and Tc1 cells, as well as between T-cells and keratinocytes. The activation of the local cell immunity may be induced by contact allergens. Immunological events in the development of psoriasis are very similar to cell immunity of delayed-type hypersensitivity. Palmo-plantar lesions are common in psoriasis and in different studies vary from 2 to 21%. The clinical picture of psoriasis with palmo-plantar involvement, as a course of disease in which new lesions develop, the aggravation of existing lesions and/or therapy resistance in some patients, suggests an involvement of local triggering factors and contact allergy. The involvement of these areas (palmo-plantar) is of great importance because it may invalidate patients and impair their social and professional activities. Every day in dermatology practice we work out these problems with palmo-plantar psoriasis and so we decided to elaborate this study.

Materials and methods

The study was conducted over a three-year period (2002–2004) at the Department of Dermato-venereology, Medical Faculty in Skopje. The subject of this study were 101 patients with different clinical presentations of psoriasis and were divided into two groups, based on clinical aspects and localizations of lesions (morphological and topographical forms).

38 patients with a clinical picture of palmar and plantar psoriasis were included in the first group, with sharply demarcated erythematous plaques and/or diffuse keratoderma, well bordered by an erythematous halo and deep, painful fissures.

The control group consisted of 63 patients with typical psoriasis vulgaris but without palmar and plantar lesions. For each patient a protocol was prepared containing data about personal history, family and past history of other diseases, occupation and domestic circumstances, including topical treatment. Clinical parameters that were considered were sex, age, clinical diagnosis and location of the lesions. The diagnosis was made on the basis of clinical and histopathological examination. Mycological examinations were carried out in most of the cases to exclude tinea. Patch-testing procedures for evaluation of delayed-type hypersensitivity to contact allergens were examined in all patients. 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. The same was the case for systemic therapy (methotrexat, retinoids, cyclosporin) or UV therapy (PUVA/UVB).

In the present study, 101 patients with psoriasis were evaluated for the possibility of contact allergy by using a patch-test with European standard series, extended series in some patients and corticosteroid series. We followed the standard procedures of the International Contact Dermatitis Research Group (ICDRG). All patch-test results were read after 48 and 72 hours: in some patients after 96 hours. Scores of the tests were: + redness, ++ redness and papules; +++ redness, papules and vesicles; ++++ reaction with eczema within the test area.

Descriptive and analytic statistical methods were used in statistical analysis. Frequency and percentages were used as descriptive methods and the χ^2 test method as tables of contingency 2x2 was used as an analytic method.

Results

Over a period of three years, 101 patients with psoriasis vulgaris were processed. According to the clinical and histopathological examination, patients were divided into 2 groups: 38 patients had isolated palmo-plantar psoriasis and 63 patients had a clinical picture (morphology and topography) of psoriasis vulgaris, but without palmar and plantar lesions. Patch-tests were performed on all 101 patients.

The first group consisted of 38 patients (22 men and 16 women) with palmo-plantar psoriasis, additionally verified using histological examination. The laboratory results of all patients in the group were within the normal range. Mycological findings were negative in all patients. All patients had a negative history the atopic constitution and hypersensitivity to some medicaments. Nails

were involved in 25 cases in the form of yellow-brown discoloration, subungval hyperkeratosis, pitting and onycholysis. A positive patch-test was found in 15 patients (39.5%); 9 men (23.7%) and 6 women (15.8%). The summary of positive patch-tests in group I is given in Table 1. The most common allergens were: nickel (7x) and cobalt (8x).

Table 1 – Табела 1

Positive patch-tests in 15 out of 38 patients with palmo-plantar psoriasis

Позитивен patch-тест кај 15 од 38 пациенти со палмо-плантарна псоријаза

Patient No.	Age (years)	Sex	Occupation	Positive patch-test
1.	42	f	housewife	nickel sulphate
2.	57	f	worker	epoxy resin, cobalt chloride
3.	64	m	pensioner	phenylenediamine, paraben mix
4.	33	f	housewife	nickel, cobalt, detergent (Ariel)
5.	62	m	worker	paraphenylenediamine
6.	53	f	professor	nickel sulphate
7.	48	m	employee	cobalt chloride
8.	42	m	worker	potassium dichromate, nickel sulphate
9.	39	f	housewife	cobalt chloride, nickel sulphate
10.	55	f	pensioner	nickel, cobalt, detergent (biljana)
11.	47	m	employee	cobalt chloride
12.	62	m	worker	detergent (ariel), soap for hands
13.	38	m	unemployed	thiuram mix, neomycin sulfat, cobalt
14.	59	m	employee	nickel
15.	44	m	worker	cobalt

In the second, control, group there were 63 patients (37 male and 26 female) with other forms of psoriasis: chronic plaque psoriasis, psoriasis inversa, psoriasis guttata, seborrhoic psoriasis; which showed no psoriatic lesions on palms or soles. The age structure was similar to that in the first group tested. The diagnosis was made on the basis of clinical and histopathological examinations. 8 patients (12.7%) had a positive patch-test; 5 male (7.9%) and 3 female (4.8%). All patients from this group had a negative personal and family history of allergic diseases. The positive patch-test in the control group is given in Table 2.

Table 2 – Табела 2

Positive patch-test in 8 out of 63 patients with psoriasis without palmo-plantar lesions

Позитивен patch-тест кај 8 од 63 пациенти со псоријаза без палмо-плантарни лезии

Patient No.	Age (years)	Sex	Occupation	Positive patch-test
1.	45	f	housewife	nickel, cobalt
2.	58	m	facade worker	kliokvinol, paraffin, tar, brick, panel paste
3.	38	f	housewife	soap for hands, detergent (Ariel)
4.	59	f	employee	nickel
5.	52	m	worker	cobalt
6.	40	m	unemployed	2 methoxy 6-n pentyl-4
7.	62	m	pensioner	colophony, potassium dichromate
8.	65	m	pensioner	thiuram mix

Dependence, between the two groups, was tested by the χ^2 test pointing: $\chi^2 = 9.663$; $df = 1$; $p < 0.01$, that means there was highly statistically significant difference in the frequency of positive patch-tests between groups. Fig.1.

Fig. 1. Patch -test in investigated groups

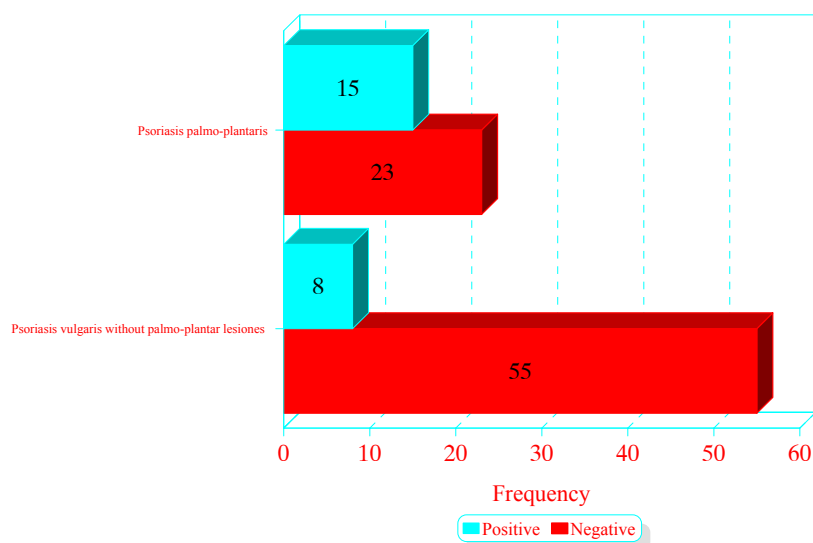


Figure 1 – Patch -test in investigated groups

Слика 1 – Patch-тест кај испитуваните групи

In the first group of patients with palmo-plantar psoriasis there was noted a statistically significantly greater number of positive patch-tests, that means greater hypersensitivity to contact allergens. Table 3.

Table 3 – Табела 3

χ^2 test

χ^2 тест

χ^2 test	Positive patch-test	Negative patch-test	Total
I Group	15	23	38
II Group	8	55	63

Discussion

The clinical manifestations of psoriatic lesions can be extremely variable in intensity and extensity [3]. The first group of patients with palmo-plantar psoriasis had a typical clinical picture for that localisation: sharply demarcated erythematous plaques and/or diffuse keratoderma, well bordered by an erythematous halo and deep, painful fissures. Localization, course and duration of lesions, itching or therapeutic resistance may suggest the involvement of an underlying trigger in the form of an irritant or contact allergen such as tar or dithranol [5, 6]. 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 allergic immune response must be considered. These factors are potential risk for antigen stimulation of delayed-type hypersensitivity, which is a really basic pathomechanism in psoriasis. Palmo-plantar psoriasis is difficult to diagnose in its solitary form, mistakes are made with chronic contact dermatitis. Palmar psoriasis is most frequently an undiagnosed dermatose, as, especially in its early stages, it has eczematous overtones. Contact allergens may help in provoking and/or maintaining psoriatic lesions, especially when mechanical factors are involved, as part of the Koebner phenomenon.

Results, in studies focusing on allergic contact dermatitis in psoriasis support the role of contact allergy in provoking psoriatic lesions on palms and soles. Studies of incidence of contact allergy in patients with palmar and plantar psoriasis report following results.

In our study, positive patch-tests were found in 39.5% of the psoriatic cases with palmo-plantar involvement, and in the control group (psoriatic without palmo-plantar lesions) only 12.7% had positive patch-tests (Table 1, 2). The global difference was highly significant (χ^2 test: $p < 0.01$) which points to

the significantly greater hypersensitivity to contact allergen in the group of patients with palmo-plantar psoriatic lesions.

Our results support the role of contact allergy in provoking psoriatic lesions on palms and soles.

Fransson *et al.* [7] investigated the influence of contact allergy in palmo-plantar psoriasis. Positive patch-tests were obtained in 17% out of 47 patients.

Patch-tests were positive in 41.7% psoriatic with palmar-plantar psoriasis and in only 6.6% of psoriatic without palmar-plantar involvement. The most frequent contact allergens were: nickel sulphate, mercapto mix, balsam of Peru, potassium dichromate, mercury mix and fragrance mix. The study showed an increased incidence of contact allergy in patients with palmar-plantar psoriasis [8].

Other authors [9] have received lower results, 13 patients (20%) out of 65 with palmo-plantar psoriasis had a positive patch-test. In the control group (psoriatic without palmo-plantar involvement), only 6.56% had positive patch-tests. The most frequently involved allergens were: chromium nitrate, potassium bichromate, cobalt nitrate and formaldehyde [9].

The same authors concluded that there is a significantly greater hypersensitivity to the contact allergens in the group of patients with palmoplantar psoriatic lesions ($p < 0.027$). Christensen was surprised that the authors did not find any single case of nickel hypersensitivity in their country.

The previous studies showed an association between local psoriasis (palmoplantar) and allergic contact dermatitis [8, 9], but there are many reports on other forms of psoriasis.

Based on own experience Heule *et al.* [10] reported an overall result of 68% positive patch test on contact allergens in patients with different clinical pictures of psoriasis vulgaris. Considering these results, a preference for some allergens can be noted: tars, nickel sulphate, perfume and balsam of Peru. The authors concluded that this result of 68% points to delayed type hypersensitivity to contact allergens as a possibly relevant factor in the presentation or course of psoriasis.

In their study, the groups of authors [11], found 19 patients (25%) with different forms of psoriasis (ps. inversa, palmoplantar ps., chronic plaque ps., ps. guttata and ps.pustulosa) who had positive patch tests. The most common were to nickel, fragrance mix, coal tar, colophony and neomycin. There were no significant differences in the frequency of contact sensitivity between the patients with different clinical pictures of psoriasis ($p > 0.05$).

In many patients with "long-standing" psoriasis and unresponsive to local corticosteroids therapy contact sensitivity to corticosteroids was detected [12].

In 3 patch test clinics, 305 consecutive psoriatic patients with different forms of psoriasis (including pustular and excluding erythroderma) were studied [13]. This large study provided different answers from previous studies. 74 psoriatics (24%) were sensitized to 1 or more allergens. 18 of these sensitized patients had palmoplantar lesions, and 56 had other distributions [13]. No relationship was noted with involved areas. 339 patients (46%) in the control group proved to be sensitized. The global difference was highly significant ($p < 0.01$). Psoriatics proved to be less frequently sensitized than patients in the control group. This contrast may be explained by the clinical heterogeneity of psoriasis [13].

Some authors [14] have reported that contact allergy in psoriatic patients has been underestimated, while others [11, 13] have reported a frequent association. A high frequency of allergic contact dermatitis in flexural and palmo-plantar psoriasis has been stressed [7, 9].

Occupationally related psoriasis has been most often associated with frictional or pressure trauma, and an isomorphic (Koebner) response leading to lesions of psoriasis. The authors [15] have presented a patient who developed an eczematous eruption that evolved into lesions typical of psoriasis. This case illustrated that allergic contact dermatitis, probably in combination with frictional contact dermatitis in this individual, can precipitate plaques of psoriasis through a Koebner response.

It is very important that the allergic contact dermatitis in psoriasis should be recognized, and very often, despite the therapy, the psoriasis persists and in that case we were thinking about a more aggressive therapy.

The study was designed [16] to indicate whether there is a need for increased vigilance in the recognition of and testing for contact allergy (patch-test) in patients with psoriasis. 20% of patients with psoriasis had positive allergic reactions on patch testing [16]. Therefore, often screening contact and atopic history in psoriasis patients may help to identify relevant contact allergens with patch-test evaluation. This could improve treatment strategies and possibly reduce disability.

In our study, all patients with positive patch-tests have shown improvement in their psoriasis after avoiding topical products containing the incriminated allergens.

This study has suggested that hypersensitivity to contact allergens in psoriasis is a relevant provocative/perpetuating factor in manifestations and the course of psoriasis.

Conclusions

On the basis of the results present in our study we can conclude the following:

- allergic contact dermatitis has a great role in the provoking and maintenance of the psoriasis lesions.
- Patch-tests have to be included as a routine diagnostic procedure in psoriasis, especially in palmo-plantar psoriasis, in long standing psoriasis and in psoriasis resistant to therapy.
- avoidance/elimination of selective, previously identified materials/antigens with epicutaneous tests (patch-test) may alleviate and make the treatment of chronic, recalcitrant psoriasis more effective.

REFERENCES

1. Kastelan M. *et al.*, (1291): New trends in the immunopathogenesis of psoriasis. *Acta Dermatovenerol Croat* 2004; 26–29.
2. Griffiths C., Kirby B. Psoriasis. Martin Dunitz Ltd 1999; 1–22.
3. Vlckova L. M., Starova A. (2000): *Klinicka dermatologija so praktikum za studenti i lekari*. Hib Dresko Skopje, 363–368.
4. Fly L. (2004): An atlas of psoriasis, Second edition. Taylor and Francis Group, 15–33.
5. Binden A. D., Muston H., Beck M. H. (1994): Intolerance and contact allergy to tar and dithranol in psoriasis. *Contact Dermatitis*. 31: 185–186.
6. Lowlor F., Hindson C. (1982): Allergy to dithranol. *Contact Dermatitis* 8: 137–138.
7. Fransson J., Stogards K., Hammar H. (1985): Palmoplantar lesions in psoriatic patients and their relation to inverse psoriasis, tinea infection and contact allergy. *Acta Derm Venereol* (Stockh). 65: 218–223.
8. Lipozencic J., Milavec-Puretic V., Pasic A. (1992): Contact allergy and psoriasis. *Arhiv Za Higijenu Rada i Toksikologiju*. 43: 249–254.
9. Pasic A., Lipozencic J., Kansky A., Ben-Ghazeil M. (1989): Contact allergy in psoriasis patients with palmar and plantar lesions. *Acta Derm Venereol* (Stockh) Suppl. 146: 66–68.
10. Heule F., Tahapary G. J. M., Bello C. R. Th. van Joost. (1998): Delayed-type hypersensitivity to contact allergens in psoriasis. *Contact Dermatitis*. 38: 78–82.
11. Fleming C. J., Burden A. D. (1997): *Contact allergy in psoriasis*. *Contact Dermatitis*. 36: 274–276.
12. Burden A. D., Beck M. N. (1992): Contact hypersensitivity to topical corticosteroids. *Br J Dermatol*. 127: 497–500.

13. Barile M., Cozzani E., Anonide A., Usiglio D., Buttioni A., Guarrera M. (1996): Is contact allergy rare in psoriatics? *Contact Dermatitis*. 35: 113–114.
14. Henseler T., Christopher E. (1995): Disease concomitance in psoriasis. *J Am Acad Dermatol*. 32: 982–6.
15. Sherertz E. F., Zanolli M. D. (1991): Occupational allergic contact and frictional dermatitis leading to plaques of psoriasis: A challenge in diagnosis. *Am J Contact Dermatitis*, Vol 2, No 1, 52–55.
16. Clark A. R., Sherertz E. F. (1998): The incidence of allergic contact dermatitis in patients with psoriasis vulgaris. *A. J Contact Dermatitis*, Vol 9, No 2, 96–99.

Резиме

ФРЕКВЕНЦИЈА НА ОДЛОЖЕН-ТИП ХИПЕРСЕНЗИТИВНОСТ НА КОНТАКТНИ АЛЕРГЕНИ КАЈ ПАЛМО-ПЛАНТАРНА ПСОРИЈАЗА

**Нина Цаца-Билјановска, Марија В'лчкова-Лашкоска,
Мargarета Балабанова-Стефанова, Весна Гривчева-Пановска**

*Клиника за дерматовенерологија, Клинички центар,
Медицински факултет, Скопје, Р. Македонија*

Апстракт: Псоријазата е честа, генетски детерминирана, хронична инфламаторна Т-клеточно медирана дерматоза.

Цел на истражувањето (Aim): да се одреди фреквенцијата на одложениот тип хиперсензитивност на контактни алергени кај палмо-плантарна псоријаза и нејзиното значење во тригерирање и/или перпетуирање на истата.

Материјал и методи: Вкупниот број на испитаници (101) со различни клинички форми на псоријаза беше поделен на две групи врз основа на клиничкиот аспект и локализацијата на лезиите. Во првата група беа обработени 38 пациенти со клиничка слика за палмо-плантарна псоријаза, додека втората, контролна група, броеше 63 испитаника со типична морфологија и дистрибуција на лезиите за вулгарна псоријаза, но без афекција на шаките и стопалата. Двете групи беа епикутано тестирани со patch-тест.

Резултати: Кај првата група на испитаници со палмо-плантарна псоријаза, позитивен patch-тест имаа 15 испитаника, т.е. 39.5%, додека кај контролната група позитивен patch-тест добивме само кај 8 испитаника т.е. 12.7%. Студијата покажа дека постои високо статистички сигнификантна разлика во фреквенциите на позитивните patch-тестови помеѓу испитуваните групи ($p < 0.01$). Во првата група на испитаници со палмо-плантарна псори-

јаза имаме статистички високо сигнификантно поголем број на позитивен patch-тест.

Заклучок: Резултатите од оваа студија покажуваат статистички сигнификантно поголем број на позитивен patch-тест кај палмо-плантарната псоријаза, со што се потврдува улогата на контактните алергени во тригерирање и/или одржување на лезиите. Поради тоа неопходно е внесување на patch-тестот, како дијагностичка процедура за откривање на каузалните/агравирачки алергени кај палмо-плантарната псоријаза и со нивно елиминирање би се избегнале честите егзацербации на болеста и/или тераписката резистенција на конвенционалната локална терапија.

Клучни зборови: палмо-плантарна псоријаза, одложен тип хиперсензитивност, patch-тест.

Contact address:

Nina Saca-Biljanovska
Department of Dermatovenerology, Clinical Centre,
Vodnjanska 17, 1000 Skopje
Republic of Macedonia

E-mail: zbiljanovski@mt.net.mk