

CELL TYPING OF THE SCABETIC LESION AND ITS CLINICAL CORRELATION

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SUMMARY: Scabies is a pruritic dermatosis due to infestation by a mite that stimulates both humoral and cellular immune responses causing cutaneous lesions as well as pruritus. Changes in immune response pattern with treatment are associated with improvement in symptoms and clinical cure.

In this study, we analysed the cellular infiltrate types and patterns in lesions of Scabies. Treated patients were divided into 2 groups as those with and without pruritus. In the pre-treatment cases, there was a high incidence of T₃, T₄, T₆ and T₈ infiltration in the lesions, with T₄ greater than T₈. Following treatment, it was noted that T₈ density was significantly increased in patients who had resolution of symptoms. It can therefore be concluded that T₄ cell dominance is the cause of persistent itching and T₈ increase leads to improvement in the pruritus.

Key-words: scabies-T₃-T₄-T₆-T₈ cells-pruritus

INTRODUCTION

Scabies is a common skin disorder of man caused by infestation with the mite *Sarcoptes scabiei var hominis*(1). Infestation of the skin with *Sarcoptes scabiei* may stimulate both cellular and humoral immune response in an infected patient (2). The mite itself produces few symptoms in the absence of immunity. The scabies organism induces immune responses that mediate the intense pruritus and bumpy red papules and nodules characterising the disease (3).

Complaints of pruritus will persist for a certain time after therapy. Scabicides effectively kill mites and eggs but the skin retains these products. This may cause continued itching. Generally, pruritus decreases by 50% within 48 hours of treatment and continues to do so over the next several weeks (4). Patients must be warned that itching may persist for several weeks after treatment (5) because of persistence of the hypersensitivity state.

PATIENTS AND METHODS

The present study was carried out on 30 scabetic patients. The diagnosis of scabies was made according to the criteria of Pardo and Kerdel (6) which were nocturnal itching, typical lesions, characteristic distribution and affection of other family members.

A skin biopsy was taken from each patient (4 mm. punch biopsy) under local anesthesia from either the papular or nodular lesions of scabies. Each patient then received a suitable topical scabicide (properly applied) and an oral antihistamine.

Patients were classified after treatment into 2 groups. Group I involved non-itchy cases and group II itchy cases, with postscabetic pruritus not due to acarophobia or irritation from the medication.

A second biopsy was taken from each treated patient, either from the postscabetic marks in case of group I (9 biopsies), or from postscabetic lesions in group II (21 biopsies).

Biopsy specimens (before and after treatment) were subjected to indirect immunofluorescence examination using DAKO monoclonal antibodies for assessment of T₃ (pan T-lymphocytes), T₄ (helper T-lymphocytes) and T₈ (suppressor T-lymphocytes) and T₆ (Langerhans cells) according to Wilson *et al* (7). The positive slides were analysed according to the sites of fluorescence as either epidermal, dermal or dermo-epidermal. The density of infiltrate was graded as mild, moderate or severe.

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RESULTS

Results of indirect immunofluorescence

■ **Before treatment:** The results showed high incidence and density of T₃, T₄, T₆ and T₈ cell infiltrates in scabietic patients with dominance of T-helper cells (T₄) over T-suppressor cells (T₈).

■ **After treatment:** There was a statistically significant increase of T₈ cell infiltrate in non-itchy cases compared to itchy cases (table 1). The results showed statistically significant increase in T₃ and T₄ cell infiltrate densities, and an insignificant increase in T₆ cell infiltrate density in itchy cases versus non-itchy cases (table 2, 4). The density of the T₈ cell infiltrate was not statistically significantly higher in non-itchy cases versus itchy cases (table 3).

T₄ cell infiltrate density was greater than T₈ cell infiltrate density in itchy cases. T₈ cell infiltrate density was greater than T₄ cell infiltrate density in non-itchy cases (tables 2, 3).

DISCUSSION

Involvement of the immune system in the pathogenesis of scabies has been suspected for a long time on the basis of clinical (2) and epidemiological manifestation. Scabies infection is associated with a CMI reaction at the site of the bite. Humoral responses involve increased IgG, IgM and IgE (3).

The present study showed that infestation of skin with scabies might stimulate the cellular arm of the immune system as evidenced by the presence of T₃, T₄, T₈ and T₆ cell infiltrates with high incidences and densities in lesional skin, especially in the dermis. These findings are consistent to that of Van Neste (8) and Reunala *et al.* (9) who found that in scabietic lesions, T lymphocytes constituted 64-75% of dermal leucocytes. Falk and Matre (10) also showed that T lymphocytes were the predominant cells in the dermal infiltrate of scabietic lesions. Our study showed that T₄ cell infiltrate was more dominant than T₈ cell infiltrate (incidence and density) in both the epidermis and dermis. A similar result was obtained by Cabrera *et al.* (3).

T cell subsets	Post-scabietic without itching	Post-scabietic with itching	Z test	P value	Interpretation
T3	9 (100%)	21 (100%)	0.00	> 0.05	Insignificant
T4	9 (100%)	18 (85.71%)	1.871	> 0.05	Insignificant
T6	3 (33.33%)	12 (57.14%)	1.248	> 0.05	Insignificant
T8	9 (100%)	17 (80.95%)	2.223	< 0.05	Significant

Table 1: Statistical evaluation of the incidence of T-cell subsets and Langerhans cells in postscabietic patients with itching (21 patients) and postscabietic patients without itching after treatment (9 patients).

Site	Density	Postscabietic without itching		Postscabietic with itching		Z test	P value	Interpretation
		No.	%	No.	%			
Epidermis	Mild	1	11.11	3	14.28	0.243	> 0.05	Insignificant
	Moderate	0		0		0.000	> 0.05	Insignificant
	Severe	1	11.11	1	4.76	0.554	> 0.05	Insignificant
Dermo-epidermal Junction	Mild	3	33.33	1	4.76	2.11	< 0.05	Significant
	Moderate	0		5	23.8	2.560	< 0.05	Significant
	Severe	0		1	4.76	1.024	> 0.05	Insignificant
Dermis	Mild	6	66.66	3	14.28	2.998	< 0.01	Highly sign.
	Moderate	1	11.11	10	47.61	2.414	< 0.05	Significant
	Severe	0		4	19.04	2.221	< 0.05	Significant

Table 2: Statistical evaluation of density of T₄ cell infiltrate and intensity of fluorescence in postscabietic patients with itching (21 patients) and postscabietic patients without itching after treatment (9 patients).

Stimulation of cell-mediated immune re-sponse in scabies is well established, and this result is consistent with that of Van Neste (8) and Reunala *et al.* (9) who stated that a delayed response would start once T lymphocytes have been produced and reach the site of mite colonization. Falk and Matre (10) stated that cell-mediated im-mune response was of importance in the patho-genesis of scabies. T cells are the prominent cells in the infiltrate, with few macrophages and very few B cells. CD45RA+ (naïve T cells) and CD8+ cells are present in varying densities throughout the epidermis and dermis. CD4+ showed a large increase during the infection phase (11). CD3 epsilon+, CD11c+, MHC class II and CD1a+ cells in the dermis play a major role in the successful immune response to scabies (12).

The intensity of the reaction is the result of opposing stimuli of T-effector cells promot-ing cellular changes and of T-suppressor cells inhibiting the reaction (13). In scabies, there is promotion of cell-mediated immune response, proved by the dominance of T-helper cells in the epidermis and dermis of lesional skin. This might play a role in the pathogenesis of itchy lesions of scabies.

These findings are consistent with that of Cabrera *et al.* (3) who re-ported that scabies organism induce immune re-sponse that mediated the intense pruritus and bumpy red papules and nodules that characterize the disease.

By comparing the findings of indirect immu-nofluorescence study after treatment of scabies in non-itchy cases and the cases with postscabi-etic pruritus, the present study showed sup-pression of cell-mediated immune response, desensitization and disappearance of itching in non-itchy group. This finding was proved by sta-tistically significant increase of T₈ cell infiltrate incidence and density in non-itchy group compared to itchy one when compared to T₄ cells.

At the same time, the present study showed promo-ting of cell-mediated immune response in itchy group evidenced by statistically significant increase of T₄ cell infiltrate density and statisti-cally insignificant increa-se of T₈ cell infiltrate density in itchy group compared to non-itchy one. The study also showed increased T₄ cell infiltrate density than T₈ cell infiltrate densi-ty in cases with postscabietic pruritus.

Site	Density	Postscabietic without itching		Postscabietic with itching		Z test	P value	Interpretation
		No.	%	No.	%			
Epidermis	Mild	1	11.11	0		1.060	> 0.05	Insignificant
	Moderate	1	11.11	4	19.04	0.584	> 0.05	Insignificant
	Severe	0		0		0.000	> 0.05	Insignificant
Dermo-epidermal junction	Mild	2	22.22	4	19.04	0.195	> 0.05	Insignificant
	Moderate	3	33.33	2	9.52	1.403	> 0.05	Insignificant
	Severe	0		0		0.000		Insignificant
Dermis	Mild	6	66.66	10	47.61	0.995	> 0.05	Insignificant
	Moderate	3	33.33	5	23.8	0.522	> 0.05	Insignificant
	Severe	0		1	4.76	1.024	> 0.05	Insignificant

Table 3: Statistical evaluation of density of T₈ cell infiltrate and intensity of fluorescence in postscabietic pa-tients with itching (21 patients) and postscabietic patients without itching after treatment (9 patients).

Site	Density	Postscabietic without itching		Postscabietic with itching		Z test	P value	Interpretation
		No.	%	No.	%			
Epidermis	Mild	1	11.11	3	14.28	0.243	> 0.05	Insignificant
	Moderate	0		2	9.52	1.485	> 0.05	Insignificant
	Severe	0		0		0.000	> 0.05	Insignificant
Dermo-epidermal junction	Mild	2		3	14.28	0.501	> 0.05	Insignificant
	Moderate	0	22.22	3	14.28	1.870	> 0.05	Insignificant
	Severe	0		0		0.000	> 0.05	Insignificant
Dermis	Mild	0		3	14.28	1.870	> 0.05	Insignificant
	Moderate	1	11.11	5	23.8	0.906	> 0.05	Insignificant
	Severe	0		0		0.000	> 0.05	Insignificant

Table 4: Statistical evaluation of density of T₆ cell infiltrate and intensity of fluorescence in postscabietic patients with itching (21 patients) and postscabietic patients without itching after treatment (9 pa-tients).

The sequence of immunity in scabies involves antigen identification by antigen presenting cell (Langerhans cells), clonal proliferation of T-cell lymphocytes specific to mite antigens, clonal proliferation of B-lymphocytes which differentiate into plasma cells producing mite specific antibodies, binding to IgE onto mast cells and proliferation of T-suppressor lymphocytes that suppress the immune response and result in de-sensitization (14). Throughout this sequence, pathological alterations resulting in lesions and itching are caused by lymphokines, complement subunits and histamine and serotonin released from mast cells and basophils (15).

The presence of various types of cells constituting the infiltrate was in agreement with the stimulation of cell-mediated immune reactions (16). Krueger (17) reported that through the lymphokines released as a result of cell mediated immune response, many cells were recruited to the area of inflammation as lymphocytes, macrophages or monocytes, neutrophils, basophils and eosinophils.

Postscabietic nodules showed the presence of multiple active lymphocytic infiltrate and few active macrophages in the epidermis and presence of perivascular dermal infiltrate composed of active lymphocytes, mast cells, active macrophages and fibroblasts (18). Blood vessels showed marked proliferation of endothelial cells, thickened basal lamina, hypertrophy of pericytes. Immunohistochemistry showed Langerhans type cells in Nodular scabies, except for the presence of Birbeck granules (19).

CONCLUSION

Persistence of cell-mediated immune reaction with T-helper cell dominance may be the cause of persistent itching after treatment of scabies while suppression of cell-mediated immune response with T-suppressor cell dominance may relieve the itch.

References

1. Burns DA. - Disease caused by arthropods and other noxious animals. In: Textbook of Dermatology. Champion RH, Burton JL and Ebling FJG (eds). 5th ed., Vol 2, Blackwell Scientific Publications, Oxford, 1992:1300.
2. Dahl MV. - The immunology of scabies. *Ann Allergy* 1983; 51: 560-66
3. Cabrera R, Agar A, Dahl MV. The immunology of scabies. *Semin Dermatol* 1993;12:15-21.
4. Estes SA, Estes J. - Therapy of scabies. Nursing homes, hospitals and homeless. *Semin Dermatol* 1993;12:26-33.
5. Wendel K, Rimpalo A. - Scabies and Pediculosis Pubis: An Update of Treatment Regimens and General Review. *Clin Infect Dis* 2002;35:S146-51.
6. Pardo RJ, Kerdel FA. - Parasites, arthropods, hazardous animals and tropical dermatology. In: Dermatology. Moschella SL and Hurley HZ (eds). Saunders Company. Philadelphia, London, Toronto, Sydney and Tokyo. 3rd. edn. 1992; 1960-7
7. Wilson M, Sulzer AJ, Walls KW. Modified antigens in the indirect immunofluorescent test for Schistosomiasis. *Am J Trop Med Hyg*, 1974;23:1072-76.
8. Van Neste D. - Immuno-allergological aspects of scabies. A comparative study of spontaneous blastogenesis in the dermal infiltrate of common and hyperkeratotic scabies, allergic contact dermatitis and irritant dermatitis. *Arch Dermatol Res* 1982;274:159-67.
9. Reunala T, Ranki A, Rantanen T, Salo OP. - Inflammatory cells in the skin lesions of scabies. *Clin Exp Dermatol* 1984;9:70-77.
10. Falk ES, Matre RM. - In-situ characterization of cell infiltrates in the dermis of human scabies. *Am J Dermatopathol* 1982;4:9-15.
11. Arlian LG, Rapp CM, Stemmer BL, Morgan MS, Moore PF. - Characterization of lymphocyte subtypes in scabietic skin lesions of naive and sensitized dogs. *Vet Parasitol.* 1997;68:347-58.
12. Stemmer BL, Arlian LG, Morgan MS, Rapp CM, Moore PF. - Characterization of antigen presenting cells and T-cells in progressing scabietic skin lesions. *Vet Parasitol.* 1996;67:247-58.
13. Parish WE. - Clinical immunology and allergy. In: Textbook of Dermatology. Champion RH, Burton JL, Ebling FJG (eds). 5th ed, Vol I, Blackwell Scientific Publications, Oxford, 1992:253.
14. Van Neste D. - Human scabies in perspective. *Int J Dermatol* 1988;27:10-15.
15. Clark WR. - The experimental foundations of modern immunology. 2nd Ed, Wiley. Somerset, NJ 1983.
16. Spetz AL, Strominger J, Groh-Spies V. - T cell subsets in normal human epidermis. *Am J Pathol.* 1996 Aug;149:665-74.
17. Krueger GG. - Lymphokines in health and disease. *Int J Dermatol* 1977;16:539-51.
18. Kamel MM, Aidaros MS, Abo Zaid HM, Hamdy MA. - Electron microscopic study of persistent scabietic nodules. *Afr J Dermatol* 1988;1:41.
19. Hashimoto K, Fujiwara K, Punwaney J, DiGregorio F, Bostrom P, el-Hoshy K, Aronson PJ, Schoenfeld RJ. - Post-scabietic nodules: a lymphohistiocytic reaction rich in indeterminate cells. *J Dermatol.* 2000;27:181-94.

