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COMPARATIVE STUDY OF THE IMMUNE RESPONSE INVOLVEMENT IN ATOPIC DERMATITIS AND PSORIASIS

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Abstract. Immunological and pbarmacological disturbances in atopic dermatitis and psoriasis are compared. This comparative study revealed several analogies: T cell deficiency; hyperfunction of B cells leading to antibody production, defect in the beta-adrenergic response. The role of immunological and pharmacological factors in the pathogenesis of the two diseases is discussed.

Key words: T cell deficiency; Hyperfunction of B cells; Psoriasis; Atopic dermatitis

Atopic dermatitis (AD) and psoriasis, two major inflammatory skin diseases, differ markedly from a clinical and histopathological point of view. Recently, immunological disturbances have been described in the two diseases and are presumably involved in their pathogenesis. It is surprising to note numerous analogies between AD and psoriasis concerning these immunological factors (8–11). Even more striking is the pharmacological hypothesis indicating a defect of the beta adrenergic response in the two diseases (20–22). In this short paper we try to give a comparative view of the possible immune response involvement in the pathogenesis of AD and psoriasis.

IMMUNOLOGICAL FEATURES

Humoral and immunopathological findings

In AD the most striking feature is the increase in serum IgE level (14). This increase is non-specific (17) and IgG-cytotropic antibodies can be present (19). These IgE could participate in recently found circulating immune complexes (3). IgE-bearing B cells are more common (5). In AD skin, immunoglobulin and complement deposits can be observed (18).

In psoriasis, serum IgA and IgG levels are elevated. High IgE levels are found in 20% of patients, and rheumatoid factors consistent with IgG anti-IgG are present in half of them (6). Circulating immune complexes have recently been described (1–10). Immunoglobulins, complement, rheumatoid factors, antinuclear antibodies and fixed antistratum corneum antibodies are present in involved epidermis and can account for keratinocyte membrane alterations (for review see 8).

In the two diseases these features reflect a hyperactivity of B-cell clones, resulting in a hyperproduction of immunoglobulins.

Cellular immunity

In AD a defect of T cells has been demonstrated in vitro by low levels of E rosettes and low stimulation by PHA and Con A (for review, see 11–9). In our own work (9) the dissociation of decreased E rosettes and normal HTLA values could indicate a defect of T cell maturation, since HTLA appears earlier than sheep red blood cell receptor during the maturation of lymphocytes, but these discrepancies were not found in an other study (2). Moreover, the markedly depressed stimulation by ConA could be in favour of a T-suppressor cell defect.

In psoriasis a similar defect of T cells is demonstrated in the active stages of the disease: a decrease in E and E active rosettes and of HTLA-bearing cells (in opposition to AD), low stimulation by ConA (7). A T-suppressor cell defect has already been suggested (10).

In the two diseases, the impairment of the B-cell control by thymus-dependent lymphocytes could explain the hyperproduction of antibodies.

PHARMACOLOGICAL FEATURES

In AD a defect in the beta-adrenergic receptors has been hypothesized since 1968 (20) but has not been fully demonstrated so far. However, abnormal cAMP responses to beta agonists have been demonstrated in lymphocytes and polymorphonuclear leukocytes which are, on the contrary, normally responsive to prostaglandin E_1 (PGE_1) stimulation (16).

In psoriatic epidermis a decrease in the cAMP/cGMP ratio has been demonstrated since 1972 by Voorhees et al. (22–15) but further studies on epidermal cyclic nucleotides are conflicting (13–24). Adenyl cyclase is poorly responsive to beta agonists but more responsible to PGE2 (23).

In the two diseases, though much work still needs to be done to further clarify this subject, a defect of the beta adrenergic response has been implicated.

PATHOGENIC IMPLICATIONS (Fig. 1)

The possible pathogenic chain of AD could be: defect of T cells → antibody production → mast cell and basophil degranulation → hyperproduction of histamine and other mediators leading to some clinical features of AD (pruritus, oedema, erythema). The beta block could account directly

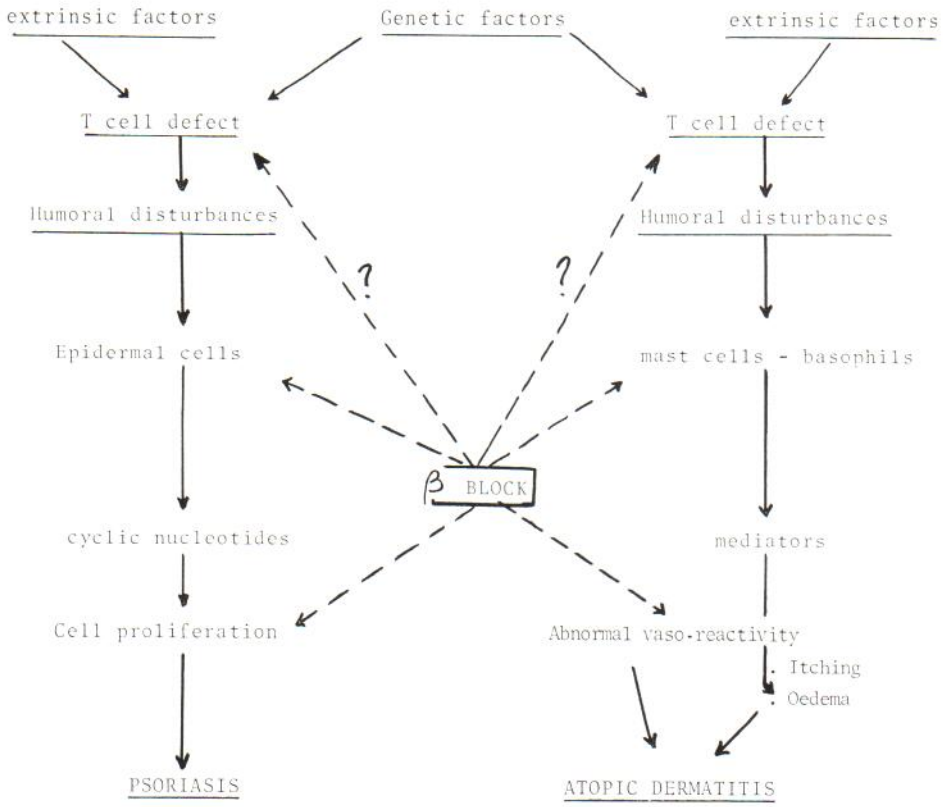

Fig. 1. Hypothetical pathogenic chain of psoriasis and atopic dermatitis and possible role of the β-adrenergic blockade.

for vasomotor and sudoral troubles. It could intervene indirectly via low levels of cAMP in enhancing humoral immunological phenomena and in the imbalance of homeostatic response to mediator secretion, resulting in alpha adrenergic and cholinergic predominant effects.

In psoriasis we have already proposed the following pathogenic chain (10): T cell defect → humoral immunological phenomena, antibodies and complement deposits in epidermis → PMN attaction → enzyme release resulting in keratinocyte membrane alterations. The membrane-bound beta-adrenergic receptor dysfunction could be due to these immunologically induced membrane alterations. This beta-receptor dysfunction could be implicated in epidermal proliferation through cyclic nucleotides and PG_s imbalance.

CONCLUSIONS

In these hypothetical pathogenic chains, some immunological differences leading to different clinical and histopathological aspects are obvious: different humoral disturbances act on different supposed targets, viz. keratinocyte membranes in psoriasis, cells responsible for immediate hypersensitivity in AD. Thus the results differ: epidermal proliferation in psoriasis, effects of hyperproduced mediators in AD.

This comparative study brings out several analogies in the immunological and pharmacological features of AD and psoriasis: (1) T cell defect, (2) hyperfunction of B cells leading to overproduction of antibodies, (3) defect of the beta-adrenergic response. But these analogies might be merely apparent and due to the fact that our knowledge of the two diseases is limited to the basic points only and real immunological and pharmacological mechanisms are poorly understood. For example, we do not know the exact lymphoid subpopulation involved in the T cell defect. This deficient subset may be different in AD and psoriasis. Direct evidence for a T-suppressor cell defect is not yet available and subsets of Fc-γ-bearing T lymphocytes, possibly modulated by immune complexes, could be implicated. The origin of the T cell defect is also under discussion (4). It could be primary, due to genetic predisposition and/or infectious agents; secondary by humoral inhibitors (12), or due to skin inflammation (21).

Likewise, we do not know the role, the origin, the nature or the exact location of the beta-receptor defect; is this deficiency restricted to epidermal cells in psoriasis and more generalized in AD?

Moreover, we are still unable to correlate exactly the immunological data with the pharmacological disturbances. In psoriasis the membrane-bound beta-adrenergic receptor dysfunction could result from epidermal immunological phenomena but inversely in the two diseases immunological features could be due to the abnormal beta-adrenergic response of immune competent cells.

Obviously much more work is necessary to elucidate the exact immunological and pharmacological disturbances in AD and psoriasis and research in immuno-pharmacology is one of the most promising fields for the future.

REFERENCES

1. Braun-Falco, O., Mannel, C. & Sherer, R.: Nachweis von zirkulierenden löslichen Immunokomplexen im Serum von Psoriasispatienten mit dem J-C1q-Ablenkungstest. Hautarzt *28:* 658, 1977.
2. Braathen, L. R., Förre, O., Natvig, J. B., Rajka, G.: Lymphocyte subpopulations, serum immunoglobulins and complement factors in patients with atopic dermatitis. Br J Dermatol *98*: 521, 1978.
3. Brostoff, J., Johns, P. & Stanworth, D. R.: Complexed IgE in atopy. Lancet *ii:* 741, 1977.
4. Clot, J., Guilhou, J. J., Meynadier, J., Paradis, B. & Andary, M.: Immunological aspects of psoriasis. III. Fc-γ-receptor bearing mononuclear cells in peripheral blood. Br J Dermatol *99:* 25, 1978.
5. Cormane, R. H., Husz, S. & Hamerlinck, F. F.: Immunoglobulin and complement bearing lymphocytes in allergic contact dermatitis and atopic dermatitis (eczema). Br J Dermatol *90:* 597, 1974.
6. Guilhou, J. J., Clot, J., Meynadier, J. & Lapinski, H.: Immunological aspects of psoriasis. I. Immunoglobulins and anti-IgG factors. Br J Dermatol *94:* 501, 1976.
7. Guilhou, J. J., Clot, J. & Meynadier, J.: T cell defect in psoriasis: further studies on membrane markers and T cell functions from 60 patients. Arch Dermatol Res *260:* 163, 1977.
8. — New concepts in the pathogenesis of psoriasis. Br J Dermatol *98:* 585, 1978.
9. Guilhou, J. J., Clot, J., Bousquet, J., Teot, M. & Meynadier, J.: Étude in vitro de l'immunité cellulaire dans l'eczéma constitutionnel et dans l'eczéma de contact. Ann Dermatol Venerol *105:* 513, 1978.
10. Guilhou, J. J., Clot, J., Guillot, B. & Meynadier, J.: Immunological aspects of psoriasis IV. Presence of circulating immune complexes in patients before and after PUVA therapy; correlations with T cell markers (submitted).
11. Hanifin, J. M. & Lobitz, W. C.: Newer concepts in atopic dermatitis. Arch Dermatol *113:* 663, 1977.
12. Hanifin, J. M. & Gottlier, B. R.: IgE inhibits T cell rosette formation. Clin Res *22:* 328A, 1974.
13. Harkonen, M., Hopsu-Havu, U. K. & Raij, K.: Cyclic-adenosine-monophosphate, adeny-cyclase and cyclic-nucleotide phosphodiesterase in psoriatic epidermis. Acta Dermatovener (Stockholm) *54:* 13, 1974.
14. Juhlin, L., Johansson, S. G. O. & Bennich, H.: Immunoglobulin E in dermatoses. Levels in atopic dermatitis and urticaria. Arch Dermatol *100:* 12, 1969.
15. Marcelo, C. L., Duell, E. A., Stawiski, M. A., Anderson, T. F. & Voorhees, J. J.: Cyclic nucleotide levels in psoriatic and normal keratomed epidermis. J Invest Dermatol *72:* 20, 1979.
16. Reed, C. E., Busse, W. W. & Lee, T. P.: Adrenergic mechanisms and the adenyl cyclase system in atopic dermatitis. J Invest Dermatol *67:* 333, 1976.
17. Rimbaud, P., Meynadier, J., Robinet-Levy, M., Guilhou, J. J. & Elharar, S.: Les immunoglobulines E dans diverses dermatoses. Bull Soc Fr Dermatol Syph *80:* 472, 1973.
18. Ring, J., Senter, T., Coriell, R. C., Arroyave, C. M. & Tan, E. M.: Complement and immunoglobulin deposits in the skin of patients with atopic dermatitis. Br J Dermatol *99:* 495, 1978.
19. Shakib, F., McLaughlan, M., Stanworth, A. R., Smith, E. & Fairburn, E.: Elevated serum IgE and IgG4 in patients with atopic dermatitis. Br J Dermatol *97:* 59, 1977.
20. Szentivanyi, A., The beta adrenergic theory of the atopic abnormality in bronchial asthma. J Allergy Clin Immunol *42:* 203, 1968.
21. Uehara, M.: Atopic dermatitis and tuberculin reactivity. Arch Dermatol *113:* 1226, 1977.
22. Voorhees, J. J., Duell, E. A., Bass, L. J., Powell, J. A. & Harrell, E. R.: Decreased cyclic AMP in the epidermis of lesions of psoriasis. Arch Dermatol *105:* 695, 1972.
23. Yoshikawa, K., Adachi, K., Halprin, K. M. & Levine, V.: On the lack of response to catecholamine stimulation by the adenyl cyclase system in psoriatic skin. Br J Dermatol *92:* 619, 1975.
24. — Is the cyclic AMP in psoriatic epidermis low? Br J Dermatol *93:* 253, 1975.