Psoriasis: A Disease of a Thousand Key Words

Sir,

As chronic inflammatory disease, psoriasis involves many different cell types and numerous phenomena can be observed in its course. To mention only the most important: a) psoriatic keratinocytes produce many cytokines (1), b) increased number of mast cells (MC) in the lesions, the MC degranulate and release tryptase and chymotryptase, prostaglandins, leukotriene B4, histamine, tumor necrosis factor (TNF) (2), etc., c) enhanced activities of neutral proteinases, including plasminogen activator (3), neutrophil cathepsin G and elastase, the latter being bound to the basement membrane zone of psoriatic lesions (4), d) specific clones of helper T cells might start autoimmune response in psoriatic epidermis to still hypothetical autoantigen (5), e) excessive autocrine regulation of psoriatic keratinocyte proliferation by transforming growth factor alpha and interleukin-6 (6, 7), f) expression of adhesion molecules: intercellular adhesion molecule (ICAM-1) both on lesional keratinocytes and dermal endotthelial cells (EC), and endothelial-leukocyte adhesion molecule-1 (ELAM-1) on the endothelium (8), g) EC of high endothelial venule morphology express molecules responsible for promotion of helper T cell migration (9), h) altered function of Langerhans cells in psoriatic epidermis (10).

The limited journal space given for publication of experimental data forces authors to shorten the discussion to the most sound arguments supporting the explanation of the pathological phenomenon under study. The fact that neuropeptides is used as a key word in our paper (11) concentrates the attention of the reader to the field of neuromodulatory effects in psoriasis, only partly explored. As to the distribution of nerve fibers in psoriatic skin (12), they are unfrequent, and subsequent sections should be studied to collect a sufficient number of fibers for statistical analysis. Immunocytochemical techniques to visualize nerve fibers due to the presence of specific neuropeptides such as substance P (SP) or calcitonin gene-related peptide (CGRP) are more precise. The generation of nerve growth factors in the psoriatic skin should also be taken into account when the elongation and the higher density of nerve fibers are considered.

From the point of view of immunologists, the study of various mediators in psoriatic skin, such as neuropeptides, should include identification of mediator-producing cell, quantitation of mediator, and expression of its specific receptors (number, distribution, changes in affinity, etc). All these factors determine the final effect of mediator on psoriatic skin, i.e. SP. An increased amount of SP in psoriatic skin occurs possibly in nerve fibers but not in extracellular space (13), which after release might be responsible for the desensitization of specific receptors for SP on MC, etc.

I would like to comment on some recent publications on the effect of SP on the skin. An article by Matis et al. (14) describes that ELAM-1 is rapidly induced on postcapillary dermal venules as a direct consequence of experimentally elicited degranulation of adjacent MC. It seems likely that this reaction depends on SP-stimulated release of TNF from degranulating MC. The production of cytokines by keratinocytes in response to SP has also been suggested by Brown et al. (15).

Our recent data on decreased activity of specific skin elastase inhibitor (SCALP) (16) throw some new light on the concentration of various low molecular mediators in psoriatic skin. Reduced activity of SCALP is responsible for the increased activity of neutrophil elastase, which in turn accelerates degradation of polypeptides. Many low-molecular weight mediators and cytokines might be degraded more efficiently and their biological activity might last much shorter in psoriatic skin than in normal skin. This seems to explain at least in part why a higher dose of capsaicin is needed in psoriatics to induce SP-mediated neurogenic erythema (11). SP secreted from nerve fibers is presumably degraded more readily after its release, which reduces its effective concentration in the tissue. Thus, higher doses of capsaicin are needed to release more SP to produce the neurogenic inflammation of the same intensity. In addition, our preliminary studies (17) have shown that serum beta-endorphin in psoriatic patients is about two-fold elevated which may be responsible for the stimulation of opioid receptors on dermal nerves and antinoceptive effect. It is likely that this in turn may change the effect of capsaicin on the SP release from nerve endings in psoriatic skin.

Summing up, the role of neuropeptides in the pathogenesis of psoriasis is no conclusive explanation. It might be a secondary phenomenon but an important factor modulating inflammatory response in patients. We thank Dr Olle Johansson for high evaluation of our paper (11).

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