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LETTERS TO THE EDITOR

"Neurogenic Inflammation Induced by Capsaicin in Patients with Psoriasis" – Is really only "Neuropeptides" the Key Word?

Sir,

In a recent paper, Glinski and collaborators (1) studied the effect of capsaicin-induced neurogenic inflammation in patients with psoriasis or with systemic scleroderma as well as in healthy volunteers. They used increasing doses of the active substance and applied it topically to the forearm skin. By using capsaicin with a concentration of 0.125 or 0.25 μg/cm^2, all normal controls showed a positive skin reaction pattern, and 81% of the scleroderma patients. However, only approximately 33% of the psoriatic patients responded with the classical signs of neurogenic inflammation: local redness, flare and wheal. Only higher doses of capsaicin (0.5–4 μg/cm^2) were able to elicit erythema and flare in late-onset psoriatic patients as well as in patients having more than 40% involved skin. In contrast, patients with early-onset of psoriatic lesions had a reaction to capsaicin similar to that of normal controls (mean capsaicin response index ±SD being 4.46 ± 0.88 for early-onset patients and 5.44 ± 0.51 for normal controls).

No correlation was found between the erythemal response to capsaicin and the clinical parameters, except for age at onset of psoriasis as well as body surface area covered by lesional skin (break-point: 40%). The authors discuss their interesting findings in comparison to the well-known coupling between capsaicin – substance P (SP) – histamine – leukotrienes – neutral proteinases. The different explanatory possibilities regarding this biochemical cascade phenomenon all emanate from the neuropeptides, and the latter term is also used as the only key word. They conclude that the unresponsiveness to capsaicin of the psoriatic patients may be related to a: 1) lower content of SP in the nerve fibres; 2) lower content of inflammatory mediators in mast cells; 3) lower affinity of specific mast cell-associated SP-receptors; and 4) faster degradation of SP by tissue endopeptidases. However, in summary, the authors find most of the above-mentioned explanations less plausible, concluding that secondary alterations of the mast cells are likely responsible for this abnormal response. Since the test area in the psoriatic patients was *uninvolved* skin, Glinski et al. (1) right-fully points to the observation that the psoriatic process involves not only psoriatic plaques, but even the whole skin (2–4).

In the following, I would like to point to another observation recently being done by us, namely the finding that psoriatic involved skin has a significant reduced number of intraepidermal nerve fibre profiles (5). The mean number of intraepidermal nerve fibre profiles in involved skin was 134/mm^2, in uninvolved skin 478/mm^2 and in normal skin from healthy volunteers 581/mm^2, thus, the reduction of innervation in involved skin was down, in average, to 23% of normal (at the 99% confidence level). *However, the uninvolved skin was not statistically significantly different to skin from healthy volunteers. No differences at all could be seen in the dermis of involved, uninvolved and normal skin, respectively.*

This is seemingly in contrast to Naukkarinen et al. (6) who claimed that psoriatic involved, but not uninvolved, skin was significantly *more densely* innervated with SP containing nerve fibres. Furthermore, Eedy et al. (7) reported higher levels of SP, however, Anand et al. (8) did not find any significant differences in SP between psoriatic skin and normal skin of healthy volunteers. Most recently, Johannsen et al. (9) also reported significantly more calcitonin gene-related peptide (CGRP) containing nerve fibres in psoriatic lesions than in lesion-free psoriatic skin. It is, of course, very difficult for us to make a correct comparison of the five different studies. One has to understand the completely different marker tools used in the various studies and, furthermore, neither Naukkarinen et al. (6) nor Johannsen et al. (9) revealed exactly which reference space that was used, and if model-based or design-based counting methods was utilized. Finally, even if the total number of intraepidermal nerve fibres is decreased, at the same time, of course, a subset of intraepidermal or dermal peptide containing fibres can be numerically increased.

These different findings regarding the number of certain nerve fibres in involved *versus* uninvolved psoriatic skin and the abnormal response to capsaicin in uninvolved psoriatic skin may actually suggest that studies of nerve fibres and/or neuronal SP/CGRP *is not* the most fruitful way to take in order to unfold the primary mysteries of psoriatic changes, since observed changes just may be secondary or tertiary to completely other phenomena. The explanatory models used by the authors appear, from a neuroscientific horizon, less plausible in view of our own results. More efforts should perhaps be put on direct investigations of the normal and psoriatic keratinocyte or mast cell, thus, although Glinski et al. (1) only had one key word, namely "Neuropeptides", perhaps our focus should be put somewhere else?

Only future studies, like the above-mentioned ones, can solve these questions, and I strongly look forward to the publication of further papers from Glinski and colleagues and congratulate them to their highly intriguing and interesting observations!

REFERENCES

1. Glinski W, Glinska-Ferenz M, Pierozynska-Dubowska M. Neurogenic inflammation induced by capsaicin in patients with psoriasis. Acta Derm Venereol (Stockh) 1991; 71: 51–54.
2. Farber EM, Nall L, Strefling A. Psoriasis: a disease of the total skin. J Am Acad Dermatol 1985; 12: 150–156.
3. Johansson O, Olsson A, Enhamre A, Hammar H, Goldstein M. Phenylethanolamine N-methyltransferase-like immunoreactivity in psoriasis: An immunohistochemical study on catecholamine synthesizing enzymes and neuropeptides of the skin. Acta Derm Venereol (Stockh) 1987; 67: 1–7.

4. Johansson O, Olsson A, Enhamre A, Fransson J, Hammar H, Han S-W, Goldstein M. The specificity and cellular origin of phenylethanolamine N-methyltransferase (PNMT)-like immunoreactivity in psoriatic skin. Br J Dermatol 1990; 122: 195–200.
5. Johansson O, Han S-W, Enhamre A. Altered cutaneous innervation in psoriatic skin as revealed by PGP 9.5 immunohistochemistry. Arch Dermatol Res 1991; 283: 519–523.
6. Naukkarinen A, Nickoloff BJ, Farber EM. Quantification of cutaneous sensory nerves and their substance P content in psoriasis. J Invest Dermatol 1989; 92: 126–129.
7. Eedy DJ, Johnston CF, Shaw C, Buchanan KD. Neuropeptides in psoriasis: An immunocytochemical and radioimmunoassay study. J Invest Dermatol 1991; 96: 434–438.
8. Anand P, Springall DR, Blank MA, Sellu D, Polak JM, Bloom SR. Neuropeptides in skin disease: increased VIP in eczema and psoriasis but not axillary hyperhidrosis. Br J Dermatol 1991; 124: 547–549.
9. Johannsen L, Schifter S, Schrøder HD, Kragballe K. Calcitonin gene-related peptide (CGRP) is increased in skin lesions and in serum of psoriatic patients. In: Proceedings of the 20th Annual Meeting of the European Society for Dermatological Research (abstr.) Turin 1990; p 54.

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