

SHORT REPORTS

Lack of Increase in Granulocyte Colony-stimulating Factor in Psoriatic Skin

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Previously, we showed an elevated level of pro-inflammatory cytokine granulocyte-macrophage colony-stimulating factor (GM-CSF) in psoriatic skin. Granulocyte (G)-CSF, which is also released from the infiltrating cells and epidermal keratinocytes, profoundly influences the biological activities of terminally differentiated neutrophils, in addition to its supporting effects on the proliferation and differentiation of progenitor cells of neutrophil lineage. We have carried out enzyme immunoassay for G-CSF in suction blister fluids and horny tissue extracts from psoriatic skin. Although some samples of the blister fluids and stratum corneum extracts showed G-CSF, there were no significant differences between the concentration in normal and psoriatic skin. These results suggest that, among CSFs, GM-CSF plays a more important role than G-CSF in the local immune responses in psoriasis. **Key words:** G-CSF; Psoriasis; Suction blister fluid; Stratum corneum.

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Proliferation and differentiation of hematopoietic cells is under the control of a group of glycoproteins, known collectively as colony-stimulating factors (CSFs), including interleukin 3 (IL-3), granulocyte (G)-, granulocyte-macrophage (GM), and macrophage-CSF. G-CSF, 18–22 kDa in protein size (1), is produced by a variety of cell types, including keratinocytes (2).

Besides supporting the proliferation and differentiation of hematopoietic precursor of progenitor cells, G-CSF shows that binding to terminally differentiated neutrophils profoundly influences their biological activities, for example, by exerting chemotactic activity (3), or by enhancing chemotactic peptide binding (4), superoxide release stimulated by a chemotactic peptide (5), respiratory burst in adher-

ent neutrophils (6), and antibody-dependent cell-mediated cytotoxicity (7). Thus, G-CSF is a growth and differentiating factor for a neutrophil lineage, and also a priming factor for the resulting mature cells (1).

Psoriasis represents inflammatory skin disorders characterized by significant changes in cellular immunity, particularly alterations in T lymphocyte- and monocyte-related functions, and by transepidermal neutrophil chemotaxis (8). A variety of cytokines, including interleukin 2 (IL-2) (9), interferon (IFN)- γ (9–11), and GM-CSF (12), have been shown to mediate these inflammatory reactions in psoriasis. Although we demonstrated the involvement of GM-CSF in the pathogenesis of psoriasis and sterile pustular dermatoses in a previous report (12), it is not clear whether G-CSF, another CSF, which is also released from the infiltrating cells and keratinocytes, mediates inflammatory reactions in psoriasis. We therefore measured the levels of G-CSF in the suction blister fluids and stratum corneum extracts from psoriasis in the same way.

MATERIALS AND METHODS

Suction blister formation

Twenty-two psoriatic patients (16 males and 6 females, age range 18–59 years, mean 34 years) and 15 healthy volunteers (13 males and 2 females, age range 5–23 years, mean 21 years) were studied. None of the psoriatic patients had received any kind of treatment for at least 2 weeks before examination. Suction blisters were raised on the skin of the abdomen or forearms by means of an attachment device using a hollow syringe, whose broad flat end was placed on the skin, and a negative pressure of 200–300 mmHg was applied. Within 1–2 h of constant suction, tiny vesicles appeared. Shortly thereafter, the vesicles coalesced to form blisters. Some of the blister fluids raised on the psoriatic involved skin were contaminated with blood. The blister fluids were collected, and supernatant was obtained after centrifugation at 3,000 rpm for 15 min. Only blister fluids without much blood contamination were stored at –70°C before use.

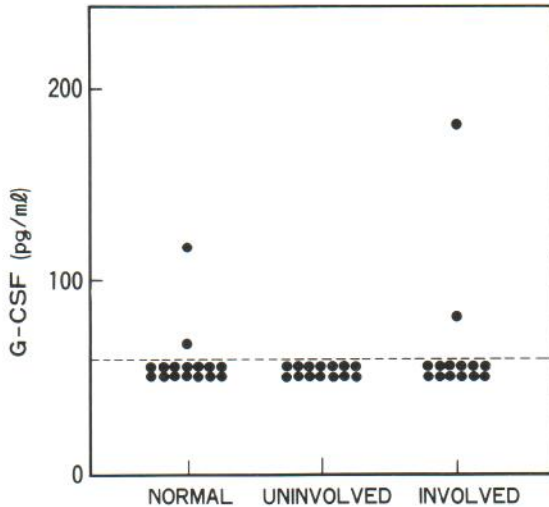


Fig. 1. Levels of G-CSF in the suction blister fluids raised on the normal, psoriatic uninvolved, and involved skin. ----, background level.

Extracts of stratum corneum

Scales were collected from skin lesions of 9 patients with psoriasis vulgaris, 2 with erythrodermic psoriasis, and 9 with pustular psoriasis. Water-soluble components were extracted from the stratum corneum in phosphate-buffered saline, pH 7.4, containing 100 µg/ml streptomycin, as reported previously (12).

Measurement of G-CSF

Concentrations of G-CSF were measured using enzyme immunoassay (EIA) for human G-CSF (13).

Statistical analysis

Levels of G-CSF were compared using the Wilcoxon rank-sum test.

RESULTS

G-CSF in the suction blister fluids

No G-CSF was detected in suction blister fluid raised on psoriatic uninvolved skin (Fig. 1). Two out of 15 normal and 2 out of 14 psoriatic involved skin samples showed G-CSF.

G-CSF in the scale extracts

Among non-inflammatory skin extracts, 1 out of 14 samples showed G-CSF (Fig. 2). Although 4 out of 20 psoriatic scale extracts showed G-CSF, its concentration in the scale extracts from psoriasis was not significantly greater than that from the stratum corneum of non-inflammatory skin.

DISCUSSION

We showed previously that EIA employed in the present study gave satisfactory reproducibility with an excellent correlation between the values of G-CSF obtained by EIA and the biological assay (13). Pro-inflammatory activities of G-CSF, especially the chemotactic activity for neutrophils (3), enhancement of chemotactic peptide binding (4), superoxide release stimulated by a chemotactic peptide (5), and induction of respiratory burst in neutrophils (6), have all suggested its role in the inflammatory reactions in psoriasis because it is also released from keratinocytes (2). However, in contrast to another pro-inflammatory cytokine, GM-CSF, whose increase was noted in the psoriatic skin (12), we found no extraordinary increase in G-CSF in the suction blister fluids or stratum corneum extracts in psoriatic lesions. It is unlikely that the low level of G-CSF in the present study was due to inadequate sample preparations. The suction blister fluids and stratum corneum have been assumed to reflect the preceding events in the epidermal keratinocytes, and we have already found that suction blister fluids or stratum corneum extracts from normal or psoriatic skin contain significant amounts of IL-1 (14), secretory IL-2 receptor, IFN-γ (9), and GM-CSF (12).

Although we failed to find an increase in G-CSF in the psoriatic skin, GM-CSF, whose increase we found in psoriatic lesions, was found to be more potent than G-CSF in the superoxide release by

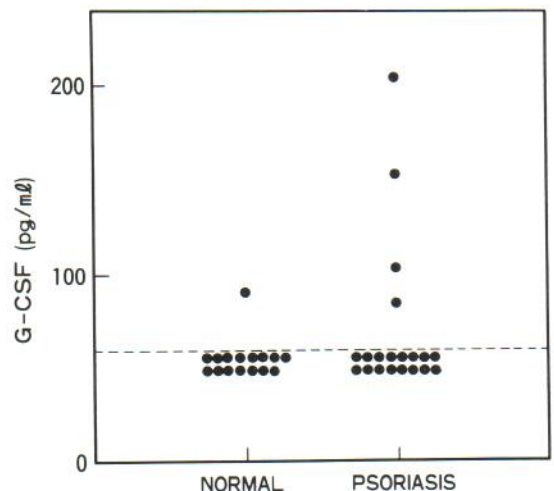


Fig. 2. Levels of G-CSF in the stratum corneum extracts from non-inflammatory skin and psoriasis. ----, background level.

neutrophils stimulated by a chemotactic peptide (15). Thus, it is likely that, among CSFs, GM-CSF plays a more important role than G-CSF in the local immune or inflammatory responses in psoriasis. These data, however, do not exclude the need for further studies to elucidate the involvement of G-CSF in inflammatory skin diseases.

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