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Neutrophil Responsiveness in Psoriasis

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During recent years, several studies have been focused on the involvement of immunological factors in the pathogenesis of psoriasis. In this regard, the accumulation of $CD4^+DR^+CD25^+$ lymphocytes into active psoriatic plaques appears to play a key role (1), even if recent data point out that also $CD8^+$ cells and $CD11c^+$ macrophages are implicated in the development of full-blown psoriatic lesions (2). At the same time, the psoriasis-related exaggerated release of several cytokines (CKs), such as interleukin 1 (IL-1), IL-6, IL-8, interferon τ (IFN-τ) and Tumour Necrosis Factor α (TNF-α), may either stimulate keratinocyte proliferation or trigger adhesion molecule expression on both endothelial and T cell surface, which is in turn responsible for T lymphocyte extravasation (3). The recent demonstration of an increased serum concentration of soluble intercellular adhesion molecule-1 in active psoriasis fully supports these findings (4).

On the other hand, the skin infiltration by polymorphonuclear cells (PMN), as detected in spongiform pustules of Kogoj and Munro's microabscesses, represents one of the salient histological features in active psoriasis (1). In the light of these results and on the basis of the elevated CK synthesis, a PMN activation has been suggested to occur at either skin or blood level. With regard to the latter point, our recent data clearly indicate that circulating PMN from active psoriatic subjects display a significant increase in their chemotactic responsiveness, superoxide anion (O_2^-) release, hydrogen peroxide (H_2O_2) generation, adherence property to either nylon fibers or fetal calf serum (FCS)-coated plates and lysosomal enzyme release (5).

Psoriatic scale-derived factors may account for the observed effects. Evidence has actually been provided for an enhanced production in psoriatic lesions of C5a anaphylatoxin, a peptide which stimulates PMN chemotaxis (6). Nevertheless, PMN enzyme activation might either upregulate the expression of surface chemotactic receptors or accelerate intracellular signal transduction (5). In this framework, a role for IL-8 cannot be ruled out, since an increase of surface IL-8 receptor density has recently been shown in PMN from psoriatic individuals (7). The augmented CK release may also be selectively involved in the triggering of PMN respiratory burst. TNF-α and IFN-τ are able to prime neutrophil suspensions for O_2^- generation by shortening the lag period following agonist stimulation (5). The resulting enhancement of oxidative metabolism may have an important in vivo counterpart, since reactive oxygen metabolites may exert noxious effects for host tissue by the induction of auto-oxidation processes (5).

The observation of an increased PMN adhesiveness to FCS-coated plastic substrates in active psoriasis implies the occurrence of a β_2 integrin-dependent mechanism. Proinflammatory CKs may, in fact, stimulate adhesion molecule expression on neutrophil membrane by favouring CD11b and CD11c translocation from intracellular stores to PMN surface (8). The pivotal role of these structures in such a phenomenon is also confirmed by the demonstration that monoclonal antibodies to β_2 integrins specifically inhibit PMN adherence to FCS-coated plastic plates (5). Finally, it should be stressed out that the augmented PMN adhesiveness gives rise to a further increase in respiratory burst, thus supporting a critical role for oxygen radicals in psoriasis-related skin damage (5).

In the light of these findings, the question arises whether peripheral blood PMN-mediated functional capacities and/or metabolic pathway positively correlate with disease activity. Our results clearly outline that PMN chemotactic and adhesiveness properties merely parallel the clinical course of psoriasis, since a strict relationship (85.7%) has been found between immunological and clinical data in a closed protocol (9).

As far as the mechanisms accounting for these effects are concerned, the possible influence of CK level on PMN-mediated responsiveness has to be pointed out. Elevated IFN-τ and TNF-α serum concentrations have been shown in untreated psoriatic patients, while cyclosporin-A or etretinate treatment down-modulates CK levels (10). Moreover, a transient IFN-τ increase usually precedes lesion relapses (10). Therefore, a drug-induced reduction of CK synthesis may account for the normalization of PMN chemotactic and adherence capacities. On the other hand, this is not the case for O_2^- generation, which is significantly enhanced in both active and inactive psoriatic individuals (9). A possible explanation for the unmodified response pattern might be represented by the elevated C5a serum levels in psoriatic-treated subjects, which is in turn responsible for the increased oxidative metabolism through complement pathway activation (9).

Taken together, these findings indicate that an activation status of circulating PMN occurs in active psoriasis and suggest the potential usefulness of PMN chemotactic and adhesiveness assays in the follow-up of the disease.

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