Serum-soluble Interleukin 2 Receptor in Psoriasis

Failure to Reflect Clinical Improvement

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Interleukin 2 (IL-2) is a T-cell growth factor produced by activated T cells. The cellular receptor for IL-2 is also expressed on activated T cells and one of its component molecules can be shed from the cell and measured as a soluble protein (sIL-2R). Blood levels of sIL-2R can be used to monitor in vivo immune activation and have been shown to correlate with clinical disease activity in conditions such as rheumatoid arthritis and atopic eczema. The present study shows that serum sIL-2R levels are raised in patients with chronic plaque psoriasis. These elevated serum levels were maintained during successful treatment of the skin lesions with topical tar preparations. This is in contrast to atopic eczema where serum sIL-2R levels fall with treatment and may indicate that topical treatment of psoriasis does not correct the underlying state of immune activation, even when resolution of the skin plaques is achieved. ***Key words: Cytokine, ELISA, Underlying mechanism.***

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Genetic and immune factors are involved in the pathogenesis of psoriasis (1,2). For example, lesional psoriatic skin contains more mRNA for IL-1 beta than non-lesional skin does, and in situ hybridization has shown that in plaques, dermal cells (probably macrophages) are actively producing this cytokine (3). The dermal infiltrate in stable plaque psoriasis consists predominantly of activated T cells (4). T-cell activation by antigen leads to production of the T-cell growth factor, interleukin 2 (IL-2), and its membrane receptor (IL-2R), resulting in T-cell clonal proliferation (5). The interleukin 2 receptor consists of at least two peptides (6) and one of these, p55 or Tac protein, is shed from the cell surface in proportion to the level of T-cell activation (7).

The soluble form of the receptor protein (sIL-2R) can be detected in the blood. The level of sIL-2R is raised in patients with immune-mediated diseases such as rheumatoid arthritis (RA) (8,9) and atopic eczema (10). Recently it has been shown that the levels are also raised in the serum of patients with psoriasis (11). In the present study we have monitored serum levels in sIL-2R in patients with psoriasis throughout a period of in-patient treatment where the end-point was clearance of all skin lesions.

PATIENTS AND METHODS

Subjects

Twelve patients (age range 18–72 years; mean 46 ± 5 [SEM] years) with widespread, stable plaque psoriasis were admitted to hospital for treatment with topical tar paste and tubular bandaging. A topical corticosteroid (Betamethasone valerate 0.025%) was used initially in some patients. No systemic treatment or ultraviolet radiation was given. Patients were discharged when the psoriatic plaques were no longer palpable (range 22–60 days; mean 41 days). Blood samples were obtained on admission and at dis-

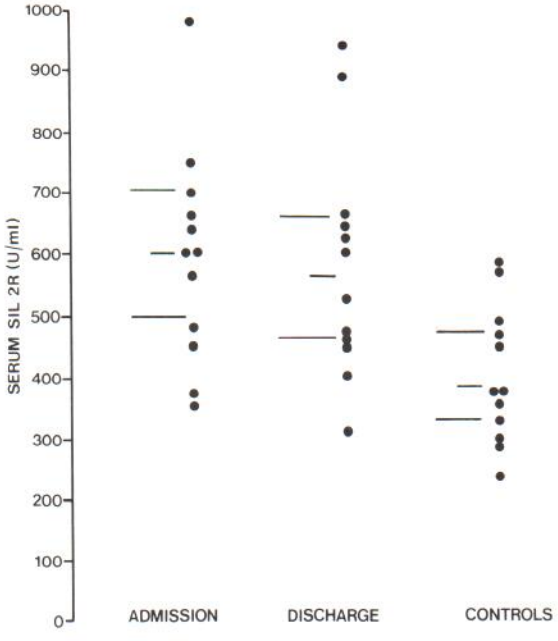

Fig. 1. Serum levels of sIL-2R in patients with psoriasis and controls. Serum samples were taken from patients on admission to hospital and at discharge when plaques were no longer palpable and from an age-matched control population sIL-2R levels were measured by ELISA. Bars denote median and 95% confidence intervals.

No systemic treatment or ultraviolet radiation was given. Patients were discharged when the psoriatic plaques were no longer palpable (range 22–60 days; mean 41 days). Blood samples were obtained on admission and at discharge and at least weekly during the period of hospitalization. The control group was formed by 12 healthy individuals (age range 22–63, mean 45±4 [SEM] years) with no inflammatory skin disease.

Measurement of sIL-2R in serum

Blood samples were drawn into dry glass tubes. After centrifugation, serum was removed and stored at −70°C until analysis. sIL-2R levels were measured by an ELISA technique using two non-competing murine monoclonal antibodies to the p55 chain (Tac protein) of the interleukin 2 receptor (T Cell Sciences Inc;). We have described this method previously (8).

Statistical analysis

The Wilcoxon paired rank sum test was used to compare levels of sIL-2R. The first comparison was between values for patients on admission and those on discharge. Second, the levels for patients on admission and at the time of discharge were both compared with controls, using the same test on age-matched pairs.

RESULTS

Serum sIL-2R levels on admission and discharge

Fig. 1 shows the levels of sIL-2R for patients on admission and at discharge and for the control group. The median values and 95% confidence intervals are shown for each group. Admission levels were significantly higher than controls ($p < 0.01$). During in-patient treatment, levels did not fall significantly ($p > 0.05$) and at the time of discharge remained significantly higher than controls ($p < 0.02$).

Serum sIL-2R in individuals

Eight patients had multiple blood samples taken during their hospital admission. Fig. 2 shows levels on admission and discharge and at intermediate time points. There was no consistent rise or fall during the period of response to treatment.

DISCUSSION

There is some evidence that the T-cell growth factor IL-2 is implicated in the pathogenesis of psoriatic lesions. Lee et al. (12) have reported marked exacerbation of psoriasis in 3 individuals undergoing IL-2 immunotherapy for metastatic renal carcinoma. Cyclosporin-A has a beneficial effect in psoriasis and this drug inhibits IL-2 production and receptor expression in vivo (13). Using immunoperoxidase staining with a monoclonal antibody against IL-2R, it has been shown that psoriatic plaques contain IL-2R-positive cells in the dermal infiltrate. There were significantly more of these cells in lesional skin

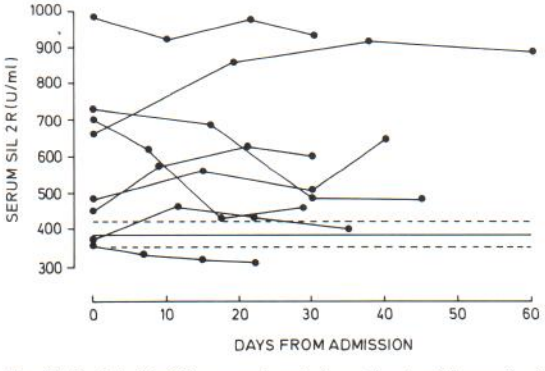

Fig. 2. Serial sIL-2R serum levels in patients with psoriasis receiving treatment in hospital. Eight patients were tested on admission, at discharge, and at two intermediate time points and serum sIL-2R levels assessed by ELISA. Solid and broken lines represent median and 95% confidence intervals for age-matched healthy control populations.

activation in vivo. They are raised in graft-versus-host disease (15) and lymphoreticular malignancy (16). In rheumatoid arthritis there is a strong correlation between serum sIL-2R and disease activity as measured by the Ritchie articular index (9) and recently sIL-2R has been shown to correlate with disease activity in atopic eczema (10). The results of the present study agree with those of Kapp et al. (11) in finding that psoriatic patients with active disease have elevated sIL-2R levels. We have also shown that topical treatment, with the end-point being clinical clearance of disease, was not associated with a significant change in sIL-2R levels. In the case of atopic eczema, it might be argued that falling levels of sIL-2R in response to treatment are associated with healing of the skin barrier and reduction of the inflammatory component caused by scratching and bacterial colonization. This argument is less convincing, however, in the light of the present study, as many of our patients also had an inflammatory component initially.

The end-point in our study was the disappearance of palpable disease. Histological abnormalities may persist for a time after clinical clearance and it is possible that the levels of sIL-2R would eventually fall to the normal range; long-term studies of psoriatics in remission are in progress.

An alternative explanation might be that in psoriatic patients, abnormal immunological activation continues despite clinical cradication of the disease with coal tar. Perhaps a further trigger is necessary in order to induce clinical exacerbation. Further studies are required with different treatment modalities to determine whether chronic immunological activation plays a primary role in pathogenesis of the skin lesions, is a secondary event in response to skin disease, or comprises elements of both.

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