Preferential Activation of the Alternative Pathway of Complement in Psoriatic Lesional Skin

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Fig. 1. Relationship between the levels of C4d and Bb expressed per milliliter (a) and milligram protein (b) in the horny tissue extracts of psoriasis vulgaris (O), erythrodermic psoriasis (•), pustular psoriasis (⊠) and pustulosis palmaris et plantaris (■). There is a significant relationship between the levels of C4d and Bb when expressed per milliliter ($R = 0.65$, $p < 0.01$).

Sir,

One of the salient histologic features of psoriatic lesions is an accumulation of neutrophils in intra- and subcorneal (Munro) or spongiform pustules (Kogoj) [1]. Psoriatic scales show chemotactic activities, apparently caused by the presence of chemotactic peptides that include complement-derived chemotactic factor C5a [2, 3]. The classical pathway of complement has been shown to be activated in psoriatic lesional skin, which leads to a generation of chemotactic C5a [2]. On the other hand, horny tissue has been shown to be capable of activating the complement system through the alternative pathway in vitro [4]. The presence of neutrophils immediately beneath the stratum corneum, therefore, suggests a possibility of the activation of complement through the alternative pathway by the stratum corneum.

During the complement activation, complement fragments C4d and Bb are released at the time of the classical and alternative pathway activation, respectively [5-8]. The presence of the C4d or Bb fragment, therefore, denotes a preceding complement activation through the classical and/or alternative pathway [9, 10]. In a previous report we showed that the scales of psoriasis and sterile pustular dermatoses contained significantly elevated enzyme immunoassayable levels of C4d and Bb compared with those in the horny tissue of noninflammatory skin, suggesting that the alternative as well as the classical pathway of complement plays an important role in the generation of the chemotactic anaphylatoxin C5a in psoriatic lesional skin [10]. However, it has not been settled which pathway plays a major role in the generation of C5a. We, therefore, reassessed the degree of classical and alternative complement activation by comparing the levels of complement fragments C4d and Bb in psoriatic scale extracts.

The relationship between the levels of C4d and Bb was examined in the horny tissue extracts of psoriasis vulgaris (9 patients), psoriatic erythroderma (4 patients), pustular psoriasis (13 patients) and pustulosis palmaris et plantaris (5 patients), which had been measured using C4d and Bb fragment enzyme immunoassay kits (Cytotech, San Diego, Calif., USA) and have been reported in the previous report [9]. The horny tissues of noninflammatory skin were excluded in the present study because the levels of C4d and Bb in these samples were very low for statistical analysis. Data were analyzed statistically by Spearman's rank correlation test.

There was a significant relationship between the enzyme immunoassayable levels of C4d and Bb in the scale extracts when expressed per milliliter ($R = 0.65$, $p < 0.01$; fig. 1a) but not per milligram protein (fig. 1b). The dots representing each sample were confined to the left upper half of the graph. These results suggest that the alternative pathway plays a major role in generating the chemotactic complement fragment C5a in psoriatic lesional skin, presumably immediately beneath the stratum corneum.

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