

Atopic dermatitis: correlation of peripheral blood T cell activation, eosinophilia and serum factors with clinical severity

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Summary

In the first part of this study peripheral blood lymphocyte subpopulations, their activation state and various serum parameters were measured in extrinsic and intrinsic atopic dermatitis (AD) patients compared to normal individuals. Beside the characteristic eosinophilia, significantly increased numbers of CD4⁺ T cells with increased expression of IL-2 receptors (IL-2R) and HLA-DR were noted in the AD patients. In addition, extrinsic AD patients showed increased numbers of CD23⁺ B cells and decreased numbers of CD16⁺ natural killer cells. Moreover, increased serum levels of eosinophil cationic protein (ECP) and soluble IL-2R as well as soluble factors that prolong survival of eosinophils *in vitro* could be demonstrated. In the second section of this study we determine how these blood immunological parameters relate to the clinical severity of the skin lesions of AD, by weekly analysis of 12 AD patients attending a high altitude clinic for 3 to 6 weeks. The patients were divided into two groups on the basis of treatment with topical steroids, but during the observation period a significant improvement in clinical status was observed in all AD patients independent of topical steroid therapy. A progressive decrease in eosinophil and activated T cell numbers, soluble IL-2R levels and serum eosinophil survival prolonging activity could be demonstrated, which closely correlated with the clinical severity of the AD.

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Introduction

Atopic dermatitis (AD) is a common inflammatory skin disease characterized by severe pruritus, a chronically relapsing course and a distinctive clinical appearance [1,2]. Although the pathogenesis of AD is unknown, several lines of evidence suggest that immunological mechanisms contribute to its development. In particular, high levels of serum total IgE and specific IgE to environmental and food allergens have been demonstrated in most AD patients [1–5].

Recent studies have demonstrated that the T cell derived lymphokines IL-4 and IFN- γ play a crucial role in the induction of IgE synthesis [6–9]. IL-4 enhances the production of IgE and induces the expression of the low

affinity IgE Fc receptor (CD23) on B cells, while IFN- γ inhibits IgE synthesis and CD23 expression [10,11]. Indeed, T cells from AD patients produce increased amounts of IL-4, while IFN- γ suppresses *in vivo* IgE synthesis in experimental animal models [12–15] and may be effective in the treatment of AD [16]. Moreover, the number of CD23 positive lymphocytes has been shown to be elevated and to be correlated with the clinical severity of AD [17,18]. The skin lesions of AD are infiltrated by activated T cells and antigen presenting cells that bind IgE on the cell surface [19–21]. IgE positive Langerhans cells may present aeroallergens to peripheral blood derived T cells by means of cell bound IgE [22]. This raises the possibility that dysfunction of the IgE related immune system provides a link between skin reaction to aeroallergen and the formation of skin lesions in AD. On the other hand, elevated IgE levels are not a prerequisite of AD as is

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Thus, this data demonstrated basic immunological differences between extrinsic and intrinsic asthma and suggests that the cytokine basis of extrinsic and intrinsic AD may also be fundamentally different.

In this study we compare immune parameters in AD patients with those in AD patients with asthma, and patients with atopic asthma (Fig. 2). Indeed, T cell activation, eosinophil survival prolonging activity and eosinophilia are a feature of both AD and asthma. It is very unlikely that the observed changes in AD patients are attributable to atopy as opposed to AD, since atopy alone is not associated with changes of the distribution of lymphocyte subpopulations, increased T cell activation, increased sIL-2R levels or peripheral blood eosinophilia [50,51]. Thus, atopic patients with hay fever were not included as controls since this study was performed outside the very short local hay fever season, and hay fever sufferers have normal T cell activation outside this hay fever season. Nevertheless, during active hay fever we can assume that similar changes in T cell activation and eosinophilia to those observed would be seen.

Analysis of eczema patients attending a high altitude clinic demonstrated clinical benefit for both extrinsic and intrinsic dermatitis. This local situation permitted us to monitor immune parameters in dermatitis patients, during a period of clinical improvement. A number of factors could be responsible for the benefits of a stay at a high altitude mountain clinic [30]. These include allergen avoidance, with decreased levels of house dust mite and grass pollen. However, in addition there are strong psychological and placebo effects with frequent alleviation of mild depression associated with long-term morbidity and a temporary respite from domestic, work and economic problems. Although this study does not explain why there is a benefit from attending the high mountain clinic, there is an improvement in both clinical and laboratory immunological parameters of eczema.

In conclusion, this study reports close correlation between T cell and eosinophil activation parameters with the clinical severity of AD. Hence these parameters should be useful to monitor the severity of AD. However, although we extend the range of peripheral blood abnormalities detectable in AD, further dissection of T cell function is required to explain the organ specific immunopathology of AD.

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