

LETTER TO THE EDITOR

Decrease in serum IL-32 level in patients with atopic dermatitis after cyclosporine treatment

Editor

Interleukin (IL)-32 is a proinflammatory cytokine that is involved in the inflammatory processes of rheumatoid arthritis, chronic obstructive pulmonary disease and Crohn disease.¹ Recent studies have reported that IL-32 also contributes to the pathophysiology of atopic dermatitis (AD) in the early stages.² IL-32 is expressed in the lesional skin of patients with AD and that serum levels of IL-32 in patients with AD are elevated.² Cyclosporine has been used as a short-term treatment for severe AD, and it effectively improves the condition of severe AD patients. However, it is suggested that the therapeutic targets of cyclosporine are suppression of the T-cell function, and it is still being evaluated. In this study, we investigated the relationship between serum IL-32 levels in AD patients and the cyclosporine treatment and demonstrated that the serum IL-32 levels in AD patients were significantly decreased after the cyclosporine treatment.

After the informed consent was obtained, 10 Japanese male AD patients aged 14–82 years (average, 39.5 years) were initiated with low-dose (3 mg/kg) oral cyclosporine treatment. The subjects continued topical corticosteroid treatments but did not take oral corticosteroid throughout the study. Serum IL-32 levels were measured with an ELISA kit (PeproTech Inc., Rocky Hill, NJ) before and 28 days after the oral cyclosporine treatment was started. Serum IL-32 levels were significantly decreased, and the skin lesions were improved in patients with AD after 4 weeks of

treatment (96.3 ± 30.4 pg/mL vs 52.0 ± 16.4 pg/mL, average $\pm$ SEM) (Fig. 1). This result indicates that systemic cyclosporine administration decreased the serum IL-32 levels, which was correlated with the skin symptom in AD patients.

IL-32 was initially detected in IL-2-activated T cells and NK cells.^{3,4} Prior studies have demonstrated that IL-32 is expressed at high levels in human epidermal keratinocytes (KCs) after stimulation with interferon (IFN)- γ and tumour necrosis factor (TNF)- α .² It is well known that KC apoptosis is an important mechanism of eczema and spongiosis in patients with AD and is mediated by IFN- γ .⁵ Moreover, it is reported that IL-32 modulates KC apoptosis and contributes to the pathophysiology of AD.² It is also suggested that TNF- α might be important in acute AD lesions.⁶

Various types of oral immunosuppressive drugs have been used for the treatment of severe AD with a prominent first choice for cyclosporine.⁷ Cyclosporine therapy can provide sustained remission in some patients.⁸ Cyclosporine effectively inhibits the transcription of cytokines, such as IL-2 and IL-4,⁹ which leads to an inhibition of T-cell activation. In addition, we have demonstrated that serum levels of IL-31, a new candidate of itch mediators, were decreased after treatment with cyclosporine.¹⁰ In this study, we have demonstrated that serum levels of IL-32 were decreased after treatment with cyclosporine. Although it still remains unclear whether cyclosporine affects directly or indirectly, this study has indicated that cyclosporine might downregulate IL-32 transcription, inhibit apoptosis of KCs and consequently improve the condition of AD patients. In conclusion, this study highlights that the mechanism of cyclosporine therapy in the treatment of AD patients might be associated with decrease in the serum levels of IL-32. Disruption of IL-32 or its signalling mechanism might provide a novel target for the treatment of AD.

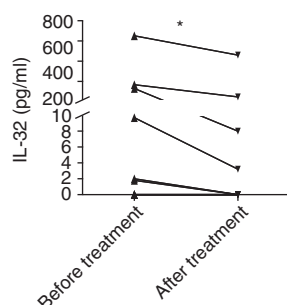


Figure 1 Serum IL-32 levels. Serum IL-32 levels in patients with AD before and after cyclosporine treatment.

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