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IL-31 and IL-33 circulating levels in allergic contact dermatitis

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KEY WORDS

Allergic contact dermatitis; cytokines; interleukin-31; interleukin-33; pruritic skin disease; pruritus

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Summary

Enhanced IL-31 expression in skin biopsies is present in allergic contact dermatitis (ACD). IL-33 expression is induced in keratinocytes and in skin of ACD patients. This overexpression is present in both allergic and irritant conditions. The aim of this work was to test the systemic involvement of IL-31 and IL-33 in ACD. IL-31 levels were significantly higher in patients than in controls. IL-33 serum levels, on the contrary, were similar in patients and controls. This work shows a possible systemic involvement of IL-31 and the absence of a systemic involvement of IL-33 in ACD. IL-31 levels do not seem related to the allergen involved, and did not change on the strength of the allergen involved. More likely, IL-31 levels are related to the itch. IL-33, instead, is secreted from damaged or inflamed tissue and might function as an early warning system at the site of skin damage. In the future, IL-31 could be a possible therapeutic target of all pruritic skin diseases resistant to conventional therapies.

Introduction

Allergic contact dermatitis (ACD) involves epidermal cells, such as keratinocytes and Langerhans cells, fibroblasts and endothelial cells, as well as invading leukocytes, interacting amongst themselves under the control of cytokines and mediators network (1). Interleukin (IL)-31, a recently discovered cytokine, is involved in both innate and adaptive immunity in tissues in close contact with the environment, such as the skin (2).

IL-31 is produced by human mast cells, monocytes, macrophages, monocyte-derived dendritic cells, human epidermal keratinocytes and dermal fibroblasts upon various stimulations (2). Enhanced IL-31 expression in skin biopsies is present in pruritic diseases as atopic dermatitis, ACD and prurigo nodularis, and elevated serum IL-31 levels have been found in chronic urticaria and pruritic skin lesions related to epidermal growth factor receptor-tyrosine kinase inhibitors treatment (3-7).

IL-33, a cytokine of the IL-1 cytokine family has recently been attributed to the epithelial "alarmin" defense system. IL-33 is released by the epithelial cells in various tissues and organs, including keratinocytes, endothelial cells, and immune cells and, as other cytokines of IL-1 family, by necrotic structural cells, as fibroblasts and keratinocytes (8,9).

The aim of this study was to measure the circulating IL-31 and IL-33 levels in patients with ACD to test the hypothesis that these cytokines could have a systemic involvement in this pruritic skin disease.

Material and Methods

We enrolled 20 patients (15 females, 5 males), with ACD (mean age 36.84 ± 12.62 years; range 18-62 years), diagnosed by patch testing with SIDAPA (Italian Society of Allergological, Occupational and Environmental Dermatology) series, in accordance