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SHORT COMMUNICATION

A Th2 Cytokine Interleukin-31 Signature in a Case of Sporadic Lichen Amyloidosis

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Lichen amyloidosis (LA), a variant form of primary localised cutaneous amyloidosis (PLCA), is a chronic itching skin disease, caused by the extracellular deposition of amyloid proteins in the dermis (1). This entity is clinically characterised by grouped hyperkeratotic papules with itchy lesions usually situated primarily on the shins. The upper back, forearms and thighs can also be involved. While the pathomechanism of PCLA still remains unclear, recent studies have identified in familial PLCA mutations in both the oncostatin M receptor (OSMR) gene, which encodes the OSMRβ (2) and in the interleukin (IL)-31RA gene (3), which encodes the IL-31 receptor α subunit.

These 2 subunits constitute the functional receptor for IL-31, a recently discovered cytokine belonging to the IL-6 cytokine family (4). In combination with gp130, OSMRβ is a component shared with the receptor for OSM, another IL-6 family related cytokine. OSMRβ and IL-31RA are widely expressed in keratinocytes, fibroblasts and cutaneous nerves. Based on these new data it has been suggested that OSMRβ or IL-31RA mutants, when stimulated by their ligands OSM or IL-31, trigger signalling abnormalities leading to keratinocyte apoptosis and pruritus (5). Moreover, IL-31 is associated with itchy conditions and overexpression of this cytokine is observed in prurigo and atopic dermatitis (6). Whether expression of IL-31 and/or its receptor is altered in LA is still unknown.

Here, we performed an analysis of the *OSMR* gene and cutaneous expression patterns of cytokines and anti-microbial peptides (AMP) in a 42-year-old woman with a sporadic case of LA.

METHODS

A lesional skin biopsy showed a hyperplastic epidermis with amorphous, eosinophilic deposits in the papillary dermis with Congo Red staining, confirming the diagnosis of lichen amyloidosis. In subsequent experiments, real-time PCR analysis was performed on additional lesional and non-lesional skin biopsies to analyse the expression profile of genes encoding AMP, cytokines and chemokines as compared to the skin of 6 healthy subjects.

RESULTS AND DISCUSSION

Although we did not detect mutation of the *OSMR* gene, the transcriptional profile revealed an up-regulation of the Th2-related cytokines *IL13* and *IL31* genes in lesional skin compared to non-lesional and control skin, while *IL4* and *TSLP* gene expressions were not altered (Fig. 1 and data not shown). In addition, transcription of a Th2-related chemokine gene, *CCL5*, was also higher in the patient's lesional skin. Altogether, these data suggest a Th2-biased immune response with an expression of IL-31 in our patient, which has never been reported in this itching skin condition, so far. *OSM* transcripts were also increased in lesional skin, although the induction was not as prominent as the one observed for *IL31* gene (Fig. 1). Among Th1 and Th17-related cytokines, interferon (IFN)-γ gene (*IFNG*) was the only one upregulated in lesional skin (Fig. 1), whereas *IL17* and *IL22* expressions were decreased in lesional and non-lesional skin of the patient as compared to normal skin. Finally, the expression of AMP genes such as *S100A7*, *S100A8*, *DEFB4* (encoding β-defensin 2) and *PI3* (encoding peptidase inhibitor 3, skin derived) were also increased in lesional skin (Fig. 1). The increased expression of AMP in our patient could be involved in the induction of IL-31 secretion as it was previously reported in mast cells (7). IL-17 and IL-22 are known to be potent inducers of AMP in the skin and mucosal surfaces (8). The fact that these cytokines were not up-regulated, but actually diminished in our analysis suggests that other factors are involved in AMP secretion in this patient (9). Altogether, our data suggest that this case of sporadic and itching LA is probably more dependent of IL-31 than of OSM-induced signalling pathway. IL-31 is a newly described cytokine mainly produced by Th2 polarised lymphocytes. This cytokine appears to be important during itching skin conditions since mice overexpressing IL-31 develop severe pruritus and dermatitis (4), and high levels of IL-31 are detected in prurigo nodularis, atopic dermatitis (6) and cutaneous T-cell lymphoma (10). Though our analyses are based only on a single case, elevated expression of IL-31 and another Th2-related cytokine, IL-13, suggests a role of the Th2 pathway in the pathomechanism of this disease. These data should be confirmed on more patients affected with sporadic LA. The recent development of IL-31 antibodies, which have been successfully used *in vivo* in mice to atopic dermatitis (11), might be of interest to improve patients suffering from itching conditions involving IL-31.

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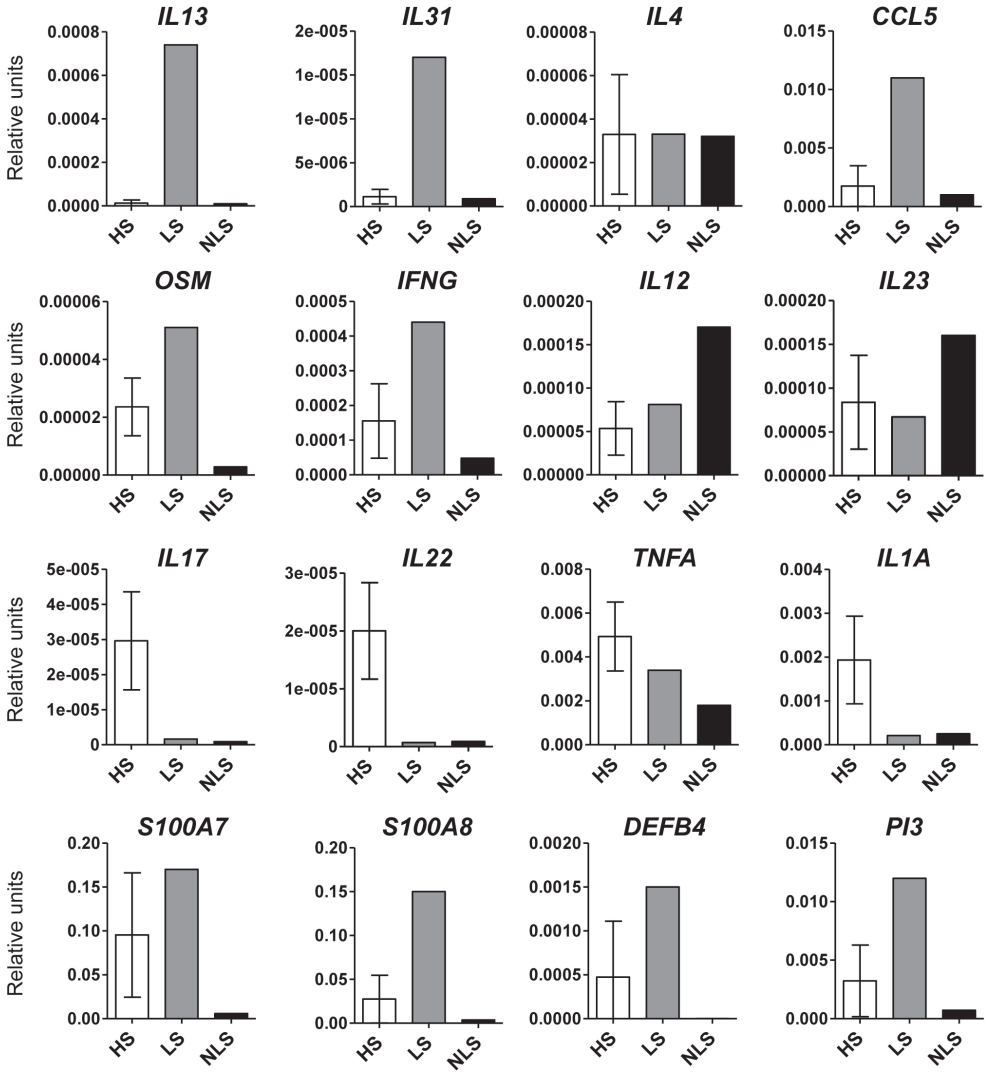

Fig. 1. Real-time RT-PCR analysis of indicated gene expression in healthy skin (HS) from control subjects ($n = 6$) as well as lesional (LS) and non-lesional skin (NLS) of the patient with lichen amyloidosis. Data are presented relative to expression of transcripts encoding GAPDH. Bars represent mean and SD.

The authors declare no conflict of interest.

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