

Concurrence of psoriasis vulgaris and atopic eczema in a single patient exhibiting different expression patterns of psoriatic autoantigens in the lesional skin



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INTRODUCTION

The systemic immune polarities in psoriasis vulgaris (Pso) and atopic dermatitis (AD) are opposing, as the T helper (Th)17/cytotoxic T (Tc) 17-type immune profile dominates in Pso and the Th2-type immune profile dominates in AD.¹⁻³ The concurrence of these 2 diseases is rare⁴ but has occasionally been reported.^{5,6} In such cases, different cytokine profiles have been found in the infiltrative T cells of lesions,⁵ thereby raising a question of what factor determines the development of such distinct skin lesions in a single patient. Because antigen-specific T-cell activation is considered crucial in the development of both diseases, it is hypothesized that the different expression of antigens in the skin might be linked to the activation of specific T-cell subsets at the site.⁵ In Pso, novel autoantigens, LL-37, and a disintegrinlike and metalloprotease domain containing thrombospondin type 1 motif-like 5 (ADAMTSL5), have recently been reported^{1,2} and are suspected to be one of the causes of Th17/Tc17 activation in psoriatic skin.

Here we present a patient that exhibited concurrent Pso and AD. We evaluated the expression levels of psoriatic autoantigens, LL37 and ADAMTSL5, in each lesion.

Abbreviations used:

AD:	atopic dermatitis
ADAMTSL5:	a disintegrinlike and metalloprotease domain containing thrombospondin type 1 motif-like 5
CAMP:	cathelicidin antimicrobial peptide
IL:	interleukin
Pso:	psoriasis vulgaris
Th:	T helper
Tc:	cytotoxic T
qPCR:	quantitative polymerase chain reaction

CASE REPORT

A 58-year-old man presented to our hospital for scaling erythema. Pso that was refractory to topical steroids, oral etretinate, oral cyclosporine, and ultraviolet A phototherapy was diagnosed 25 years ago at another hospital. Skin biopsy on arrival found the histologic characteristics of Pso. Treatment with ustekinumab, an anti-interleukin (IL)-12/23p40 blocking antibody, was started and continued for 4 years with partial reduction in the psoriatic eruptions. The patient noted exacerbated pruritic sensations during the period, however, together with the development of atopic lichenified eczema on the trunk and extremities that was clinically different

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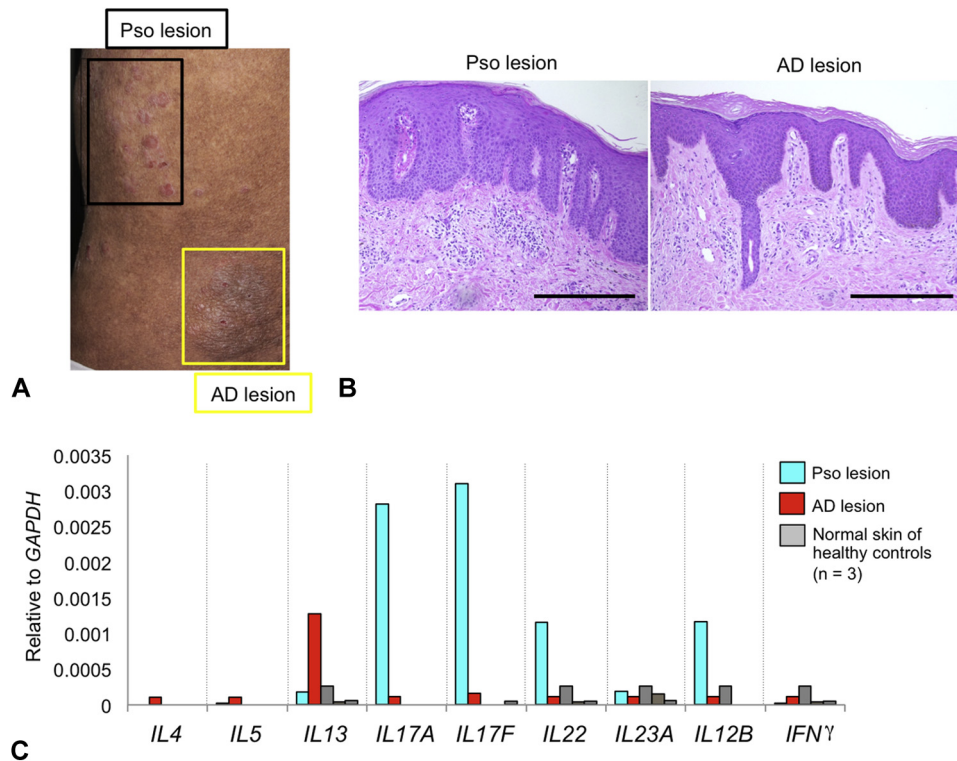


Fig 1. Concurrence of AD and Pso lesions in a single patient. **A**, Concurrence of a Pso lesion (black square) and an AD lesion (yellow square) on the trunk. **B**, Hematoxylin-eosin stain of each skin lesion. Bar = 200 μ m. **C**, mRNA expression levels of cytokines in each skin lesion and in normal skin taken from 3 healthy controls, examined by qPCR.

from the Pso eruptions and persisted for more than six months (Fig 1, A).

Both types of skin lesions on the trunk were analyzed histologically (Fig 1, B). The Pso lesion exhibited typical features of Pso, such as acanthosis with uniform elongation of rete ridges, whereas the atopic lesion exhibited features of chronic eczema, such as acanthosis with hypergranulosis and nonuniform elongation of rete ridges. Both lesions included massive perivascular cellular infiltration. The diagnosis of concurrent Pso and AD was made.

The mRNA expression levels of each lesion were examined by quantitative polymerase chain reaction (qPCR), and compared with those of normal skin taken from 3 healthy donors. Consistent with the diagnosis, the Pso lesion exhibited high expression of Pso-related genes, such as *IL17A*, *IL17F*, *IL22*, and *IL12B*, whereas the AD lesion exhibited high expression of *IL13*, an AD-related gene, compared with those of control skin samples (Fig 1, C). The expression levels of the Pso-related genes and AD-related genes in each lesion were similar to those in lesional skin of naïve Pso or AD patients, respectively (Fig 2). In contrast, flow cytometric analysis of blood-circulating CD4⁺ and

CD8⁺ T cells found no apparent differences in the cytokine-producing capacity (IL-4, IL-13, IL-17A, IL-17F, IL-22, and interferon- γ) between the patient and healthy controls (data not shown). Only mild increases in the percentage of eosinophils (11.8%; faculty normal range, 3%-5%), immunoglobulin E level (359 IU/mL; normal, <170 IU/mL), and thymus and activation-regulated chemokine level (614 pg/mL; normal, <450 pg/mL) were noted in the blood. These results showed that there is no apparent systemic immune polarization in the patient, although each skin lesion has a distinct immune shift toward the Th17/Tc17-dominant or Th2-dominant condition.

Next, we evaluated the expression of ADAMTSL5 and LL-37 in each skin lesion by immunohistochemistry. ADAMTSL5 and LL-37 were detected in keratinocytes and perivascular infiltrating cells in both Pso and AD lesions. The expression of both proteins in the Pso lesion was more prominent than that in the AD lesion (Fig 3, A and B, left). In addition, the mRNA expression of cathelicidin antimicrobial peptide (*CAMP*), a gene encoding LL-37, was detected only in the Pso lesion (Fig 3, B, right).

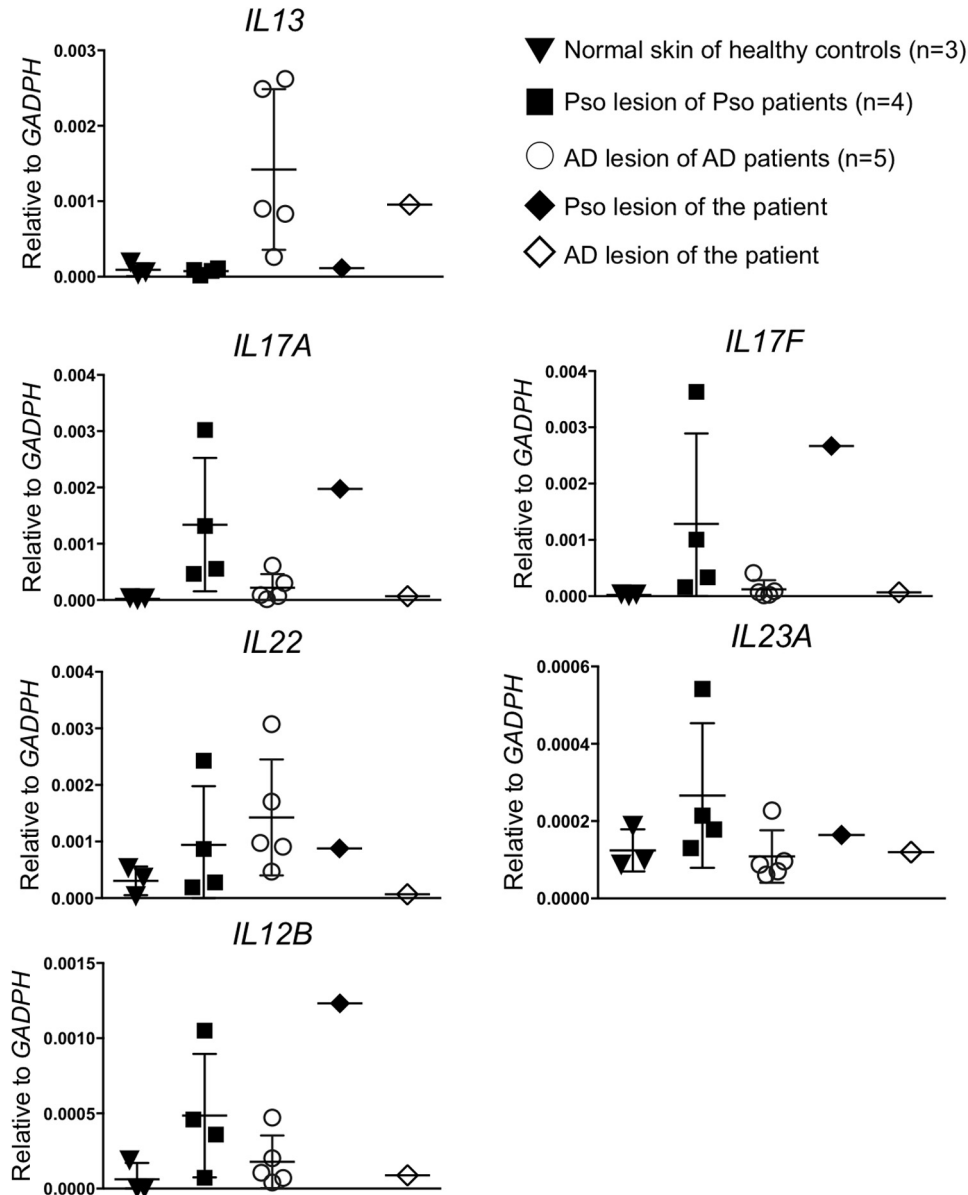


Fig 2. Expression levels of cytokines in the patient compared with those of naïve AD and PSO. qPCR analysis of mRNA expression levels of *IL13*, *IL17A*, *IL17F*, *IL22*, and *IL23A* in different skin lesions. Samples were taken from the Pso lesion and AD lesion of the patient, the Pso lesion of naïve Pso patients (n = 4), the AD lesion of naïve AD patients (n = 5), and normal skin of healthy controls (n = 3). Expression levels of *IL4*, *IL5*, and *IFN γ* were under detection limit in most samples in this trial.

DISCUSSION

Herein, we confirmed the different cytokine profiles and expression levels of LL-37 and ADAMTSL5 in a Pso and an AD lesion in a single patient. Our results suggested the possibility that the high expression of psoriatic autoantigens might be necessary to induce Th17/Tc17 activation at the sites, which might have caused the Pso lesions.

Elevation of LL-37 and ADAMTSL5 in psoriatic lesions has been reported^{1,2}; however, the precise

mechanisms by which the expression of LL-37 and ADAMTSL5 is regulated remains unknown. In addition, the expression of LL-37 in AD is conflicting among reports,^{7,8} and there have been no studies assessing the expression of ADAMTSL5 in AD to date. Indeed, we could not find a general trend in the expression levels of LL-37 or ADAMTSL5 in the AD lesion; the expression levels were quite variable among the patients (n = 10) (data not shown). It might be interesting to explore whether the

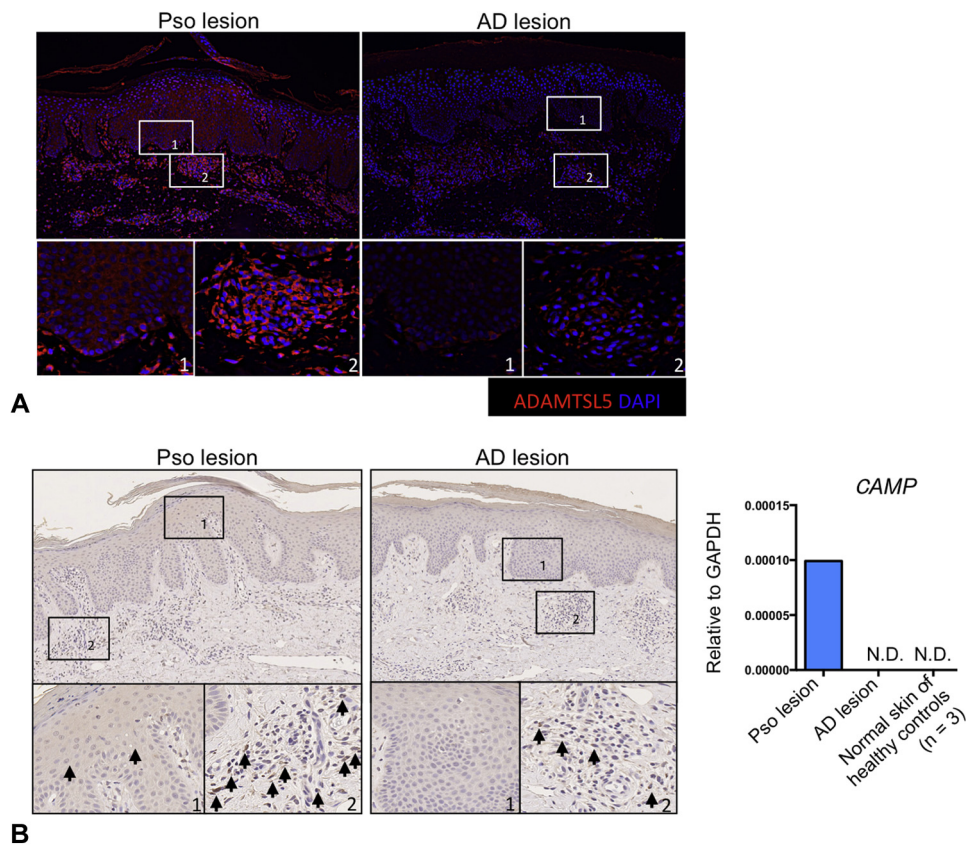


Fig 3. Expression of psoriatic autoantigens in the lesional skin. Immunohistochemical staining of ADAMTSL5 (red) (**A**) or LL-37 (brown) (**B**, left) in the Pso and AD lesions. Blue in (**A**) indicates nuclei stained with DAPI. Arrows indicate positive-staining cells. Lower panels indicate the high magnification of squares in the upper panels. mRNA expression levels of *CAMP* in each skin lesion compared with samples of healthy controls (**B**, right). *ND*, Not detected.

Th2-dominant or Th17/Tc17-dominant environment directly affects the expression of psoriatic autoantigens. In addition, because Th17 immune polarization could also be observed in some AD patients,³ an evaluation of these proteins together with AD subtypes and local cytokine profiles might provide clues to aid in our understanding of the pathogenesis of AD accompanied by Th17 activation.

It is of note that the present AD lesions appeared after the development of the Pso lesions in the patient. We assumed that additional invasion of external antigens, such as mite antigens, or the down-regulation of psoriatic autoantigens might have allowed Th2 polarization. In addition, treatment with ustekinumab might have influenced the development of AD lesions, because blockade of IL-12/23p40 will impair the differentiation of Th1 cells and the maintenance of Th17 cells, which might have facilitated Th2 cell differentiation and triggered AD.⁹

In a concomitant case of Pso and AD, the expression levels of psoriatic autoantigens were

associated with the phenotype and the immune shift in the lesions. Although this is a limited observation from a single patient, our case may highlight the importance of antigens in the skin for the development of Pso and AD.

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