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SHORT COMMUNICATION

Variations in Serum TARC and I-TAC Levels Reflect Minor Changes in Disease Activity and Pruritus in Atopic Dermatitis

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Atopic dermatitis (AD) is a chronic or relapsing inflammatory skin disease. Scratching in AD patients results in proinflammatory cytokine and chemokine production. Thus, serum levels of monocyte chemotactic protein-1 (MCP-1), regulated on activation, normal T-cell expressed and secreted (RANTES), macrophage inflammatory protein (MIP)-1β, eotaxin, thymus and activation-regulated chemokine (TARC), and macrophage-derived chemokine (MDC) were increased in AD patients, compared with normal controls (1–4). With regards to Th1 chemokines such as interferon (IFN)-γ-inducible protein 10 (IP-10), IFN-γ-inducible T-cell α-chemoattractant (I-TAC), and monokine induced by IFN-γ (MIG), their expression in lesional AD skin was confirmed by immunohistochemistry (5). They may negatively contribute to the development of AD because macrophages from AD patients produced lower levels of IP-10 compared to cells from healthy controls in response to α-toxin (6) and the expression of MIG and IP-10 was lower in Langerhans cells from patients with AD than from patients with psoriasis, whereas the opposite was observed for TARC and MDC (7).

Visual analogue scale (VAS) is a valuable method to assess pruritus intensity in patients with pruritic dermatoses (8). In this study, we focus on temporal variation of pruritus in each patient and compare serum samples taken at different time points when there were only slight, if any, changes in disease activity. The aim of this study was to highlight the most sensitive chemokine associated with changes in pruritus in AD patients.

MATERIALS AND METHODS

Seventeen Japanese outpatients with moderately-controlled AD, diagnosed according to the criteria of Rajka & Langeland (9), were enrolled in this study (11 men and 6 women, mean age 34.4 ± 10.4 years). Clinical severity: 8 mild cases, 5 moderate cases, and 4 severe cases. Blood samples were collected twice with an 8-week interval after informed consent. We rated itch by VAS 0–10, asking the patients to mark a point on the line corresponding to mean itch during the last 7 days before blood draw. The clinical severity of AD was evaluated using the scoring system proposed by Rajka & Langeland (9). They were treated with topical corticosteroids and moisturizers in combination with oral antihistamine, which were not changed. during the study. None of the patients showed dramatic changes in disease activity during the observation period. All studies were approved by the ethics review board of the Faculty of Medicine, the University of Tokyo and conducted according to the Declaration of Helsinki Principles.

Serum cytokine levels of 12 chemokines, i.e., interleukin-8, MCP-1, RANTES, MIP-1α, MIP-1β, IP-10, I-TAC, MIG, eotaxin, TARC, MDC, and GROα were analysed with Multi-Analyte ELISArray Kits (QIAGEN, Frederick, MD) according to the manufacturer's protocol.

Correlation coefficients between ⊿VAS (VAS at the 2nd visit subtracted by VAS at the 1st visit) and ratio of absorbance (serum chemokine absorbance at the 2nd visit divided by serum chemokine absorbance at the 1st visit) were determined using the Spearman's rank correlation test. *P*-values of < 0.05 were considered statistically significant.

RESULTS

Pruritus VAS score (mean±standard deviation) at the 1st visit in mild, moderate, and severe AD was 4.6 ± 0.74, 6.2 ± 0.8 and 4.8 ± 2.4, respectively (Fig. 1a). Pruritus VAS scores at two different visits are shown in Fig. 1b and example of serum chemokines levels in Fig. 1c and d. After the 8 weeks, pruritus was improved in 10 patients, in 4 patients itch sensation got worse, while there was no change in pruritus in 3 patients. Only minor changes in chemokine levels occurred (all data not shown). The variations in pruritus correlated positively with the before and after ratio of serum TARC levels and negatively with ratio of I-TAC levels (Fig. 1e, f). On the other hand, absolute VAS scores did not significantly correlate with any serum chemokine levels (data not shown).

DISCUSSION

Although TARC and I-TAC may not directly regulate pruritus in AD patients, it may be safely said that these chemokines are very sensitive disease markers of AD. Plenty of data have been accumulated to suggest that serum TARC levels reflect disease activity of AD (4, 10). The expression of TARC and MDC was reported to be higher in Langerhans cells from patients with AD than from patients with psoriasis (7). Moreover, TARC was reported to be superior to other markers of AD. When mRNA expression levels of 14 CC chemokines in the skin were examined, TARC and other two chemokines went along with eczema development in AD (11). Similary, out of 10 examined cytokines/chemokines, serum concentrations of TARC were increased in adult AD patients (12). These findings, together with our results, suggest that TARC is the most sensitive disease

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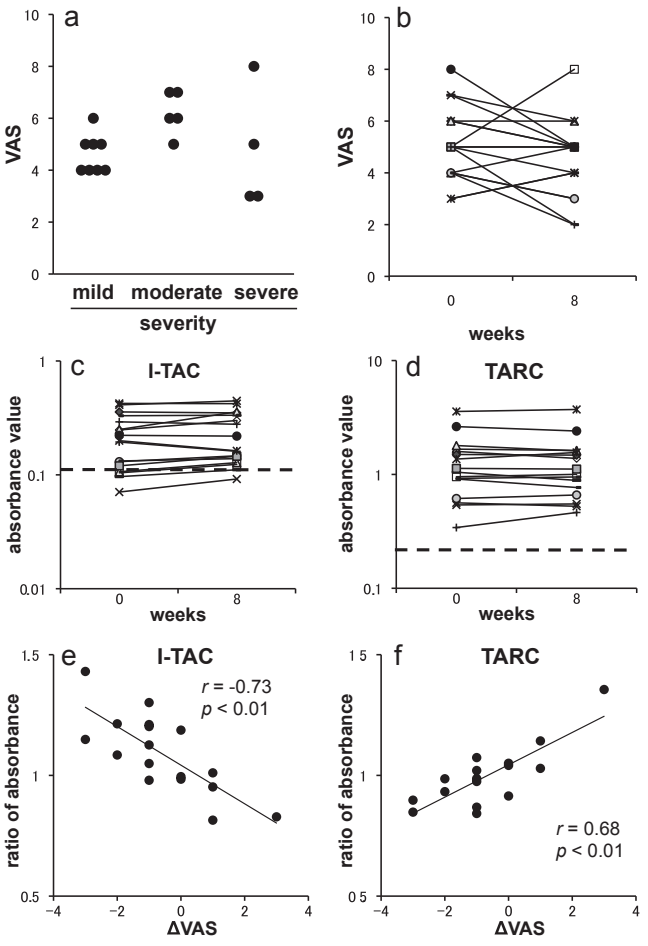

Fig. 1. (a) Pruritus visual analogue scale (VAS) scores at the first visit of AD patients. (b) Pruritus VAS scores at two different visits. (c, d) Absorbance values of IFN-γ-inducible T-cell α-chemoattractant (I-TAC) (c) and thymus and activation-regulated chemokine (TARC) (d) at two different visits. Dotted lines represent the mean level of each chemokine in healthy controls. (e, f) Association between variations in VAS score and ratio of serum absorbance values of I-TAC (e) and TARC (f) at the 2 observation time-points.

marker of AD. On the other hand, the role of I-TAC in the development of AD is yet to be investigated. It was previously reported that IFN-γ response was attenuated in monocyte-derived dendritic cells in patients with AD (13). Plasma levels of IP-10, another Th1 chemokine, tended to be decreased in severe AD compared to mild AD, although they were higher in AD patients than in normal controls (14). These previous studies suggest that Th1 chemokines might be expressed in response to Th2-mediated inflammation and that decrease in their expression might be associated with deterioration of AD.

The authors declare no conflict of interest.

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