

Immunohistochemical Analysis of CCR6 Expression in Four Psoriasis Patients

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TO THE EDITOR

Chemokines and chemokine receptors have been known to play a crucial role in directing the movement of mononuclear cells that is involved in the systemic immune system. In recent years, the acquired immunity involving Interleukin 23 (IL-23) / T helper 17 (Th17) axis has been considered to have an important role in pathophysiology of psoriasis [1]. Among the chemokines and chemokine receptors having an association with IL-23/ Th17 axis, chemokine (C-C motif) ligand (CCL) 20, and CC-chemokine receptor (CCR) 6, only known receptor for CCL20, has been focused attention according to the following findings of the studies. (1) Both CCR6 and CCL20 have reported to be expressed at significantly higher levels in lesional psoriatic skin than in non-lesional skin. (2) CCR6 is expressed on almost all IL-17A- and IL-22-producing CD4⁺ T cells those are expected as a key player in an IL-23/ Th17 axis. (3) Mice deficient in CCR6 fail to develop IL-23-induced psoriasis-like lesion. On the other hand, it has been reported that more than 75% of resident T cells in normal skin also express CCR6, accordingly, CCR6 may be involved in migration of T cells not only in inflammation state, but also in the steady state. According to the previous studies using clinical samples of psoriasis patients, up-regulation of CCR6 mRNA expression and immunohistochemical localization of CCR6 protein in the skin lesions has been reported. Nevertheless, the association between CCR6 expression and clinical characteristics has never been argued. In this paper, we performed immunohistochemical analysis of CCR6 in four psoriasis patients, and discuss about an association between CCR6 expression and clinical characteristics of the patients.

The four patients clinically diagnosed as plaque-type psoriasis vulgaris were recruited for the investigation (Table 1). Samples of lesional skin were taken using 4 mm punch biopsy. To confirm the diagnosis of psoriasis,

histopathological examination was performed in all lesional skin samples. Psoriasis Area and Severity Index (PASI) was determined subjectively by dermatologists. Clinical characteristics of the patients were obtained from the medical records. Normal skin samples were obtained from three persons who underwent skin grafting. Informed consent was given to all participants. Formalin-fixed, paraffin-embedded tissue samples were cut at 3µm. The applied antibody was a rabbit polyclonal anti-CCR6 antibody (1:50, clone; LSBio, WA). Immunohistochemical stains were performed on an automated slide stainer for immunohistochemistry (Leica BOND-III, Leica Biosystems).

The immunohistochemical results were demonstrated in Figure 2. All psoriatic samples showed similar results, namely, robust expression of CCR6 in the inflammatory lymphocytes which had infiltrated into the papillary and perivascular superficial dermis (Figure 2a-2d). Although the normal skin contained a few dermal lymphocytes, CCR6 expression in those cells was less prominent than in the psoriatic samples (Figure 2e). On the other hand, in both psoriatic and normal skin, keratinocytes in the basal and suprabasal layer of the epidermis showed comparable CCR6 expression.

There have been a large number of studies investigating pathophysiological roles of IL-23/ Th17 axis. To our knowledge, only a few studies of immunohistochemical

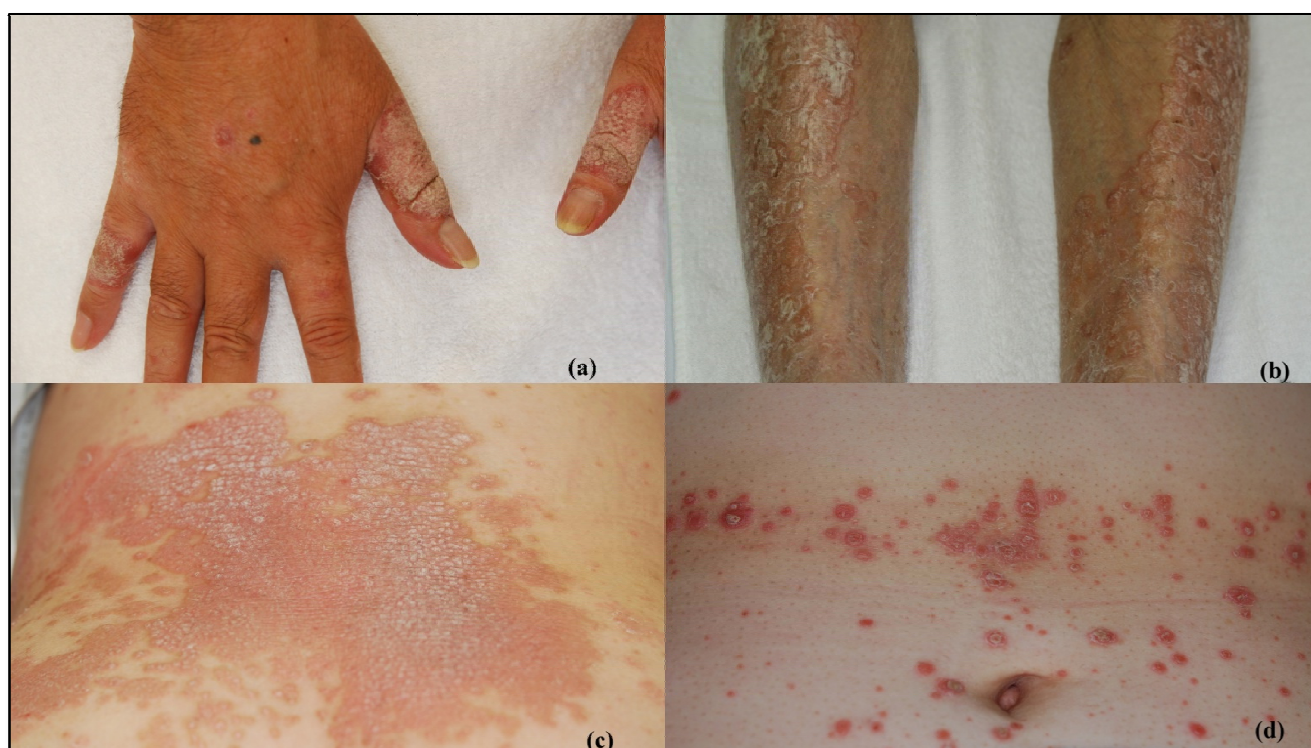
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Table 1. Clinical characteristics of four psoriasis patients

	Age/ Sex	PASI	Disease duration	Treatment of the most recent two months	Comorbidities
Case 1	54 M	9.6	10 years	Topical steroids and topical vitamin D3	hypertension
Case 2	88 M	21.6	2 years	Topical steroids	Hypertension
Case 3	70 M	16.5	13 years	Topical steroids	Hyperlipidemia
Case 4	58 F	16.6	1 years	Topical steroids and topical vitamin D3	None
Mean value	67.5	16.1	6.5 years		

**Figure 1.** Clinical pictures of the patients: (a) Case 1, (b) Case 2, (c) Case 3, (d) Case 4**PASI; Psoriasis Area and Severity Index.**

CCR6 expression in psoriasis patients has been published. Antiga et al. [2] reported that CCR6-positive and CD4-positive cells were both mainly located in the superficial dermis, an observation consistent with our own. Moreover, in our study, immunohistochemical results demonstrated that CCR6 was also expressed on basal and suprabasal layer of epidermis, which was consistent with the previous report by Charbonnier et al. [3]. They theorized that epidermis-expressed CCR6 had a role for a homing of Langerhans cells and a keratinocyte homeostasis. Although we could not elucidate precise characteristics of the CCR6-positive

infiltrative lymphocytes, it may be possible that such lymphocytes in the lesional psoriatic skin play a role in promotion of inflammatory cell migration. Besides, recent studies noted that CCR6 is expressed on almost all Th17 cells (IL-17A- and IL-22-producing CD4⁺ T cells). Accordingly, we speculate that the CCR6-positive infiltrative lymphocytes shown in the lesional psoriatic skin contain some Th17 cells.

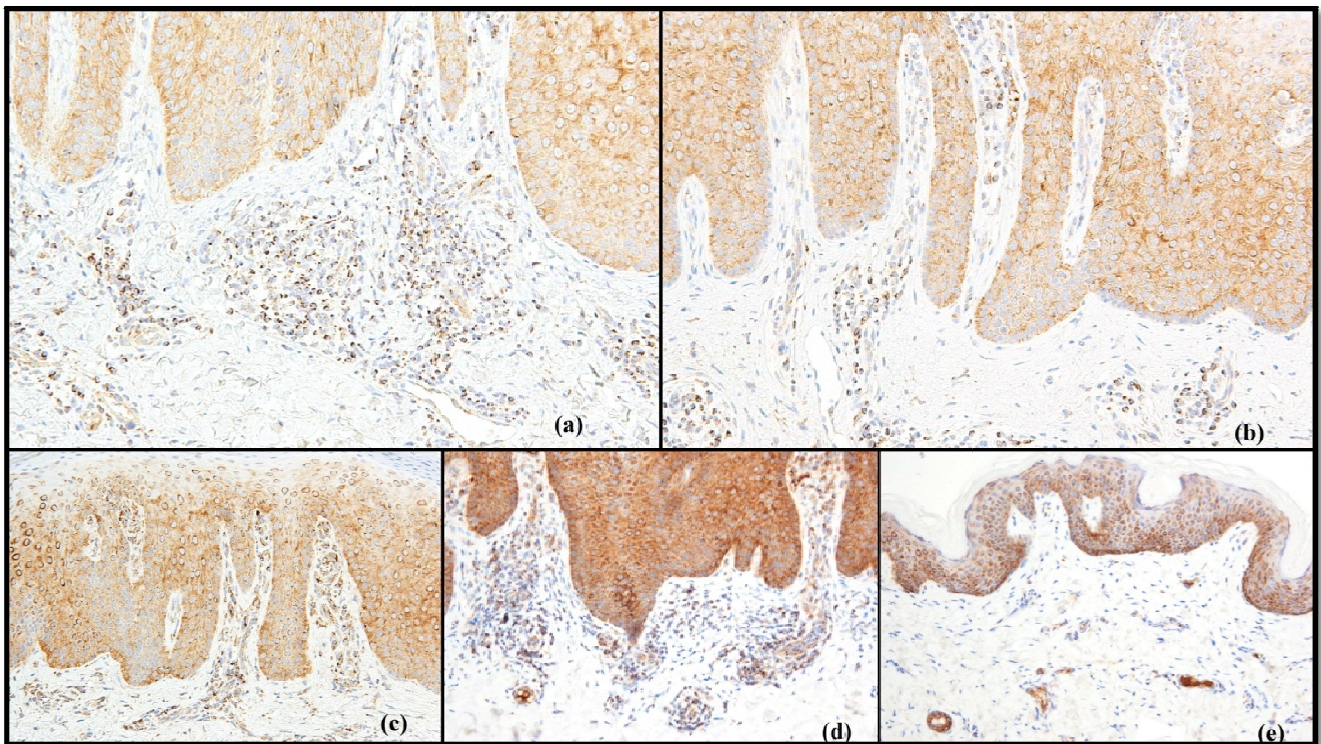


Figure 2. Immunohistochemical results (original magnification; x200): (a) Case 1, (b) Case 2, (c) Case 3, (d) Case 4, (e) Representative normal skin

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CONFLICT OF INTEREST

None declared.

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