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Differential Expression of ICAM-1, E-selectin and VCAM-1 by Endothelial Cells in Psoriasis and Contact Dermatitis

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Adhesion receptors on endothelial cells are considered to be important for cellular influx in tissue. In this regard, skin constitutes a specialised environment for migration of leukocytes during inflammation. Using immuno-enzymatic staining techniques, we compared the in situ expression of ICAM-1, E-selectin, and VCAM-1 on endothelial cells and inflammatory infiltrates in both lesional and non-lesional biopsied skin from two immuno-inflammatory diseases, viz. psoriasis and contact dermatitis. The results were compared with those in skin specimens obtained from normal healthy individuals free from any history of skin disease. Our results show that ICAM-1 and ELAM-1 are upregulated in psoriatic non-lesional and lesional skin. On the other hand, in non-lesional biopsy from contact dermatitis patients, all three AR molecules are sparsely present, similar to the situation in normal skin although they are overtly expressed in the lesional sites. Moreover, VCAM-1 was found to be significantly increased on endothelial cells in the lesional sites of contact dermatitis as compared with biopsied psoriatic specimens. Interestingly VCAM-1 was also found to be present on some T-cells and Langerhans cells in contact dermatitis alone. The present data suggest that in different inflammatory dermatitis, varying adhesion receptor-ligand interactions involving endothelial cells and leukocytes are involved, which may be due to the differing cytokine profiles of perivascularly located T-cells.

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The main constituents of inflammatory dermatoses are characterized by the presence of mutually interacting activated subsets of T cells and antigen-presenting cells (APC) at the lesional sites (1). Adhesion receptor (AR) expression on endothelial cells (EC) is regarded as important for cellular influx in tissue. In recent years, various AR on both EC and immunocompetent cells have been identified which are involved in adhesion and homing into various tissues and also causing their regional activation (2). The interactions between the accumulating cellular infiltrates cause the release of proinflammatory cytokines which then lead to tissue damage. Psoriasis is a disease which spontaneously exacerbate but also undergo remission. During our ongoing studies on cellular interaction in psoriasis pathology, we observed that the expression of various AR is upregulated in both non-lesional (NL) and lesional (L) skin of psoriasis patients, as compared with that in skin of normal healthy individuals (3–4). Our findings, together with those in the literature (5), show that the upregulation of AR in non-lesional psoriatic skin is due to an ongoing local hyperimmune reactivity as a constitutive phenomenon of the disease. However, in order to establish the validity of such a hypothesis, one essential prerequisite is to evaluate the status of AR in both NL and L skin from patients with other known inflammatory dermatoses, such as contact dermatitis, during the active phase of the disease.

The best characterized AR expressed by EC in relation to leukocyte migration and adhesion are ICAM-1, VCAM-1, and E-selectin (6). Consequently we examined the expression of these AR, particularly on EC and on immunocompetent cells, by immunohistochemical single and multiple staining methods.

MATERIALS AND METHODS

The details are similar to those described earlier (3–7). Patients: Groups of 6 patients, each with active psoriasis, and 72 h patch-tested contact dermatitis (CD) patients with DTH reaction, together with 6 healthy volunteers were included in this present study.

Skin biopsies were removed from the inside border of respective lesions and also from the non-involved area on a location at least 5 cm away from the involved area. Cryostat sections (5 μm) were cut, fixed in acetone and stored at −20°C until use.

Immunohistology and lightmicroscopic examination: Immunohist-

Table I. *Expression of ICAM-1, E-selectin and VCAM-1 by endothelial cells in cryostat sections from normal, lesional and non-lesional psor/asis and contact dermatitis skin biopsies*

	Normal skin	Psoriasis		Contact dermatitis	
		NL	L	NL	L
ICAM-1	+	+–>++	+++	+	+++
E-Selectin	±	+	+++	+	+++
VCAM-1	–	–	±	–	+++

-: no staining; ±: weak staining; +: positive staining; ++: strong staining; +++: very strong staining.

Table II. *Mean percentages of Langerhans cells and T cells expressing ICAM-1 and VCAM-1 in cryostat sections from normal, lesional and non-lesional psoriasis and contact dermatitis skil biopsies*

	N	Psoriasis		Contact dermatitis	
		NL	L	NL	L
CD1a/ICAM-1	0	10±8	38±30	5±8	70±30
CD1a/VCAM-1	0	0	0	0	35±12
CD3/ICAM-1	20±20	65±15	70±15	15±10	38±18
CD3/VCAM-1	0	0	0	0	8±8

N: normal human skin; NL: non-lesional skin; L: lesional skin.

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ological analysis by both single and multiple staining methods (using serial sections) were carried out described earlier before (3–7). MAbs used in this study were anti-ICAM-1 and VCAM-1 (both purchased from British Biotechnology, Abingdon, Berks, England), anti E-selectin (a gift from Dr D. Haskard, Rheumatology Unit, Postgraduate Medical School, London, England), Leu (4) (Becton & Dickinson, Mountain View, USA), OKT 6 (Ortho Diagnostics, Raritan, USA).

RESULTS AND DISCUSSION

The results of the immunostainings on AR expressed by endothelium are summarized in Table I. Endothelial cells in normal skin are ICAM-1 +, and increased expression of this adhesion receptor can be found in lesional psoriasis and CD skin biopsies. On the other hand, only the non-lesional psoriatic (and not CD) skin also shows increased expression of ICAM-1. E-selectin was found to be weakly expressed in normal as well as in non-lesional CD skin, but was increased in non-lesional psoriasis. This adhesion molecule was strongly expressed in lesional sites in both the diseases. On the other hand, VCAM-1 expression was negative in all normal and non-lesional skin specimens. However, strong expression of this AR was seen in lesional CD skin, while weak expression was evident in lesional psoriatic biopsies. These results show that EC in non-lesional psoriatic skin are in an activated state because of the higher expression of E-selectin and ICAM-1 as compared with non-involved CD and normal skin. The upregulation of these AR facilitates the recruitment of specific populations of T cell subsets.

The migration of lymphocytes into skin is thought to be a multistep mechanism, involving the initial adhesion, activation of leukocyte integrins, eventually leading to transendothelial migration (8). Regulation of lymphocyte migration into lesional psoriasis skin appears to be mediated mainly by ICAM-1 and LFA-1, and to a minor extent VCAM-1/VLA-4. In contrast, the migration of lymphocytes into CD skin involves both ICAM-1/LFA-1 and VCAM-1/VLA-4. In agreement with the present findings of low levels of VCAM-1 in psoriasis it can be reasoned that the critical time period for identifying the in situ identification of this molecule had already lapsed when the biopsy was taken. On the other hand, in CD lesions the biopsy was taken at the peak time of 72 h for *de novo* VCAM-1 expression on cytokine-stimulated endothelial cells.

Since both ICAM-1 and VCAM-1 also showed staining with mononuclear cells in the different skin specimens, double stainings with MAbs against LC and T cells were also performed. Double stainings of ICAM-1 and VCAM-1 against CD68 could not be performed since the MAbs were of the same isotype. In normal and CD lesional skin we found that a certain proportion of T cells were invariably ICAM-1+ (15–20%). However, the proportion of CD3 + ICAM-1+ cells was significantly increased in both non-lesional and lesional psoriasis skin biopsies. Quantities of ICAM-1+ CD3+ cells in CD lesional and non-lesional sites were less than those observed in psoriasis. We did not find any CD3+ or CD1a+ cells which were also VCAM-1 + in any of the normal or psoriasis skin specimens. Interestingly, VCAM-1+ Langerhans cells as well as occasionally T cells were encountered only at the site of DTH reaction. This indicates that VCAM-1+ Langerhans cells as well as T cells are important in interactions with antigen (contact allergen) specific T cell populations. Such an interpretation should be evaluated further by making in vitro studies.

In conclusion, our results show that the endothelium of non-lesional psoriatic skin is constitutively activated. Additionally, we hypothesize that, although psoriasis and CD are both hyperimmune skin disorders, leukocyte infiltration and migration into the lesional sites is regulated by varying adhesion pathways in different dermatoses.

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