Acta Derm Venereol (Stockh) 1989; 69: 403–406

Expression of CD36 (OKM5) Antigen on Epidermal Cells in Normal and Diseased Skin

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The expression of the CD36 (OKM5) antigen was studied with the PAP technique on sections of skin from healthy subjects and of normal and diseased skin from patients with various skin diseases. In specimens from healthy subjects the antigen was found on vascular and perivascular structures and in some cases it was seen on cells of the acrosyringium. A net-like pattern of CD36 was observed in the upper part of the stratum spinosum in skin lesions of patients with psoriasis, lichen planus, pityriasis rosea, morbilliform drug reactions, necrobiosis lipoidica, lichen amyloidosus, Darier's disease and ichthyosis vulgaris. Expression of CD36 was also seen in the nonlesional skin just below the granular layer in 3 of 5 patients with factitial urticaria with immediate dermographism, but not in delayed dermographism or chronic urticaria. In ichthyosis vulgaris CD36 was also expressed in dendritic cells of the basal layer and in a patient with a graft versus host reaction it was recognized both on scattered keratinocytes and on dendritic cells in the epidermis. The role of the expression of the CD36 antigen in the skin is unknown. The activated cells might possibly serve as antigen-presenting cells and/or have a modulatory influence on an inflammatory reaction.

(Accepted May 31, 1989.)

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The monoclonal antibody OKM5 recognizes an 88 kD antigen CD36 on blood monocytes and platelets. In normal epidermis the antigen expression was only confined to cells of the acrosyringium (1). It has been observed in a net-like pattern on keratinocytes in the stratum spinosum from lesions in patients with delayed intracutaneous test reactions, lichen planus, subacute lupus erythematosus and chronic eczematoid purpura (1–5). In mycosis fungoides and tuberculin reactions the CD36 antigen has been found to be expressed on a few of the keratinocytes (6–7). Melanophages can also carry CD36 antigen in inflammatory skin diseases (8). CD36 might function as an adhesion molecule of leukocytes, since it also reacts with thrombospondin, which is a cellular adhesion protein (9). Since the CD36 expressed on keratinocytes may serve as a target for inflammation, we have studied its occurrence in patients with various skin disorders in an attempt to obtain more information about their conditions.

MATERIAL AND METHODS

Punch biopsy specimens (3 mm) were obtained from five healthy subjects and from patients listed in Table I. In five patients with factitial urticaria biopsy specimens were taken both from apparently normal and from lesional skin and in patients with psoriasis both before and after treatment with anthralin. None of the patients had been exposed to UV-B irradiation in the last 3 weeks. The specimens were quick-frozen in isopentane at -70°C and stored at the same temperature until sectioned in a cryostat. Acetone-fixed sections, 6 mm thick, were investigated for binding of the monoclonal antibody CD36 (OKM5 dilution 1/40, Ortho Diagnostic Systems, Raritan, NJ, USA), using the peroxidase-antiperoxidase (PAP) technique (10). Monoclonal anti-HLA-DR or anti-Leu 6 antibodies were used as positive controls. Omission of the primary antibodies served as negative controls.

RESULTS

The main results are summarized in Table I. In the stratum spinosum the net-like expression of CD36 was most marked in patients with lichen planus and necrobiosis lipoidica (Fig. 1). In two patients with Darier's disease it was also marked around and in the hair follicles. The cancer area in basalioma was negative but the overlying apparently normal uppermost stratum spinosum was positive with accentuation in a hair follicle. In 3 of 5 patients with immediate dermographism both the apparently normal skin and the 15-minute-old dermographic area showed a weak expression of CD36 just below the stratum granulosum (Fig. 2). In a psoriatic plaque treated with anthralin for 3 weeks and in which previous erythema and infiltration had disappeared, the net-like epidermal distribution of CD36 was still present. An area of lichen amyloidosus which was clinically healed after application of betamethasone lotion (Betnovat, Glaxo) under Actiderm (Convatec, Squibb USA)

Table I. *CD36 expression in various dermatoses*

Subjects studied	Nos.	Site of CD36 expression
Healthy controls	5	Vascular and perivascular dermal cells. Acrosyringium positive when seen in 3 subjects
Chronic urticaria	5	
Delayed dermographism	1	
Immediate dermographism	2	
GVH reaction	1	Also in epidermal cell membranes and dendritic cells
Lichen planus	2	In a net-like intercellular or cell-membrane pattern in the upper part of the stratum spinosum and in dermal cells as above (Figs. 1–3)
Necrobiosis lipoidica	1	
Psoriasis	3	
Darier's disease	2	
Immediate dermographism	3	
Lichen amyloidosis	2	
Basalioma	1	
Morbilliform drug eruption	1	
Pityriasis rosea	2	
KID syndrome (11)	1	
Ichthyosis vulgaris	1	Also CD1 negative dendritic cells in the basal layer (Fig. 4)

once weekly for 3 weeks showed no CD36 expression in the epidermis, in contrast to a strong epidermal reactivity in an untreated lesion.

DISCUSSION

The expression of CD36 antigen in a net-like intracellular configuration in the upper stratum spinosum was found in several skin lesions investigated, but not in normal skin. The results confirm the findings in some earlier investigations, but also make it clear that expression of this antigen is more common than has previously been known. It is interesting that not only lesional but also apparently normal skin of some patients with dermographism showed CD36 below the stratum granulosum. The cause of the initial OKM5 expression on the keratinocytes is not known. Expression of both DR antigen and CD36 on keratinocytes has been observed in vitro, however, after stimulation by gamma interferon (12). It has been speculated that the CD36 antigen serves as an adhesion molecule for inflammatory cells and is thus able to maintain T cells and other leukocytes in the epidermis (9). The lymphokines formed might then further upregulate the CD36 expression on keratinocytes in the upper stratum spinosum. CD36-positive cells in the blood can act as antigen presenting cells (13) and it is possible that the activated keratinocytes may have similar functions. It is also conceivable that the CD36 expression could have a modulatory influence on cell proliferation or on an inflammatory response. The strong CD36 expression in more chronic inflammatory lesions such as necrobiosis lipoidica and lichen planus might suggest that the expression is influenced by the duration of the inflammation. Our findings do not indicate, however, that expression of CD36 in the upper epidermis is related to the severity of inflammation, as no marked difference in CD36 expression was found between a severe erythematous and indurated psoriatic lesion and an area healed after treatment with anthralin. Nor was the possibility of a relationship between CD36 expression and degree of inflammation strengthened by the findings of CD36 expression just below the granular layer in a patient with ichthyosis and in certain patients with urticaria factitia. The latter would rather favour a trigger effect on vascular elements. That the CD36 expression is located just under the stratum granulosum could also imply that its purpose might be related to the functions of the granular layer.

It has been reported that CD36 antigen has been observed in scattered melanophages of the basal layer 72 hours after UV irradiation (4MED) and in inflammatory disorders such as lupus erythematosus (3,8).

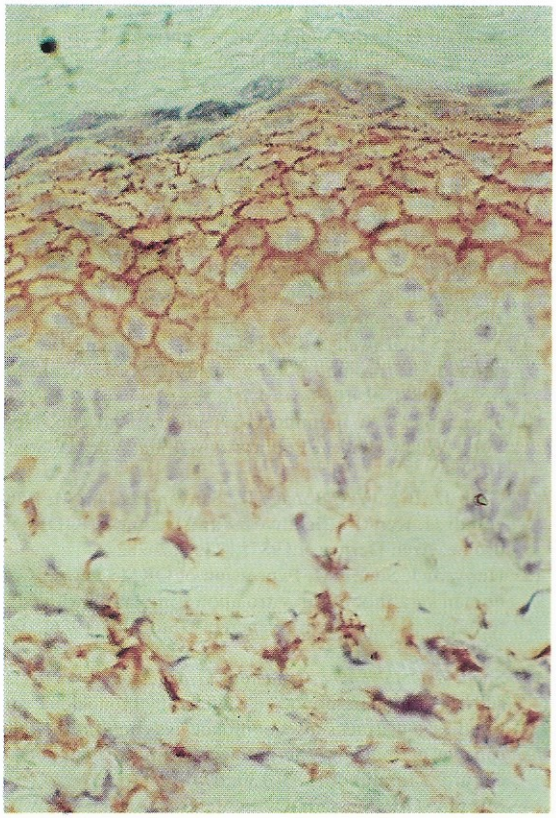

Fig. 1. Expression of CD36 antigen in necrobiosis lipoidica. ×360.

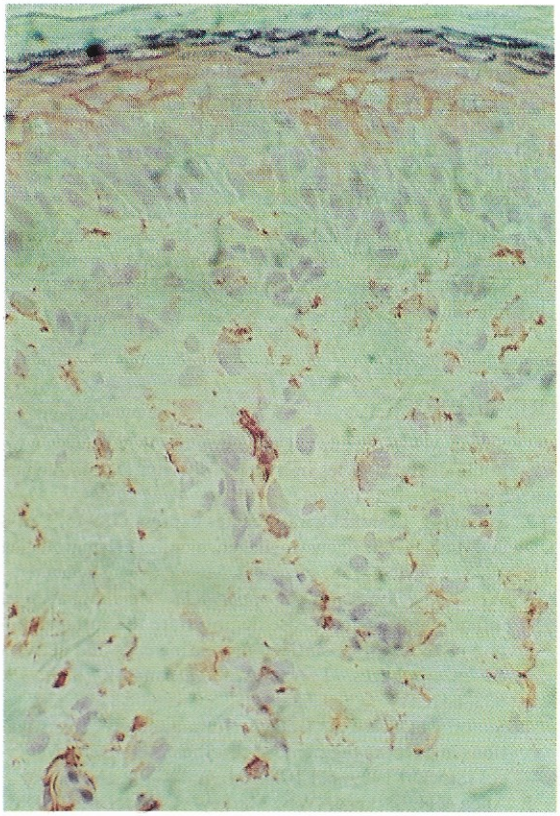

Fig. 3. Expression of CD36 antigen in pityriasis rosea. ×290.

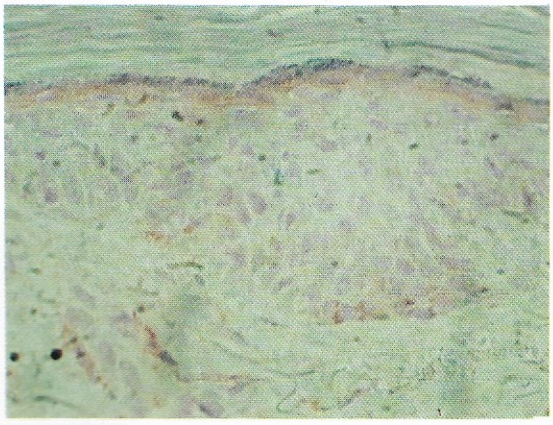

Fig. 2. Expression of CD36 antigen in immediate dermographism. ×310.

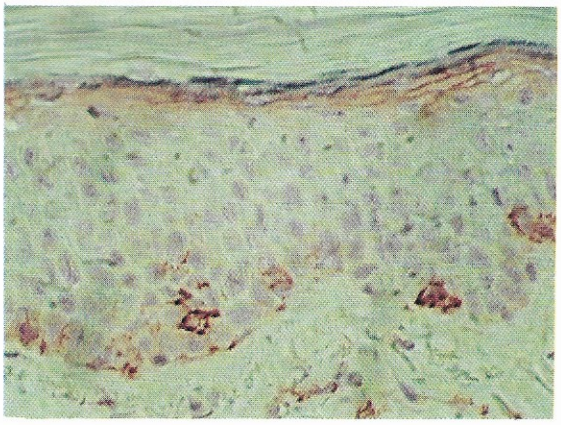

Fig. 4. Expression of CD36 antigen in ichthyosis vulgaris. ×310.

Why a non-UV-irradiated and noninflammatory disorder such as ichthyosis showed similar cells in the basal cell layer is not clear. The dendritic shape of the cells in the basal layer does not rule out the possibility that they are melanocytes. The cells were also seen in the middle of the epidermis in the specimen from the patient with a GVH reaction and might be similar to the phagocytic cells described by Murphy et al. (14),

which migrated into the epidermis and assumed phenotypic characteristics of Langerhans' cells. Some of them, however, seem to be isolated keratinocytes with a cell membrane reacting to CD36.

ACKNOWLEDGEMENTS

The author wishes to thank Mrs Eva Hagforsen for skilful technical assistance. This work was supported by grants from the Swedish Psoriasis Association and the Edvard Welander Foundation.

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