

SHORT REPORTS

Immunological Markers of Langerhans' Cells in Mycosis fungoides Skin Lesions

Ulla Tjernlund

*Department of Dermatology, University Hospital,
Uppsala, Sweden*

Received October 19, 1981

Abstract. The patterns of two immunological markers of epidermal Langerhans' cells were compared in normal skin and mycosis fungoides (MF) skin lesions. A double-staining indirect immunofluorescence method was used. Cells suggestive of keratinocytes reacted with the anti-Ia antibodies in some cases of MF lesions, while no such pattern was seen with the thymocyte-antigen antibodies (OK T6). In other cases of MF, as in normal skin, the epidermal picture was mainly the same with the two markers. A great many of the dermal mononuclear cells in MF were reactive with the anti-Ia antibodies but only occasional dermal cells in MF and no dermal cells in normal skin stained with OK T6.

Key words: Mycosis fungoides; Ia-like antigens; thymocyte (OK T6) antigens

Earlier work in our group has suggested an increase in epidermal cells expressing Ia antigens in some cases of mycosis fungoides (MF) lesions (11, 14). This is an unexpected finding, since Ia antigens in normal epidermis seem to be confined to Langerhans' cells or their precursors (1, 6, 7, 10) and since ultrastructural studies on MF have not indicated a corresponding increase in cells containing Birbeck granules (8). In order to further evaluate epidermal membrane markers in MF, the pattern of anti-Ia reactivity was compared with that seen with another immunological marker for Langerhans' cells, namely OK T6, which is a monoclonal antibody that reacts with most thymocytes, but not with peripheral T cells (5). This antibody has recently been claimed to react also with Birbeck granule containing cells as the only cells within the normal epidermis (4).

MATERIAL AND METHODS

The presence of cells expressing Ia antigens and thymocyte antigens was investigated by an indirect immunofluorescence method (IIF) on thin sections of frozen biopsies from normal skin and 4 cases of MF. The sections were double-stained with immunosorbent-purified rabbit-anti-human-Ia antibodies (14) and monoclonal murine anti-human-thymocyte antibodies (OK T6-Ortho) in the first incubation stage, followed by a second incubation with swine-anti-rabbit IgG (DACO) and goat-anti-mouse IgG-F (ab')₂ (Kappel). The tracing antibodies were labelled with green fluorescein-isothiocyanate and red tetramethyl-rhodamine-isothiocyanate respectively. This allowed the identification of both Ia-like antigens and OK T6 antigens on the same sections when the slides were read in a Leitz microscope with incident light and interchangeable filter combinations for the fluorochromes used.

Monoclonal anti-Ia antibodies (OK Ia1, Ortho) were also used in single-stained IIF to assess the specificity of the binding of the rabbit-heteroantibodies. Further specificity tests included replacements of the heteroantibodies with normal rabbit IgG and omission of the primary antibodies.

RESULTS

In normal skin, Ia antigens and OK T6 antigens were found on the same dendritic cells, mainly in the mid-portion of the epidermis (Fig. 1a, b). In one case of normal skin one OK T6-stained cell was observed that did not bind the anti-Ia antibodies. In the dermis of normal skin there were several cells expressing Ia antigens, but no cells reacting with the OK T6 antibodies (Fig. 1a, b).

In 2 patients with MF (stage II) scattered dendritic epidermal cells were seen, that expressed both Ia- and thymocyte antigens. Only occasionally in these 2 patients was an epidermal cell seen that expressed only one of the markers. In the other 2 patients (stage III and erythroderma MF) an epidermal intercellular anti-Ia reactivity was seen, with both the rabbit- and monoclonal anti-Ia antibodies (Fig. 1c). OK T6, however, in these cases as in the other two, only stained epidermal dendritic cells (Fig. 1d).

In the dermis of all MF lesions a majority of mononuclear cells stained with the anti-Ia antibodies but only occasional cells reacted with the OK T6 antibodies. The controls were negative.

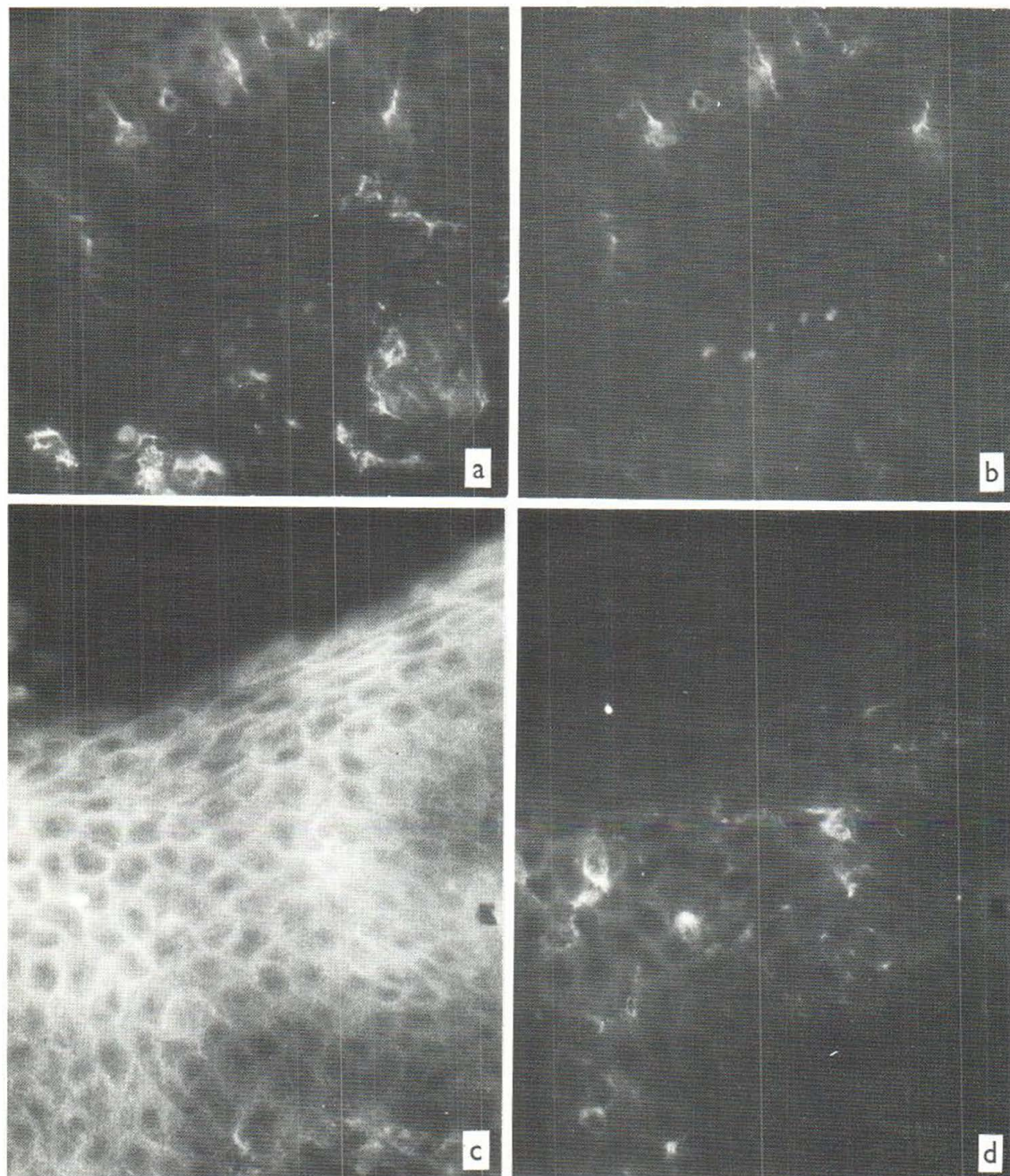


Fig. 1. Immunofluorescence microscopy of thin sections of skin biopsies after indirect double-staining with immunosorbent-purified anti-Ia antigen antibodies and monoclonal anti-thymocyte antigen antibodies (OK T6) $\times 320$. (*a*) Dendritic cells in the epidermis and dermis

expressing Ia-like antigens in normal human skin. (*b*) Epidermal (but no dermal) cells, stained with OK T6 in the same section as in (*a*). (*c*) Epidermal intercellular anti-Ia staining in mycosis fungoides (stage III). (*d*) OK T6 reactivity in the same mycosis fungoides section as in (*c*).

DISCUSSION

This study showed that in the normal epidermis, in contrast to the dermis, Ia- and OK T6 antigens are expressed mainly by the same dendritic cells. It also showed that in those MF lesions where no epidermal dendritic cells expressing Ia antigens could be detected, OK T6 antibody reactive dendritic cells were still unaffected. One possible explanation for the epidermal intercellular Ia pattern seen in these patients and in other MF cases described before (11, 14) could be that Ia antigens are shedded from Langerhans or other dendritic cells as a part of the disease process. Otherwise the Ia antigens could be shedded from activated T lymphocytes deposited in the skin, since an increased number of anti-Ia-reactive circulating T cells have been noticed in many patients with MF (14).

Another possibility is that, on certain stimuli, keratinocytes might start to synthesize Ia-like antigens (13). The fact that neither extensive washing of the sections before the incubation of the anti-Ia antibodies nor dilution of the antibodies eventually replaced the intercellular pattern with that of dendritic cells might favor this explanation. So might also the earlier findings in single epidermal cell suspensions of Ia-like antigens on cells suggestive of keratinocytes (14).

Besides, in some cases MF (11, 14), we have earlier observed the epidermal intercellular Ia pattern also in acute lichen planus (12), while others have noted anti-Ia-reactive keratinocytes in graft-versus-host disease (2, 3) in the rat. Interestingly, lichen planus-like lesions indistinguishable from the idiopathic form can be seen as the skin manifestations of graft-versus-host disease in man (9).

ACKNOWLEDGEMENTS

Lars Klareskog is thanked for immunosorbent-purified anti-Ia antibodies, Eva Hagforsen for technical assistance and Susanne Gebre-Medhin for typing the manuscript.

This work was supported by grants from the Swedish Medical Research Council (No. B81-12X-00769-16) and the Welander Foundation.

REFERENCES

1. Klareskog, L., Tjernlund, U. M., Forsum, U. & Peterson, P. A.: Epidermal Langerhans' cells express Ia antigens. *Nature* 268: 248, 1977.
2. Lampert, I. A., Suitters, A. J. & Chisholm, P. M.: Expression of Ia antigen on epidermal keratinocytes in graft-versus-host disease. *Nature* 293: 149, 1981.

3. Mason, D. W., Dallman, M. & Barclay, A. N.: Graft-versus-host disease induces expression of Ia antigens in rat epidermal cells and gut epithelium. *Nature* 293: 150, 1981.
4. Murphy, G. F., Bhan, A. K., Sato, S., Mihm, M. C. & Harriest, T. I.: A new immunological marker for human Langerhans' cells. *N Engl J Med* 304: 791, 1981.
5. Reinherz, E. L. & Schlossman, S. F.: Regulation of the immune response-inducer and suppressor T-lymphocyte subsets in human beings. *N Engl J Med* 303: 370, 1980.
6. Rowden, G., Lewis, M. G. & Sullivan, A. K.: Ia antigen expression on human epidermal Langerhans' cells. *Nature* 268: 247, 1977.
7. Rowden, G., Phillips, T. M. & Lewis, M. G.: Ia antigens on indeterminate cells of the epidermis. *Br J Dermatol* 100: 531, 1979.
8. Rowden, G., Phillips, T. M., Lewis, M. G. & Wilkinson, R. D.: Target role of Langerhans' cells in mycosis fungoides. Transmission and immunoelectron microscopic studies. *J Cut Pathol* 6: 364, 1979.
9. Saurat, J. H., Didier-Jean, L., Gluckman, E. & Busse, A.: Graft-versus-host reaction and lichen planus-like eruptions in man. *Br J Dermatol* 92: 591, 1975.
10. Stingl, G., Katz, S. I., Abelson, L. D. & Mann, D. L.: Immunofluorescent detection of human B cell alloantigens in S-Ig-positive lymphocytes and epidermal Langerhans' cells. *J Immunol* 120: 661, 1978.
11. Tjernlund, U. M.: Epidermal expression of HLA-DR antigens in mycosis fungoides. *Arch Dermatol Res* 261: 81, 1978.
12. — Ia-like antigens in lichen planus. *Acta Dermatovener (Stockholm)* 60: 309, 1980.
13. — Beta-2 microglobulin and Ia antigens in normal and pathological skin. *Acta Dermatovener (Stockholm)* 61: Suppl. 94, 1981.
14. Tjernlund, U. M., Scheynius, A., Kabelitz, D. & Klareskog, L.: Anti-Ia-reactive cells in mycosis fungoides: A study of skin biopsies, single epidermal cells and circulating T lymphocytes. *Acta Dermatovener (Stockholm)* 61: 291, 1981.

Thiol Levels in Normal and Psoriatic Corneocytes

P. D. Mier and Helga van Rennes

*Department of Dermatology,
University of Nijmegen, 6524 MJ Nijmegen,
The Netherlands*

Received November 3, 1981

Abstract. A technique is described for obtaining small samples of corneocytes suitable for chemical analysis. Thiol and protein levels have been measured in water- and detergent-extracts of corneocytes from healthy controls,