Virchows Archiv A Pathol Anat (1991) 418:311–314

Virchows Archiv A
Pathological Anatomy and Histopathology

Dermal dendrocytes and photochemotherapy

G.E. Piérard, A. Nikkels, J. Arrese Estrada, T. Ben Mosbah, and C. Piérard-Franchimont

Department of Dermatopathology, University of Liège, Liège, Belgium

Received September 14, 1990 / Accepted Novemberr 20, 1990

Summary. We studied the fate of dermal dendrocytes in patients treated with psoralens and ultraviolet light by combining immunohistochemistry and computerized image analysis. Factor-XIIIa-positive dermal dendrocytes were found to be altered in these patients. When compared with controls, dermal dendrocytes were often increased in number and had an uneven size and tissue distribution. Their cytoplasm was occasionally fragmented. These changes were more pronounced when early photosclerosis was present. The alterations described probably reflect vascular changes, and may be responsible for immunomodulating actions and disorder of the connective tissue structure induced by ultraviolet light.

Key words: Dendrocyte – Factor XIIIa – Photosclerosis – Skin – Ultraviolet light

Introduction

The term dendrocyte refers to dermal cells that are stellate or dendritic and share some cytochemical and immunohistochemical characteristics in common with cells of the mononuclear-macrophage system (Headington 1986; Arrese Estrada et al. 1989; Cerio et al. 1989, 1990; Headington and Cerio 1990). Dermal dendrocytes are conveniently revealed by antibodies to factor XIIIa (Nemes and Thomazy 1988; Cerio et al. 1988, 1989, 1990; Arrese Estrada et al. 1989; Arrese Estrada and Piérard 1990; Penneys 1990; Piérard-Franchimont et al. 1990). They represent over 80% of the cell population located in the adventitial dermis and are, to a lesser extent, dispersed in the reticular dermis. Their nature and relationship with other dendritic cells have been extensively reviewed by Headington and Cerio (1990).

Many of these cells abut onto vessels and could be considered as a component of the intrinsic cell population of the microvasculature (Arrese Estrada and Piérard 1990; Cerio et al. 1990; Penneys 1990). They display phagocytic functions (Arrese Estrada et al. 1989; Cerio et al. 1990) may act as an antigen presenting cell (Cerio et al. 1989; Headington and Cerio 1990) and could also be involved in regulatory mechanisms of deposition of extracellular macromolecules in the dermis (Piérard et al. 1990).

Photochemotherapy (PUVA), combines administration of psoralens (P) and exposure to ultraviolet A light (UVA). It is known to alter vessels and to induce deposition of collagen in the superficial dermis (Piérard and Ackerman 1979; Piérard et al. 1981), a change described as PUVA-induced photosclerosis (Piérard et al. 1981). This is defined by the presence of a sclerotic band (with rare residual cells) underlying the epidermis, in the absence of solar elastosis (Hashimoto et al. 1978; Piérard and Ackerman 1979; Ingraham et al. 1981; Niemi and Kanerva 1981; Piérard et al. 1981, 1983; Thurlimann and Harms 1982).

We have studied the fate of dermal dendrocytes in PUVA-treated patients who received more than 1,500 J/cm^2 of UVA radiation.

Materials and methods

Biopsies were taken from the shoulders of 18 psoriatic patients treated with PUVA for at least 6 years, and from 8 age- and phototype-matched psoriatic patients who never received PUVA therapy (Table 1). No biopsy site had been involved by psoriatic plaques, and none had been treated topically for the past 6 months.

Histological sections were stained with haemalum-eosin and periodic acid-Schiff in order to visualize the presence of photosclerosis.

Sections 5 μm thick were dewaxed in xylene, hydrated in graded alcohols and preincubated with 0.05% pronase E (protease XXV, Sigma, St. Louis, Mo., USA). Endogenous peroxidase was blocked with 3% hydrogen peroxide in methanol for 5 min at room temperature. The peroxidase antiperoxidase technique was used with factor XIIIa rabbit polyclonal antibody (Behringwerke, Marburg, FRG) at a dilution of 1:300 for 30 min. The 3-amino-9-ethylcarbazole was used as chromogen. In order to evaluate the presence

Offprint requests to: G.E. Piérard, Department of Dermatopathology, CHU du Sart Tilman, B-4000 Liège, Belgium

Table 1. Characteristics of patients

	PUVA treated	Controls
Age (years)		
range	29–69	36–64
mean	50.3±10.7	50.7±10.2
Phototype		
II	8	3
III	8	4
IV	2	1
UVA J/cm^2		
range	1,561–11,328	0
mean	2,913±2,359	0
Photosclerosis		
absent	10	8
<50 μm	4	0
>50 μm	4	0

of other cells of the monocyte-macrophage lineage, selected serial sections were immunolabelled for S100 protein (Dakopatts, Copenhagen, Denmark) and L1 antigen (Mac 387, Prosan, Gent, Belgium) using the aforementioned technique.

Sections were examined by optical microscopy and the papillary dermis was studied by computerized image analysis (MOP Videoplan Kontron, Eching, FRG). We considered the number of nuclei of factor-XIIIa-positive dermal dendrocytes in a 150-μm-thick band of the superficial dermis. We measured the mean area and the total area covered by the cytoplasm of all factor-XIIIa-positive dermal dendrocytes. We also evaluated the mean thickness of photosclerosis from the epidermal basement membrane to above the superficial vascular plexus by dividing its area by the length of the sections. All morphometric data were expressed per millimetre length of the sections, and were evaluated on statistical grounds by the Kolmogoroff-Smirnow test.

Results

In the superfical dermis of PUVA-treated patients and our controls, we found factor-XIIIa-positive dendrocytes. These cells were negative for S100 protein and for the L1 antigen.

Modifications were found in the factor-XIIIa-positive dermal dendrocytes of PUVA-treated patients with or without photosclerosis (Fig. 1). When compared with controls, they appeared plump, their dendrites were sometimes fragmented (Figs. 2, 3), their distribution in the adventitial dermis was uneven, and their number was significantly larger (75.3±38.5 vs 42.3±16.6, $P<0.05$). These changes were more prominent beneath early photosclerosis (thickness <50 μm), except for the number of dendrocytes. This was not significantly different when we compared PUVA-treated skin with and without early photosclerosis. When photosclerosis was thicker than 50 μm, the density of dendrocytes was markedly reduced (17.7±5.9).

In PUVA-treated patients, image analysis revealed an inverse relationship between the number of dendrocytes and the mean size of dermal dendrocytes (Fig. 4). Conversely there was a positive relationship between the number of dendrocytes and the total area covered by their cytoplasm (Fig. 5). Such correlations were not seen in controls. No correlation was found between the morphometric data and age, phototype and amount of UVA.

In 3 PUVA-treated patients we saw factor XIIIa-positive dendritic cells present focally in the epidermis (Fig. 6). These cells were S100 protein and Mac 387 negative.

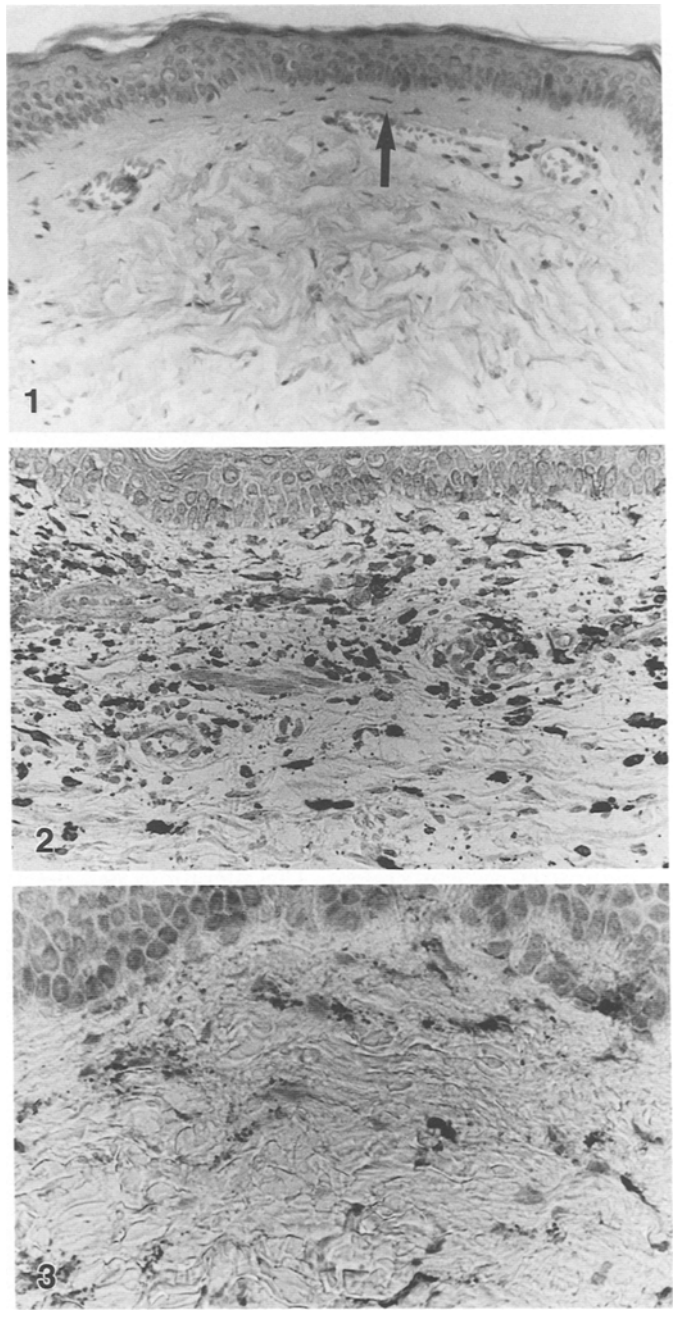

Fig. 1. Photosclerosis defined by the presence of a sclerotic band underlying the epidermis in absence of solar elastosis

Fig. 2. Presence of numerous plump factor-XIIIa-positive dendrocytes. Some of them present fragmentation of their dendrites (dendrocytoclasia)

Fig. 3. Prominent dendrocytoclasia focally present in the superficial dermis

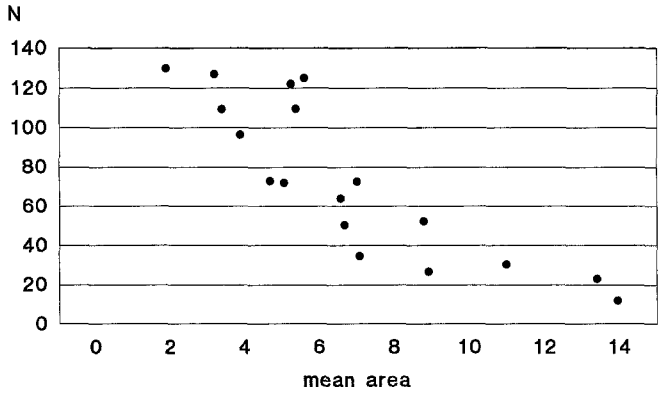

Fig. 4. Inverse relationship between the number of dendrocytes per 0.2 mm^2 papillary dermis (N) and their mean area (μm^2)

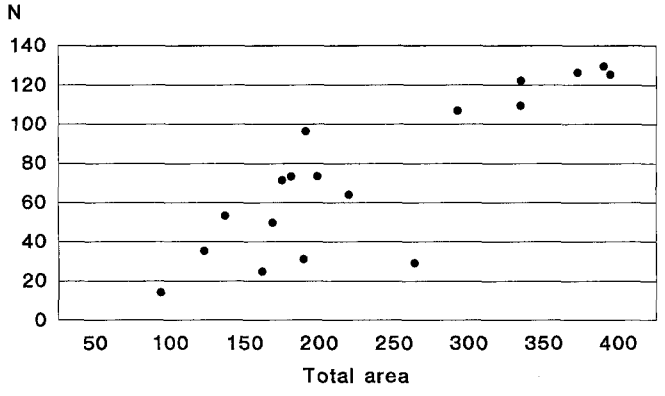

Fig. 5. Positive relationship between the number of dendrocytes per 0.2 mm^2 papillary dermis (N) and the total area (μm^2) covered by their cytoplasms

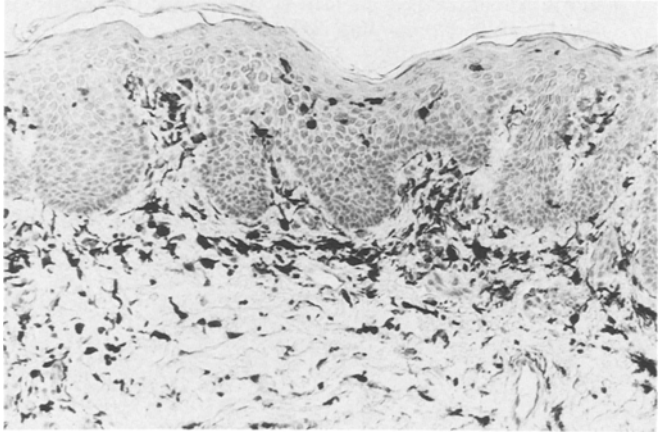

Fig. 6. Presence of intraepidermal factor-XIIIa-positive dendrocytic cells in association with numerous dermal dendrocytes

Discussion

The number and cytological appearance of dendrocytes appear to be under the influence of light, as shown in photoageing with solar elastosis (Piérard-Franchimont et al., in press) and in patients submitted to bath-PUVA therapy (Piérard-Franchimont et al. 1990). Our present findings agree with this concept and suggest that long-term PUVA therapy induces an uneven distribution of dermal dendrocytes with their disappearance in some foci, while they increase in number and size at other sites. These features may be compared to the mottled clinical and histological aspect of the skin of PUVA-treated patients (Piérard and Piérard-Franchimont 1984).

"Dendrocytoclasia" defined as a fragmentation (apoptosis) of the factor-XIIIa-positive cytoplasm of dendrocytes is, in our experience, a feature shared by patients under PUVA treatment and those with cutaneous necrotizing vasculitis (Arrese Estrada et al., in press). These alterations are easily distinguished from the nuclear fragmentation of neutrophils. As many dendrocytes are cells of the microvasculature (Arrese Estrada and Piérard 1990; Penneys 1990), such dendrocytoclasia could be a further argument suggesting that photochemotherapy alters the superficial vascular plexus.

Theoretical views linking vessels, dendrocytes, fibrosis and sclerosis (Beranek and Masseyeff 1986; Desmet 1986; Nemeth and Penneys 1989; Arrese Estrada and Piérard 1990; Piérard et al. 1990) may be applied to photosclerosis. PUVA therapy could induce an uneven accumulation and hypertrophy of dendrocytes, but in some foci destroys most of these cells. The balance between these events could play a role in the development of photosclerosis.

The presence of $S100^-L1^-$factor $XIII^+$ dendritic cells in the epidermis of a minority of our PUVA-treated patients has already been seen in other inflammatory and light-induced disorders (Cerio et al. 1989; Piérard-Franchimont et al. 1990). They resemble $CD1a^-$ DR^+ $OKM5^+$ dendritic cells appearing in UV-irradiated skin (Shen et al. 1983; Cooper et al. 1984, 1986; Weiss et al. 1988). Whether or not these cells are similar and distinct forms of Langerhans cells ($CD1a^+$ DR^+) remains speculative (Murphy et al. 1986; Cerio et al. 1989; Piérard-Franchimont et al., in press).

In summary, photochemotherapy induces changes in the dendrocyte population of the superficial dermis. These alterations may reflect a stimulatory effect by UVA and occasionally alterations of the microvasculature. Photosclerosis may be the result of the metabolic dysregulation of these cells. As these cells have a putative antigen-presenting function, the effect of photochemotherapy in some immunological disorders could be mediated by them.

Acknowledgements. We are grateful to Mr. S. Pierre and J. Sauvage and to Mrs. F. Delory, A.M. Jordant and N. Veys for their skilful technical assistance.

References

Arrese Estrada J, Piérard GE (1990) Factor XIIIa-positive dendrocytes and the dermal microvascular unit. Dermatologica 180:51–53

Arrese Estrada J, Laso Dosal F, Piérard-Franchimont C, Piérard GE (1989) Heterogeneity in the cell population of the dermis. In: Piérard GE, Piérard-Franchimont C (eds) The dermis –

from biology to diseases. Monographies Dermatopathologiques Liégeoises, Liège, pp 1–12
Arrese Estrada J, Goffin F, Cornil F, Piérard-Franchimont C, Piérard GE (1991) Dendrocytoclasia in Henoch-Schonlein purpura. Acta Derm Venereol (Stockh) (in press)
Beranek JT, Masseyeff R (1986) Hyperplastic capillaries and their possible involvement in the pathogenesis of fibrosis. Histopathology 10:543–546
Cerio R, Spaull JR, Wilson Jones E (1988) Identification of factor XIIIa in cutaneous tissue. Histopathology 13:362–363
Cerio R, Griffiths CEM, Cooper KD, Nickoloff BJ, Headington JT (1989) Characterization of factor XIIIa positive dermal dendritic cells in normal and inflamed skin. Br J Dermatol 121:421–433
Cerio R, Spaull J, Oliver GF, Wilson Jones E (1990) A study of factor XIIIa and Mac 387 immunolabeling in normal and pathological skin. Am J Dermatopathol 12:221–233
Cooper KD, Fox P, Neises G, Katz SI (1984) Effects of ultraviolet radiation on human epidermal cell alloantigen presentation: initial depression of Langerhans cell-dependent function is followed by appearance of $T6^-$ DR^+ cell which enhance epidermal alloantigen presentation. J Immunol 134:129–137
Cooper KD, Neises GR, Katz SI (1986) Antigen-presenting $OKM5^+$ melanophages appear in human epidermis after ultraviolet radiation. J Invest Dermatol 86:363–370
Desmet VJ (1986) Hyperplastic capillaries and their possible involvement in the pathogenesis of fibrosis. Histopathology 10:549–551
Hashimoto K, Kohda H, Kumakiri M, Blender SL, Willis I (1978) Psoralens UVA treated psoriatic lesions. Arch Dermatol 114:711–722
Headington JT (1986) The dermal dendrocyte. In: Callen JP, Dahl MV, Golitz LE, Rassmussen JE, Stegmen SJ (eds) Advances in dermatology. Year Book Medical, Chicago, pp 159–171
Headington JT, Cerio R (1990) Dendritic cells and the dermis in 1990. Am J Dermatopathol 12:217–220
Ingraham D, Bergfeld W, Bailin P, Steck W, Taylor J, Tomecki K (1981) Histopathologic changes after PUVA and after discontinuance of PUVA therapy. In: Farber EM, Cox AJ (eds) Psoriasis. Proceedings of the 3rd International Symposium. Grune and Stratton, New York, pp 457–458
Murphy GF, Messadi D, Fonferko E, Hancock WW (1986) Phenotypic transformation of macrophages to Langerhans cells in the skin. Am J Pathol 123:401–406
Nemes Z, Thomazy V (1988) Factor XIIIa and the classic histiocytic markers in malignant fibrous histiocytoma: a comparative immunohistochemical study. Hum Pathol 19:822–829
Nemeth AJ, Penneys NS (1989) Factor XIIIa is expressed by fibroblasts in fibrovascular tumours. J Cut Pathol 16:266–270
Niemi KM, Kanerva L (1981) Electron microscopic observations on photosclerosis of papillary dermis induced by long term PUVA therapy. J Cutan Pathol 8:131–132
Penneys NS (1990) Factor XIII expression in the skin: observations and a hypothesis. J Am Acad Dermatol 22:484–488
Piérard GE, Ackerman AB (1979) Histopathology of remodelling induced by PUVA in the superficial dermis. Br J Dermatol 100:251–256
Piérard GE, Piérard-Franchimont C (1984) Xerodermoid induced by photochemotherapy. Am J Dermatopathol 6:397–410
Piérard GE, Franchimont C, Brassinne M de la, Lapière CM (1981) Photosclerosis induced by long wave length ultraviolet light and psoralens. In: Marks R, Payne P (eds) Bioengineering and the skin. MTP Press, Lancaster, pp 71–78
Piérard GE, Piérard-Franchimont C, Lapière CM (1983) Alteration des loci minoris resistentiae du derme dans la photosclérose. Dermatologica 167:121–126
Piérard GE, Arrese Estrada J, Piérard-Franchimont C, Deleixhe-Mauhin F (1990) Is there a link between dendrocytes, fibrosis and sclerosis? Dermatologica 181:264–265
Piérard-Franchimont C, Nickels-Read D, Ben Mosbah T, Arrese Estrada J, Piérard GE (1990) Early dermatopathological signs during bath-PUVA therapy. J Pathol 161:227–231
Piérard-Franchimont C, Arrese Estrada J, Nikkels A, Deleixhe-Mauhin F, Piérard GE (1991) Dendrocytes et cellules dendritiques épidermiques au cours du photovieillissement. Ann Dermatol Venereol (in press)
Shen HH, Talle MA, Goldstein G, Chess L (1983) Functional subsets of human monocytes defined by monoclonal antibodies: a distinct subset of monocytes contains the cells capable of inducing the autologous mixed lymphocyte culture. J Immunol 130:698–705
Thurlimann W, Harms M (1982) Sklerodermiforme Veränderungen nach PUVA Therapie bei Vitiligo. Dermatologica 164:305–313
Weiss JS, James WD, Cooper KD (1988) Melanophages in inflammatory skin diseases demonstrate the surface phenotype of OKM5+ antigen presenting cells and activated macrophages. J Am Acad Dermatol 19:633–641