The Pathogenesis of Hypopigmented Psoriasis: Ultrastructural Study of Melanocytes in Psoriatic Lesions.

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Abstract :

Skin biopsies from the psoriatic plaques of four patients were examined by transmission electron microscopy. The well-known characteristics of psoriasis were seen, including widened intercellular spaces, hyperactive keratinocytes, a decrease in tonofilaments and kerato-hyaline granules, and basal keratinocyte herniations through a multi-laminated basal layer. Another conspicuous ultrastructural feature is the presence of few small degenerated melanocytes. This study revealed not only increased epidermal turnover but also melanocytes degeneration might be the possible causes of hypopigmentation after the resolution of psoriatic plaques.

Introduction:

A number of inflammatory dermatoses, including psoriasis, may be associated with, or on resolution may leave, hypopigmented macules corresponding to the cutaneous sites of involvement [1].

The ultrastructure of psoriasis is not entirely clear although the main characteristics have been described by several authors [2,3,4].

Melanocytes are the pigment-producing cells of the skin that reside in the basal layer of the epidermis. They are dendritic cells and their cytoplasm contains specific organelles (melanosomes) in which the melanin pigment is deposited. As the melanosomes mature and acquire melanin they migrate from a perinuclear location into the dendrites, the tips of which are then phagocytozed by the surrounding keratinocytes. This transfer of pigment from a melanocyte to a keratinocyte is necessary for normal skin pigmentation [5].

The aim of this study was to evaluate the electron microscopic structure of the psoriatic lesions with special regard to the melanocyte ultrastructure which might show changes explaining the hypopigmentation seen in resolving psoriatic lesions.

Patients and Methods:

Patients:

Four male patients of skin type IV, aged 19-37 years, with chronic plaque psoriasis were studied. Each patient had active psoriatic lesions and a few hypopigmented patches. None were receiving treatment at the time nor had they received any for at least six months prior to the evaluation. Previous treatments had included emollients, tar, salicylic acid and topical steroid preparations. Occasionally, hypopigmentation occurred during clinical remission following topical therapy, in these patients.

Methods:

Having obtained informed consent, biopsies (6 mm punch biopsy) were taken from the psoriatic lesions under local anesthesia. The material was divided and one portion was fixed in 10% neutral formalin for routine histological processing and haematoxylin and eosin staining in order to confirm the diagnosis.

The other portion was fixed immediately in 3% cold glutaraldehyde in cacodylate buffer at pH 7.4 and then fixed for two hours in 1% osmium tetraoxide. The specimen was then dehydrated in ascending grades of alcohol and propylene oxide before embedded in Epon 812. Semi-thin sections were stained with 1% toluidine blue, ultrathin sections were cut with a LKB ultramicrotome, mounted on copper grids, stained with uranyl acetate (20 minutes) and lead citrate (3 minutes) [6,7]. The sections were examined with a Philips 400 transmission electron microscope.

Results :

Light microscopy:

The epidermal histological picture showed acanthosis with regular elongation of the rete ridges with clubbing in their lower portions, a diminished granular layer, thinning of the supra-papillary epidermis, confluent parakeratosis and the presence of Munro microabscesses. In the dermis, there were dilated tortuous capillaries, a mild inflammatory infiltrate (mainly lymphocytes) in the upper dermis and elongation and edema of the dermal papillae.

Electron Microscopy :

a) Epidermis

There was replication or multilamination of the basement membrane with the basal keratinocytes showing herniations of cytoplasmic processes through gaps in the basal lamina. The intercellular spaces were widened and contained a granular substance with marked separation of the basal keratinocytes. Melanocytes were few and showed signs of degeneration. Their cytoplasm contained multiple vacuoles of variable size and shape. Vacuolated mitochondria with loss of its crestae were also noted. The scanty rough endoplasmic reticulum was seen with difficulty. The melanocytes had small short narrow dendrites and contained very few melanosomes, most of them small with a lesser degree of melanization. (Fig. 1& 2)

The melanosomes were seen rarely in the cytoplasm of keratinocytes in all the layers of the epidermis. In addition the characteristic ultrastructural features of psoriasis were detected as: widened intercellular spaces, the tonofilaments were thin and markedly decreased in number. The desmosome-tonofilaments complexes were poorly developed. The cytoplasm of the keratinocytes contained a large amount of polysomes and mitochondria and multiple cytoplasmic vacuoles. The keratohyaline granules and keratinosomes were diminished in the keratinocyte in the granular layer. Some active lymphocytes were present in between the keratinocytes of the upper and basal layers(Fig. 3).

b) Dermis

The blood capillaries have a wide lumen. The endothelial cells were swollen, there were multiple gaps and fenestrated bridges between them and their cytoplasm contained multiple vacuoles. Pericyte showed vesiculated cytoplasm. Dermal infiltration, mainly around blood vessels, included lymphocytes and mast cells (Fig. 4).

Discussion :

Psoriasis is a common chronic recurrent disease characterized by dry, well-circumscribed silvery scaling papules and plaques of varing sizes [8]. In some cases a residual post-inflammatory hypopigmentation can be observed after resolution of the psoriatic plaques [1].

Cutaneous hypopigmentation may result from any of several disturbances in the pigmentary system, including decreased number or function of melanocytes, decreased melanization of melanosomes and decreased transfer of melanosomes from melanocytes to keratinocytes [9]. In psoriasis markedly increased epidermal turnover might be responsible for the hypopigmentation due to a decreased phagocytosis of the melanosomes - containing dendrities by the surrounding keratinocytes[10].

Accelerated epidermal transit time and shortened epidermal turnover time in the active psoriatic lesions have both been reported [8,11]. In this study hyperactivity of the keratinocytes was noted by detecting large amounts of polysomes, free ribosomes, mitochondria, prominent endoplasmic reticulum and Golgi area in the cytoplasm of the keratinocytes. The keratohyaline granules were greatly reduced in size and number and the tonofilaments were thin, sparse and arranged in bundles of varying thickness. These findings are in agreement with those of others and correspond to rapid epidermal cell proliferation[2,3,11,12]. The markedly increased epidermal turnover could explain the clinical hypopigmentation as the melanosomes are rarely seen in the cytoplasm of the keratinocytes in all layers of the epidermis.

Another conspicuous feature of our findings was that the melanocytes in the psoriatic lesion were few, small and degenerated. This might explain the hypopigmentation that is seen commonly after the healing of the plaques. Signs of melanocytes degeneration included multiple intracytoplasmic vacuoles of varying size, vacuolated mitochondria, loss of its crestae, small short narrow dendrites, a scanty rough endoplasmic reticulum which was seen with difficulty, and few melanosomes with poor melanization.

Some electron microscopic studies of psoriasis[10,13,14,15] have confirmed the rarity or almost complete absence of melanosomes in all the layers of the epidermis, while others [4,16] have not reported these changes. None have reported melanocyte degeneration.

Our study suggests that rapid epidermal turnover and melanocytes degeneration might be the possible causes of hypopigmentation in resolving psoriatic plaques.

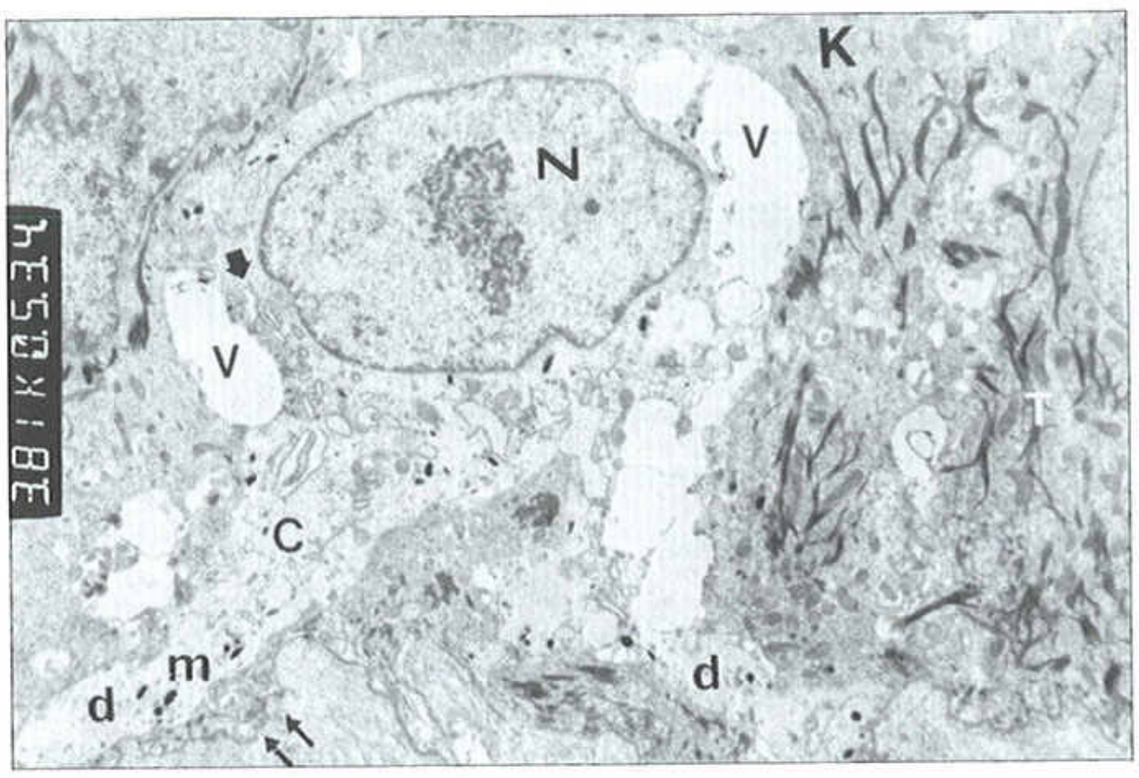

Fig.1: Electron micrograph showing melanocyte with its nucleus (N); degenerated cytoplasm (C); containing multiple vacuoles (V), (d): short dendrites containing few, small melanosomes (m); (T)= tonofilaments present inside the cytoplasm of basal keratinocytes (K), which contain few or no melanosomes. Thick arrow = scanty, inactive rough endoplasmic reticulum; long arrow = multilayed basement membrane zone (x 3.800).

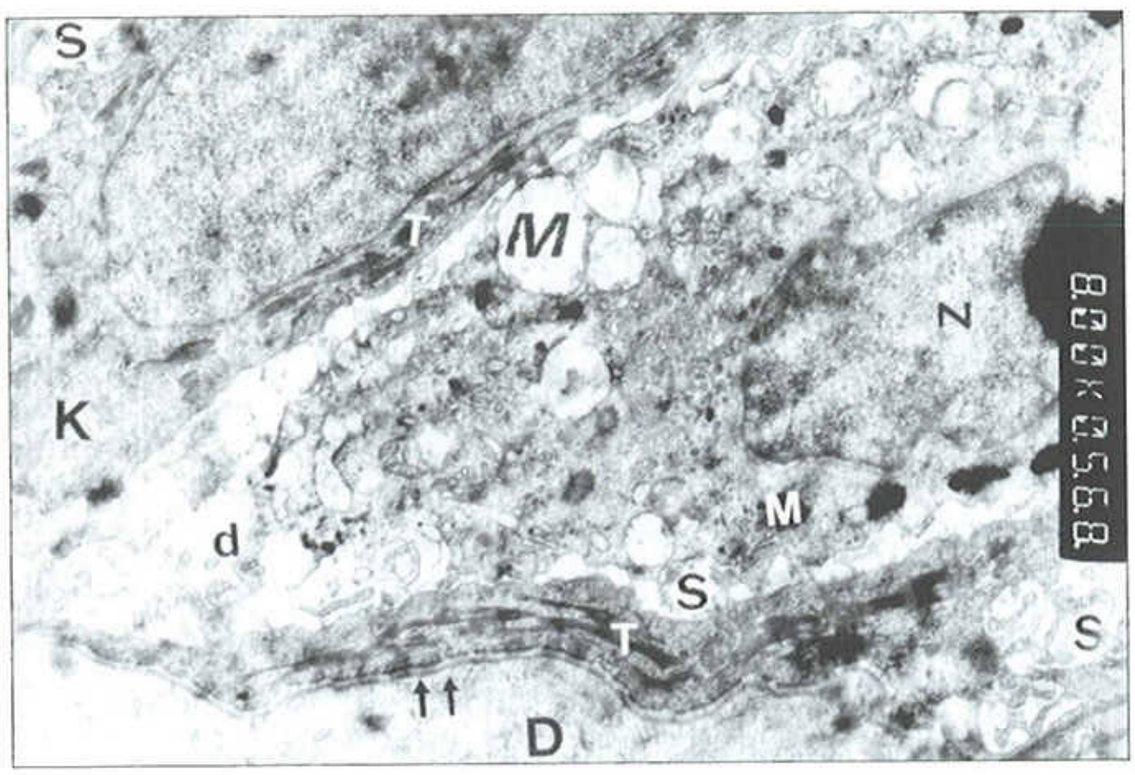

Fig.2: Electron micrograph showing higher magnification for a melanocyte with its nucleus (N); note the vacuolated mitochondria with loss of its cristae (M); The rarity of melanosomes (M) inside, (d) = short narrow dendrites. (K) = basal keratinocytes containing no melanosomes inside its cytoplasm, (T) = tonofilaments; (S) = widened intercellular spaces; arrows = basement membrane zone with some gaps; (D) = Dermis (x 8.000).

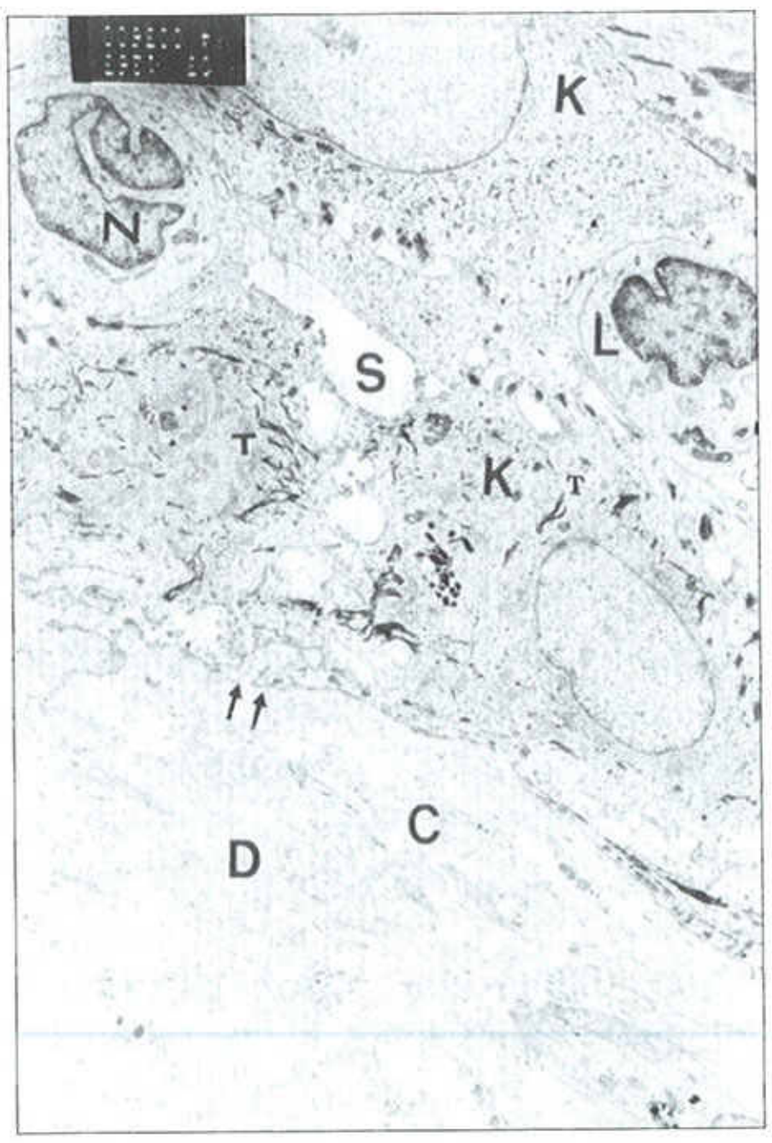

Fig.3: Electron micrograph from the active Psoriatic lesion showing multilayered basement membrane zone (arrows); (K) = Keratinocytes containing scanty small melanosomes; few thin tonofilaments (T) and poor developed desmosomes (d); widened intercellular spaces (S). N= convoluted nucleus of langerhan's cell. L = Lymphocytes in between the lower layers of keratinocytes. Arrows = laminated basement membrane zone, (D) = dermis containing collagen (c) (x 3.600).

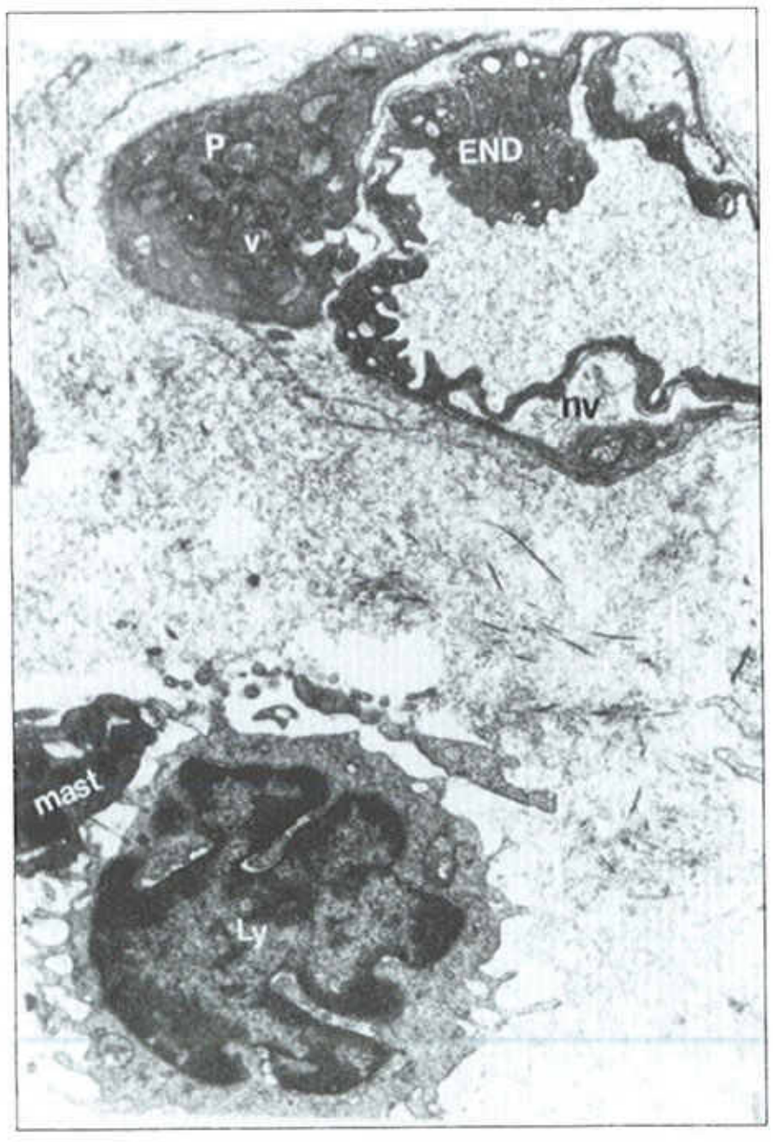

Fig.4: Electron micrograph of psoriatic dermis showing that the blood capillary has a wide lumen(Lu). Endothelial cell (END) showing hypertrophy and pinocytotic vesicles (arrow). Pericyte cell (P) has vesiculated cytoplasm, nerves of vessels (nv). Endothelium gap is present (arrow) and villi muscle (VI). There are perivascular infiltration of lymphocytes (Ly) and part of mast cell (mast). (x. 6.000)

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Oh, oh, oh for an itch

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I have itches that rashes and scratches
and it does at all the wrong place
and at odd times, causing long faces
Dare not I scratch lest it embarasses;
And when I see my dermatologist
who I wish was less of an apologist
over the skin that looks unwell
he chants long latin like a spell;
And when he has it labelled
in a long name got it obscured
looks to him as good as cured
and he is happy and satisfied;
But my itch continues to scratch
I say you: one who can scratch
and scratch when he wants
and scratch where he wants
he is the luckiest of them all !!