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Photofibrosis: A Further Histopathological Change Induced by PUVA Therapy via the Mast Cell in Guttate Psoriasis

Preliminary report

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Twenty-five psoriatic patients were studied histologically before and after PUVA therapy in order to delineate the relationship between dermal mast cells, psoriasis healing process and collagen changes. A number of mast cells were found in the psoriatic lesion both before PUVA and also after PUVA therapy in 22 of the 25 patients. Fibrosis of the papillary dermis and upper reticular dermis was found in 3 cases. Increased collagen deposition and increased numbers of fibroblasts were accompanied by verticalization of ectatic and elongated blood vessels, with an overall pattern of relatively recent scarring. Mast cells were no longer detectable in the fibrosis area. We cannot exclude the possibility that PUVA therapy exerts a further stimulus on mast cell histamine and heparin degranulation in this type of psoriasis, thus leading to dermal fibrosis and blood vessel neogenesis.
Key words: PUVA therapy; dermal changes; mast cell.

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INTRODUCTION

Histopathological changes induced by PUVA therapy in the dermis are characterized by an increased deposition of mucopolysaccharides in the papillary dermis, associated with decreased and fragmented dermal elastic fibres (1). Most of these changes are reversible after PUVA therapy is discontinued (2), although marked ultrastructural changes in the elastic fibres are still found 15 months after PUVA discontinuation (3). Disappearance of the elastic tissue from the papillary dermis and replacement with homogeneous and sclerotic material have been reported in one case after PUVA (4). Collagen is usually reported as not being affected by PUVA therapy. In addition to lymphocytes, the presence of considerable numbers of mast cells characterizes the inflammatory cell infiltrate of psoriasis (5). Mast-cell released mediators may stimulate both endothelial cells (6) and epidermal proliferation (5). The role of the mast cell in wound healing (7) and its relationship with dermal collagen deposition have been demonstrated (8).The aim of this work was to examine the relationship between dermal mast cells, PUVA-induced healing of psoriatic plaques, and possible collagen tissue changes.

MATERIALS AND METHODS

Twenty-five psoriatic patients (17 males, 8 females; mean age 40.3, range 20–72 years) were seen consecutively at the Department of Dermatology of the University of Pavia. 16 had previously been given PUVA therapy (energy dose range 109–4831 J/cm^2; mean energy dose 1247.3 ± 1689.5 J/cm^2). Skin biopsies were performed under local anaesthesia before PUVA therapy on the buttocks, both on psoriatic plaques and on perilesional skin. When no psoriatic lesion was present on the buttocks, biopsies were taken either from the elbow or from the extensor surface of the forearm. A second biopsy was made on the same area after the clearing of the pre-existing plaque, but naturally avoiding the site of the first biopsy. The 9 patients undergoing PUVA therapy for the first time received a mean exposure of 110.75 ± 35.96 J/cm^2 (range 50–160 J/cm^2). All the patients considered had avoided any local or systemic treatment for at least one month before PUVA therapy. They did not suffer from itching and had no self-induced excoriations. Haematoxylin and eosin, Toluidine Blue and Orcein-Giemsa stains were used.

RESULTS

A large number of mast cells were found in the psoriatic lesion in 22 of the 25 patients before PUVA therapy, and this number was not significantly decreased by PUVA. In 90% of the specimens, after regression of the psoriatic lesion, some degree of homogenization of the papillary dermis and a decrease in or fragmentation of the elastic fibres were seen. In 14 of the 25 cases (56%), disoriented and increased, coarse eosinophilic collagen fibres were found in the reticular dermis, with a decreased number of fibroblasts, thus featuring a variable degree of dermal sclerosis. Fibrosis of the upper and reticular dermis was found in 3 cases (Fig. 1). In these cases, epidermal atrophy was accompanied by an increased number of fibroblasts, increased collagen deposition and an increased number of neoformed, vertically oriented blood vessels (Fig. 2). The overall histopathological

Fig. 1. Fibrosis of upper dermis, with increased numbers of fibroblasts, new collagen deposition and neoformed capillaries. H&E, ×160.

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Fig. 2. Fibrosis of dermis, with atrophy of epidermis and compact hyperkeratosis. The overall pattern is that of a scar, with prominent, vertically oriented ectatic blood vessels. Orcein-Giemsa stain, ×40.

pattern was that of a relatively recent scar. In the 3 fibrosis cases, mast cells were no longer detectable in the dermis (Fig. 3).

DISCUSSION

The effects of PUVA therapy on mast cells are controversial. In fact, according to some authors (9, 10), degenerative changes are seen in mast cells of urticaria pigmentosa after PUVA. Some other authors, however, failed to demonstrate any changes in the number and structure of mast cells after PUVA (11). In our case series, the persistence of mast cells suggests that they escape the effects of PUVA therapy, even when the plaque has fully cleared. Persistence of mast cells during clearing of guttate psoriatic lesions after topical steroid therapy and after bath-PUVA therapy have been reported by Töyry et al. (12). In our series too, systemic PUVA therapy did not affect dermal mast cells, but this did occur in the 3 cases in which fibrosis was associated. We could not correlate the fibrosis finding either with clinical phototype, site, age, or with the energy dose given to these 3 patients, but rather with the type of psoriasis, which in all 3 cases was relatively recent and of the guttate and/or small nummular type. An early and constant mast cell degranulation characterizes eruptive guttate psoriasis (13). The type of psoriasis (i.e. guttate psoriasis) may thus be regarded as a main condition in leading to fibrosis after PUVA-induced healing. However, mast cells alone are unlikely to be the only factor in the induction of fibrosis, when it is recalled that some pathological conditions, such as mastocytoma and urticaria pigmentosa, may heal spontaneously without scarring fibrosis. The possibility cannot be ruled out that PUVAtherapy itself is the cause of the fibrotic response through the mast cells in guttate psoriasis (photofibrosis): nor can the possibility be excluded that the histological negativity of the mast cells in the fibrotic area may be attributable to mast cell degranulation and hence to its non-identification with the stains used. Granules may be released by mast cell cytoplasmic pseudopodia and actively taken both by fibroblasts and endothelial cells. This passage of granules (transgranulation) has been demonstrated both in vivo and in vitro (14). The transgranulation from cell to cell of heparin granules stimulates the migration of capillary endothelial cells (15), while the passage of histamine granules activates fibroblasts (16). Both these events are crucial steps in the fibrosing and/or scarring process. Our findings, albeit preliminary, suggest that in guttate psoriasis, a peculiar condition exists in which PUVA can induce a fibrosing response through increased mast cell activation.

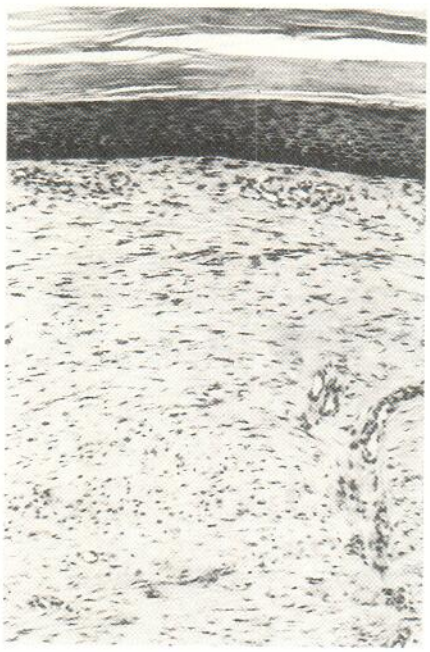

Fig. 3. Fibrosis of upper dermis after PUVA-induced healing of a psoriatic plaque. Absence of elastic tissue, inflammatory cell infiltrate and mast cell are noticeable. Orcein-Giemsa stain, ×160.

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