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MORPHOLOGY OF ATOPIC ECZEMA

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Abstract. Atopic eczema, an inflammatory skin disorder characterized by acute vesicular lesions or chronic lichenified plaques, both accompanied by pruritus, occurs at any period of life in patients with personal or family histories of atopy. Previous histologic studies of atopic eczema using biopsy specimens stained with hematoxylin and eosin or with toluidine blue and ultrastructural studies of infantile eczema are now extended by studies using 1 μm thick sections stained with Giemsa's reagent. These biopsy specimens allow better definition of both normal skin structures and cells involved in the inflammatory response. This precision leads to clearer differentiation of diagnosis between the clinically similar atopic eczema and allergic contact dermatitis.

Key words: Atopic eczema; Mast cell; 1 μm thick sections; Allergic contact dermatitis

Atopic eczema (1) is an inflammatory skin disorder that occurs in patients with a personal and/or family history of atopy as manifested by asthma, allergic rhinitis, and rarely urticaria. Some patients have typical skin lesions without an atopic history. The disorder may begin during infancy, childhood, or adulthood. The acute lesions exhibit erythema, edema, and vesiculation that may lead to oozing. The chronic lesions are recognized as lichenified plaques with prominent skin markings. In older children and adults the lesions are typically localized to the flexural areas, especially the antecubital and popliteal fossae, and may be acute or chronic. Pruritus is the major symptom.

Histologic descriptions (2, 3) of atopic eczema have been based on studies of paraffin-embedded biopsy specimens stained with hematoxylin and eosin or toluidine blue and on ultrastructural studies of infantile eczema (4, 5). Use of 1 μm thick, glutaraldehyde-fixed, Epon-embedded sections (6–8) stained with Giemsa's reagent avoids the sampling problem inherent in electron microscopy and permits better definition of normal skin structures and cells of the inflammatory response than that which can be achieved in routinely processed specimens. This paper summarizes a description of the microscopic alterations which characterize atopic eczema (8) and compares these alterations with those reported in allergic contact dermatitis.

HISTOLOGY OF ATOPIC ECZEMA IN 1 μm SECTIONS

Skin biopsy specimens of the antecubital fossae were taken from individuals with atopic eczema whose ages ranged from 23 to 35 years. Specimens were obtained from acute vesicular lesions, from lichenified plaques, and from apparently normal skin, and processed as described (6–8).

Acute vesicular lesions (Figs. 1 and 2)

Epidermal hyperplasia with focal intercellular edema, vesiculation, and an epidermal infiltrate consisting predominantly of lymphocytes and macrophages were regularly observed. Compaction of erythrocytes in the superficial capillary venule without extravasation was noted. Marked perivenular and slight intervascular infiltrates were observed about the superficial venular plexi and consisted of lymphocytes, activated lymphocytes, and macrophages. Only occasional neutrophils, eosinophils, and basophils were noted; plasma cells were absent. Activated histiocytes were distributed throughout the superficial layers of the dermis and often contained melanin. Mast cells in acute vesicular areas occurred in normal numbers when compared with clinically uninvolved skin or skin from normal control individuals. Although endothelial cells of the superficial venular plexus were enlarged and contained large nuclei with clumped chromatin and prominent nucleoli, necrosis was not present. Vascular basement membrane alterations included edema, reduplication, and in some instances homogeneous thickening. Arterioles were normal.

Lichenified plaques (Figs. 3 and 4)

Hyperkeratosis, psoriasiform hyperplasia, and dyskeratosis of the epidermis were noted with focal areas of intercellular edema and infiltration by lymphocytes. Dermal edema was minimal, although compaction of the superficial capillary venule without red blood cell extravasation was noted. A moderate cellular infiltrate containing predominantly macrophages and lymphocytes was present in both perivenular and intervascular locations. The number of mast cells was significantly increased when compared to clinically un-

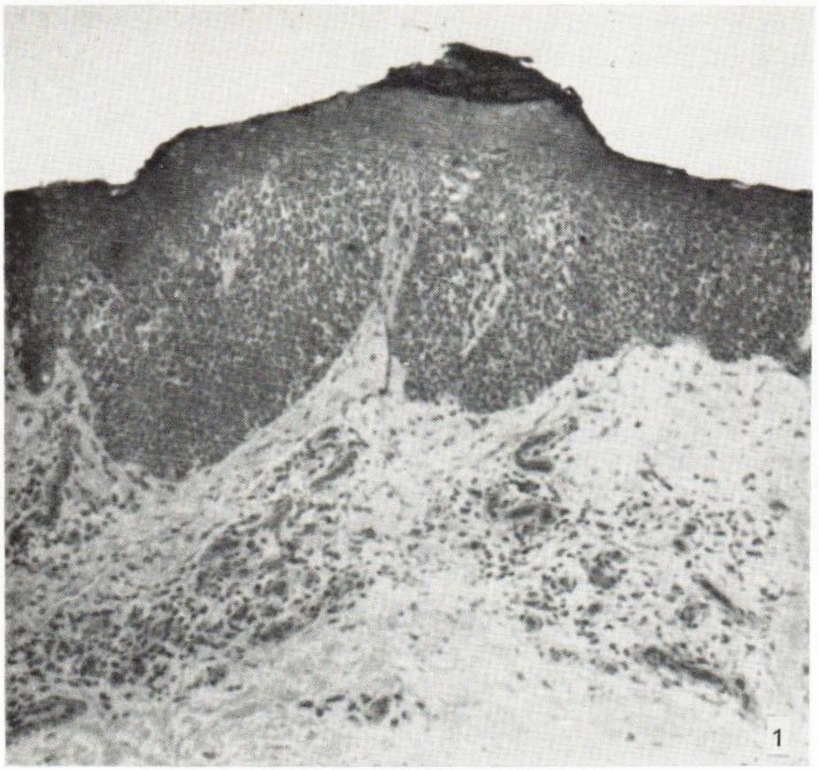
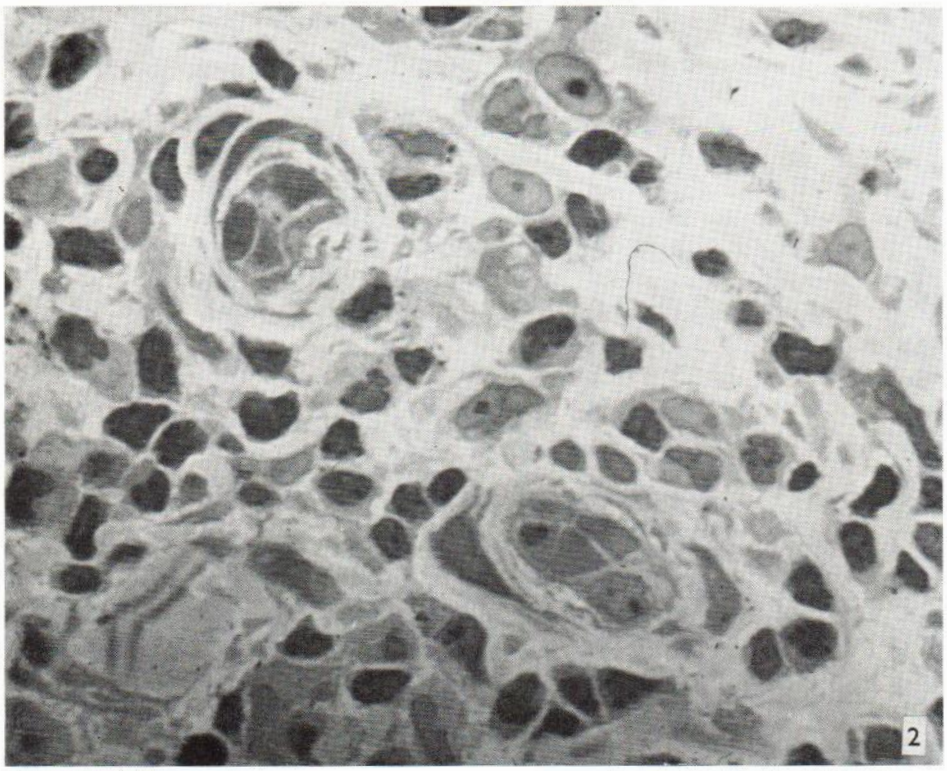
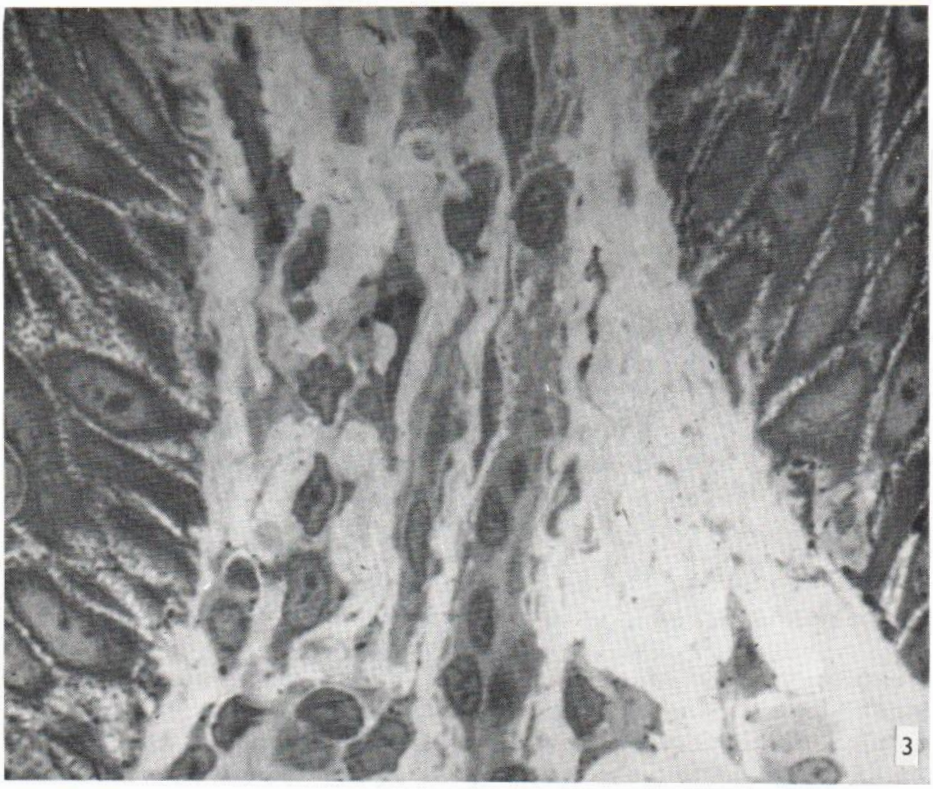


Fig. 1. Acute vesicular lesion with epidermal intercellular edema and a dermal perivenular infiltrate composed predominantly of lymphocytes. Giemsa, ×22.5.

Fig. 2. Acute vesicular lesion with lymphocytes disposed about venules which manifest hypertrophy of the endothelial cells and basement membrane reduplication. Giemsa, ×900.





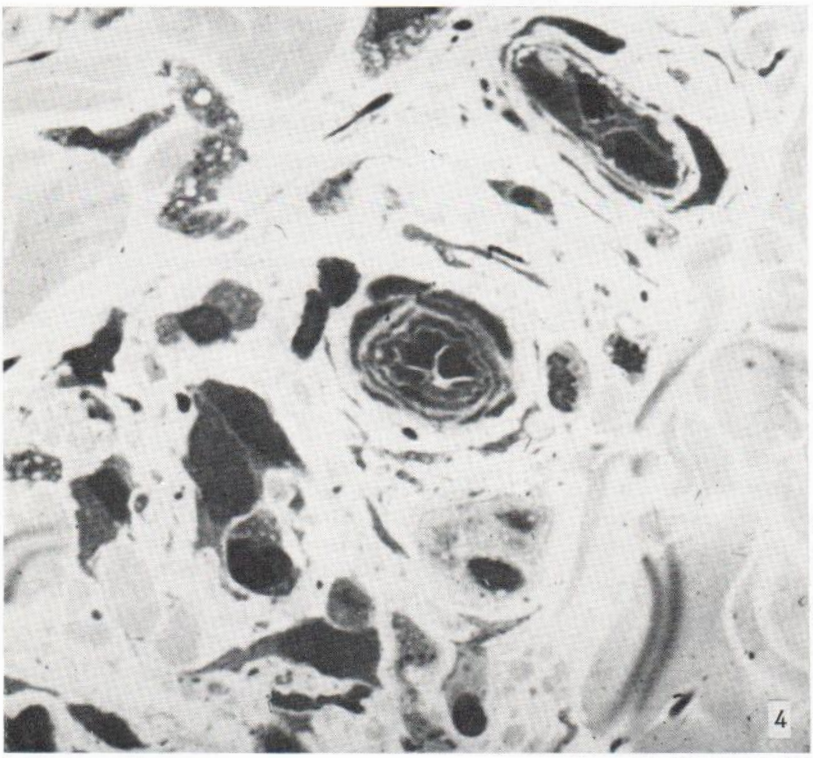


Fig. 3. Chronic lichenified plaque with focal epidermal intercellular edema and sclerosis of the superficial capillary venule. Note numerous macrophages. Giemsa, ×900.

Fig. 4. Chronic lichenified plaque with cutaneous nerve manifesting vacuoles, demyelination, and "ghost-like" remnants of nerve fibers. Note normal arteriole in center of field. Giemsa, ×900.

involved skin, acute lesions, or skin from normal individuals. Activated histiocytes were observed. Alterations of the superficial venular plexus and deeper venules included endothelial cell hypertrophy with enlarged nuclei and prominent nucleoli, basement membrane thickening, and enlarged pericytes. Cutaneous nerves at all levels of the dermis exhibited alterations including apparent demyelination and fibrosis. Occasional vacuolated areas appeared within their fibers.

Clinically normal skin

Traces of hyperkeratosis and epidermal hyperplasia, intercellular edema, and a slight dermal cellular infiltrate consisting primarily of lymphocytes were noted. Alterations occurred in most venules and included endothelial cell enlargement with focal luminal obliteration and prominent nucleoli, basement membrane thickening and/or reduplication, and enlarged pericytes. Sweat glands in all specimens appeared unaltered. Occasionally fibrosis and focal demyelination of cutaneous sensory nerves were noted.

DISCUSSION

Microscopic changes in the epidermis and dermis in atopic eczema vary with the nature of the clinical lesion. One μm thick biopsy sections from vesicular areas exhibited epidermal intercellular edema and a dermal inflammatory infiltrate of lymphocytes and activated lymphocytes disposed mainly about the superficial venular plexi. Venular alterations included endothelial cell hypertrophy with enlarged nuclei and basement membrane reduplication. In lichenified lesions there was epidermal hyperplasia with abnormalities of venules, increased numbers of lymphocytes and macrophages, and alterations in cutaneous nerves. In clinically normal skin abnormalities of the superficial venular plexi and venules similar to those of the lesional sites were observed.

The changes of atopic eczema in the 1 μm thick sections exhibit both similarities to and differences from those observed in allergic contact dermatitis (6). This method is valuable for differentiating between these two clinically similar types of eczematous dermatitis. In allergic contact dermatitis the changes in venules are noted only in relation to perivenular lymphocytic infiltrates, whereas in atopic eczema they occur both without and with a surrounding infiltrate. Allergic contact dermatitis manifests severe epidermal involvement and a dermal infiltrate which, in addition to lymphocytes and activated lymphocytes, exhibits more numerous basophils and eosinophils than are observed in atopic eczema. A striking difference between these reactions is the prominence of interstitial fibrin deposition in contact dermatitis (9) and its absence in atopic eczema. Moreover, the demyelination and fibrotic changes in cutaneous nerves found in lichenified lesions of atopic eczema have not been observed in contact dermatitis.

Previous descriptions of the venules in atopic eczema (3, 4) have been extended in this study by the recognition of endothelial cell hypertrophy, basement membrane reduplication, and homogeneous thickening. The alterations of venules in the absence of an inflammatory infiltrate in clinically normal skin may reflect previous involvement or, alternatively, an underlying vascular disorder.

The increase in absolute numbers of mast cells in lichenified plaques is compatible with the qualitative histologic observations previously made (3). It is also consistent with quantitative determinations of increased levels of tissue histamine in chronic lichenified plaques (10). Moreover, increased numbers of Langerhans' cells were noted in the epidermis of chronic lesions (11).

Cutaneous myelinated nerves from the lichenified lesional sites exhibited apparent demyelination and sclerosis without associated cellular infiltrates. Although the possibility of an ischemic mechanism must be considered, the derangement of neural structures may be related to the trauma to the skin incurred by repetitive scratching due to pruritus.

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DISCUSSION

Rørsman (Lund). Q: Can you differentiate between atopic dermatitis and atopic dermatitis with contact dermatitis in addition?

A: Such studies have not been performed.

Hanifin (Portland). Q: Is there any evidence of mast cell degranulation in acute atopic dermatitis, and have you made counts of mast cells in atopic dermatitis versus acute allergic contact dermatitis.

A: In acute vesicular areas the mast cells appeared variably hypogranulated, while those in lichenified plaques appeared full of granules.

Zachariae (Aarhus). Q: You found very few eosinophils. Would you think this is a marker that mast cell degranulation is not something very significant in atopic dermatitis in the acute stage?

A: No. Mast cells have at least 2 classes of eosinophil chemotactic factors. On the other hand, among lymphokines there are factors which are chemotactic not only for eosinophils but also for neutrophils and basophils, and we don't know what turns these on and off in the regulation.