

Morphology of atopic eczema

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The routine examination of skin biopsy specimens embedded in paraffin and strained with hematoxylin-eosin has failed to allow differentiation of atopic eczema from other types of eczematous dermatitis. The use of 1- μ m plastic-embedded sections permits the recognition of infiltrating cell types and blood vessel alterations, thus allowing a refined method to examine cutaneous lesions and permit better definition of cutaneous structures than can be achieved in routinely-processed specimens.

Acute vesicular lesions exhibited marked epidermal intercellular edema (spongiosis) and a dermal inflammatory infiltrate of lymphocytes, and activated lymphocytes with normal numbers of mast cells that exhibited various degrees of hypogranulation. Only rare eosinophils, neutrophils, and basophils were noted. Venular alterations included endothelial cell hypertrophy without necrosis. In lichenified plaques there was epidermal hyperplasia with a dermal inflammatory infiltrate that included increased numbers of fully granulated mast cells and increased numbers of lymphocytes and monocyte-macrophages. Alterations of venules included marked endothelial cell hypertrophy and basement membrane thickening. Cutaneous nerves exhibited demyelination and fibrosis.

Also, increased numbers of Langerhans' cells have been noted in the epidermis of chronic lesions. Despite the absence of eosinophils, major basic protein has been demonstrated in the dermis by direct immunofluorescence techniques. Studies of lymphocyte subsets have shown increased numbers of CD4 + T lymphocytes.

Atopic eczema (1) is an inflammatory skin disorder that occurs in patients with a personal and/or family history of atopy, although some individuals have typical skin lesions without an atopic history. The acute lesions exhibit erythema, edema, and vesiculation. 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. Pruritus is the cardinal symptom.

Traditional histological descriptions (2-4) of the alterations in atopic eczema have been based on studies of routinely processed, paraffin-embedded biopsy specimens strained with hematoxylin and eosin or toluidine blue, in which it is impossible to distinguish the morphological features of atopic eczema from other forms of eczematous dermatitis. Moreover, ultrastructural studies of infantile eczema (5, 6) have failed to show specific abnormalities. The use of 1- μ m, plastic embedded sections (7-9) avoids the sam-

pling 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. The use of this technique (9, 10) has allowed a description of the changes in the acute and chronic lesional sites of atopic eczema. This paper summarizes the microscopic alterations observed in 1- μ m, plastic-embedded sections which characterize atopic eczema (9).

Histology of atopic eczema in routine specimens

In routine sections the histopathological alterations of atopic eczema are dependent on the types of the gross morphological lesions selected for examination. Acute lesional sites showed intercellular edema (spongiosis) of the epidermis and a dermal inflammatory cell infiltrate consisting of lymphocytes and macrophages with rare eosinophils and neutrophils. Chronic

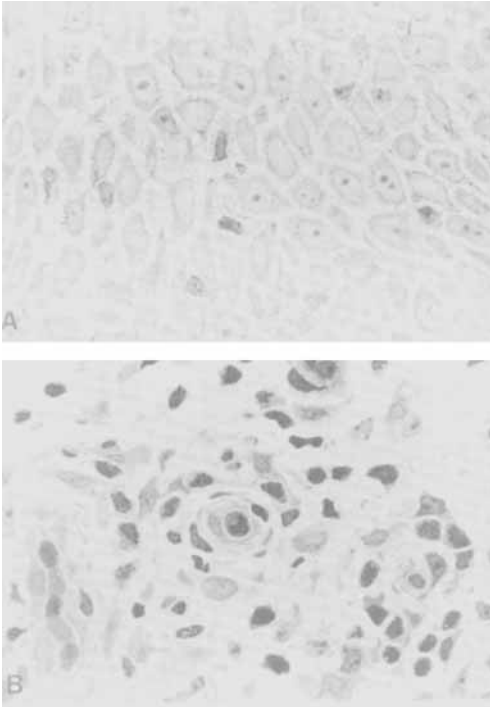


Fig. 1. Acute vesicular lesion. a. Extensive amounts of epidermal intercellular edema. b. Lymphocytes disposed about venules that manifest endothelial cell hypertrophy, basement membrane thickening, and compaction. Giemsa $\times 410$.

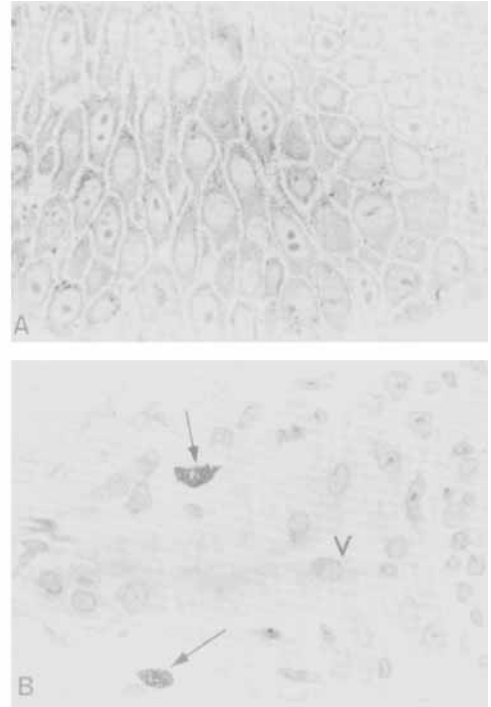


Fig. 2. Chronic lichenified lesion. a. Slight degree of epidermal intercellular edema. b. Venule (V) with extensive endothelial cell enlargement and basement membrane thickening. Infiltrate contains lymphocytes, monocyte-macrophages, and prominent fully-granulated mast cells (arrows)

lesional sites showed epidermal hyperplasia with minimal amounts of spongiosis and a dermal inflammatory cell infiltrate consisting of lymphocytes and monocyte-macrophages.

Histology of atopic eczema in 1- μ m 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 (9).

Acute vesicular lesions (Figs. 1a and b)

Epidermal alterations consisted of extensive degrees of intercellular edema, vesiculation, and

an infiltrate containing predominantly lymphocytes and activated lymphocytes. Compaction of erythrocytes in the superficial capillary venule was noted. Marked perivenular and slight intervascular infiltrates were observed about the superficial venular plexus and consisted of lymphocytes, activated lymphocytes, and macrophages. Only occasional neutrophils, eosinophils, and basophils were noted; plasma cells were absent. Macrophages were distributed throughout the superficial layers of the dermis and often contained melanin. Mast cells were hypogranulated and were present in normal numbers when compared with clinically uninvolved skin or skin from normal control individuals. The endothelial cells of the superficial venular plexus were enlarged and contained large nuclei with clumped chromatin and prominent nucleoli; however, necrosis was not pre-

sent. Vascular basement membrane alterations included reduplication and, in some instances, thickening. The arterioles were normal.

Lichenified plaques (Figs. 2a and b)

Hyperkeratosis and psoriasiform hyperplasia of the epidermis were present with focal areas of intercellular edema. In the dermis, a moderate cellular infiltrate containing predominantly monocyte-macrophages and lymphocytes was present in both perivenular and intervascular locations. Fully granulated mast cells were prominent, and the number of mast cells was significantly increased when compared to clinically uninvolved skin, acute lesions, or skin from normal individuals. 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 the fibers of the nerves.

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 focal endothelial cell enlargement, basement membrane thickening and/or reduplication, and enlarged pericytes. Occasionally, fibrosis and focal demyelination of cutaneous sensory nerves were noted.

Immunopathology

The majority of the dermal lymphocytes are T lymphocytes (10–13). Using monoclonal antibodies, the majority of the infiltrating dermal lymphocytes in both acute and chronic lesions are CD4+ (helper/inducer) T lymphocytes with only a few CD8+ (suppressor/cytotoxic) T lymphocytes. Natural killer cells are absent

(13). In acute lesional sites the epidermal lymphocytes are CD4+ (10). Although eosinophils are infrequently observed (9, 10), the major basic protein derived from the eosinophil granule is deposited in the dermis in the absence of substantial numbers of eosinophils (14). It is of note that the intracutaneous injection of a relevant antigen or of platelet activating factor into atopic skin elicited an infiltrate of eosinophils that does not occur in control subjects (15).

The Langerhans' cell number is increased in chronic lichenified plaques to a greater degree than in acute erythematous lesions (10, 17).

Direct immunofluorescence studies have shown deposited immunoglobulins and complement proteins at the dermoepidermal junction in lesional and uninvolved skin in some instances (17). IgG and C3 are the most frequently deposited proteins, although C1q, C4, C5, factor B and properdin have been detected.

DISCUSSION

The histopathological alterations in the epidermis and dermis in atopic eczema vary with the nature of the clinical lesion. The use of 1- μ m plastic-embedded sections offers the best method for refined histologic study of skin biopsy specimens. 1- μ m biopsy sections from acute 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 cutaneous microvasculature similar to those of the lesional sites were observed.

In acute vesicular lesions the mast cells were normal in number and exhibited various degrees of hypogranulation. The increase in absolute numbers of mast cells in lichenified plaques is compatible with the qualitative histological observations previously made (3). It is also consistent with quantitative determinations of in-

creased levels of tissue histamine in chronic lichenified plaques reported in one study (18) but not confirmed in another (19). Increased numbers of Langerhans' cells were noted in 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 alterations of neural structures may be related to the trauma to the skin due to repetitive scratching.

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