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Mast Cell Invasion of Peripheral Nerve in Skin Lesions of Atopic Dermatitis

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To ascertain whether or not a spatial relationship between mast cells and peripheral nerves is present in skin lesions of atopic dermatitis, 10 biopsy specimens of the skin lesions were examined with both semi-thin and ultrathin serial sections. Mast cell invasion of peripheral nerves was observed in 9 out of the 10 biopsy specimens (4 subacute lesions, 3 lichenified lesions, and 3 prurigo lesions). The mast cells within peripheral nerves often showed degranulation, and the nerve fiber bundle showed conspicuous edema. The degranulation of mast cells within peripheral nerve bundles and edema of the nerve bundle may pay a role in provoking or aggravating itchiness of atopic dermatitis.
Key words: Atopid dermatitis; Mast cell; Peripheral nerve; Pruritus.

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INTRODUCTION

Mast cells are often increased in number in the inflammatory cells in skin lesions of atopic dermatitis (AD) (1–4). Mast cells in skin lesion of AD are known to be distributed in the perivascular area, the perifollicular area, and in the epidermis (1, 5, 6). However, a topographical relationship between mast cells and peripheral nerves in the dermatosis has not been described (1–5).

In the present study, therefore, we tried to ascertain whether or not there is a close spatial relationship of mast cells to peripheral nerve fiber bundles in skin lesions of patients with AD.

MATERIALS AND METHODS

Patients

Ten patients with AD were included in the study. They ranged in age from 15 to 48 years (mean 26 years). The diagnosis was made on the basis of morphological appearance and distribution of skin lesions, the clinical course, and the family history of atopic disease. Thus, they fulfilled the criteria of Hanifin & Rajka for AD (7).

Biopsies

Three-millimeter punch biopsy specimens were taken from 4 subacute lesions, 3 lichenified lesions, and 3 prurigo lesions of AD. The skin lesions examined had not been treated with topical corticosteroids for at least one month prior to the examination.

One μm-thick semi-thin sections

Biopsy specimens were fixed with 3% glutaraldehyde in 0.1 M PBS at pH 7.4. Post-fixation in 1% osmium tetroxide was followed by dehydration and embedding in Epon. In each specimen, 100 serial 1 μm-thick sections were prepared, and stained with toluidine blue.

Ultra-thin sections

For every 20 μm of the semi-thin sections, a few ultra-thin sections were prepared and stained with uranyl acetate and lead citrate, and observed with a Philips CM-12 electron microscope.

RESULTS

Invasion

Invasion of mast cells into cutaneous nerve fiber bundles was observed in 9 out of the 10 skin lesions of AD examined (Table I). Mast cells in nerve fiber bundles were seen more frequently in prurigo lesions than in subacute and lichenified lesions. The mast cells within the nerve fiber bundle often showed degranulation, which was accompanied by conspicuous edema of the nerve fiber bundle. Fig. 1a shows an electron microscopic picture of a prurigo lesion of AD. The nerve fiber bundle is surrounded by the perineurium (arrowheads).

Table I. *Histological findings on mast cells and nerve fiber bundles in 10 patients with atopic dermatitis examined*

Case	Age	Skin lesion	Mast cell invading nerve	Degranulation of mast cell	Edema of the nerve
1	31	Subacute	+	+	+
2	15	Subacute	+	+	+
3	23	Subacute	+	+	+
4	19	Subacute	−	−	−
5	48	Lichenified	+	−	−
6	39	Lichenified	+	+	+
7	22	Lichenified	+	+	+
8	19	Prurigo	+	+	+
9	22	Prurigo	+	+	+
10	26	Prurigo	+	+	+

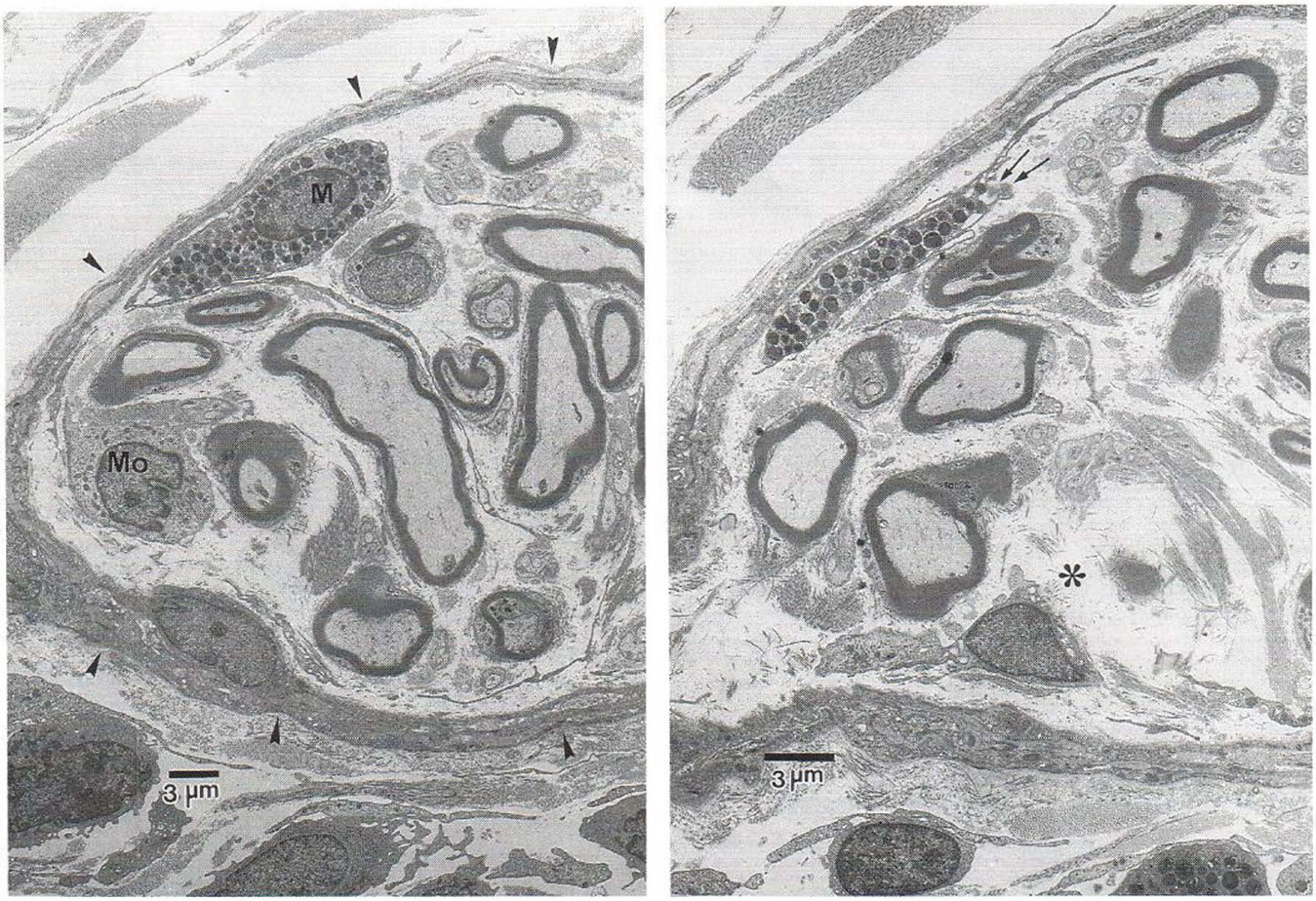

Fig. 1a. An electron microscopic picture of a prurigo nodularis lesion of atopic dermatitis. One mast cell (*M*) and one monocyte (*Mo*) are seen in a nerve fiber bundle surrounded by the perineurium (*arrowheads*). Myelinated and non-myelinated nerve fibers are observed loosely bound, showing conspicuous edematous appearance. – *Fig. 1b.* A stepped section of Fig. 1a. The degranulation process of a mast cell and the enlarged endoneurial space (*) are observed.

In the nerve fiber bundle, myelinated and non-myelinated nerve fibers are observed to be loosely bound, showing a conspicuous edematous appearance. Fig. 1b is a stepped section of Fig. 1a. Degranulation of the mast cell and edema of the nerve fiber bundle are seen. Fig. 2 is an electron-microscopic picture of a lichenified lesion of AD. A very similar cytoplasm of mast cell (arrows) is observed both within and outside the nerve fiber bundle. Fig. 3a–c consists of a series of stepped semi-thin sections of Fig. 2. Both within and outside the nerve fiber bundle, two portions of very similar mast cell cytoplasm (arrows), separated by the perineurium (arrowheads), is observed (Fig. 3a,b). One portion of mast cell cytoplasm is observed within the perineurium (Fig. 3c). The morphological relation of the mast cell and the nerve fiber bundle as observed in the stepped sections of Fig. 2 and Fig. 3a–c is shown schematically in Fig. 4.

DISCUSSION

The present study demonstrates that mast cell invasion of peripheral nerves occurs in subacute, lichenified, and prurigo lesions of atopic dermatitis. Mast cells within the peripheral nerve often showed degranulation, which was accompanied by conspicuous edema of the nerve fiber bundle.

In previous studies (1, 2), derangement of the neural structure in atopic dermatitis lesions was observed, but not mast cell invasion of nerve fiber bundles.

The main reason for our being able to observe mast cell invasion of nerve fiber bundles in AD lesions in this study may

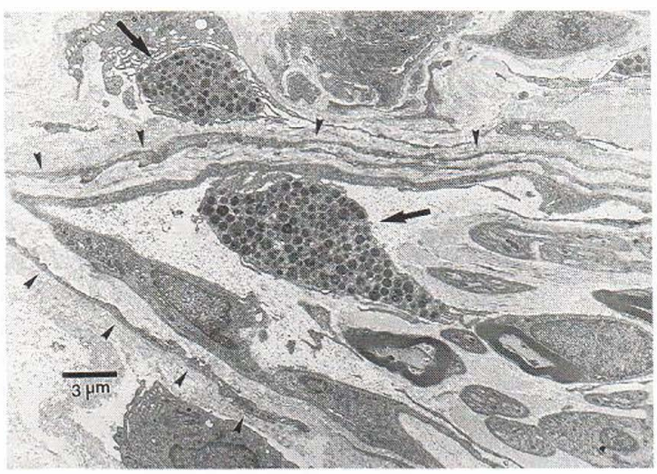

Fig. 2. An electron-microscopic picture of a lichenified lesion of atopic dermatitis. Both within and outside the nerve fiber bundle, two portions of very similar mast cell cytoplasm (*arrows*) separated by the perineurium (*arrowheads*) are observed.

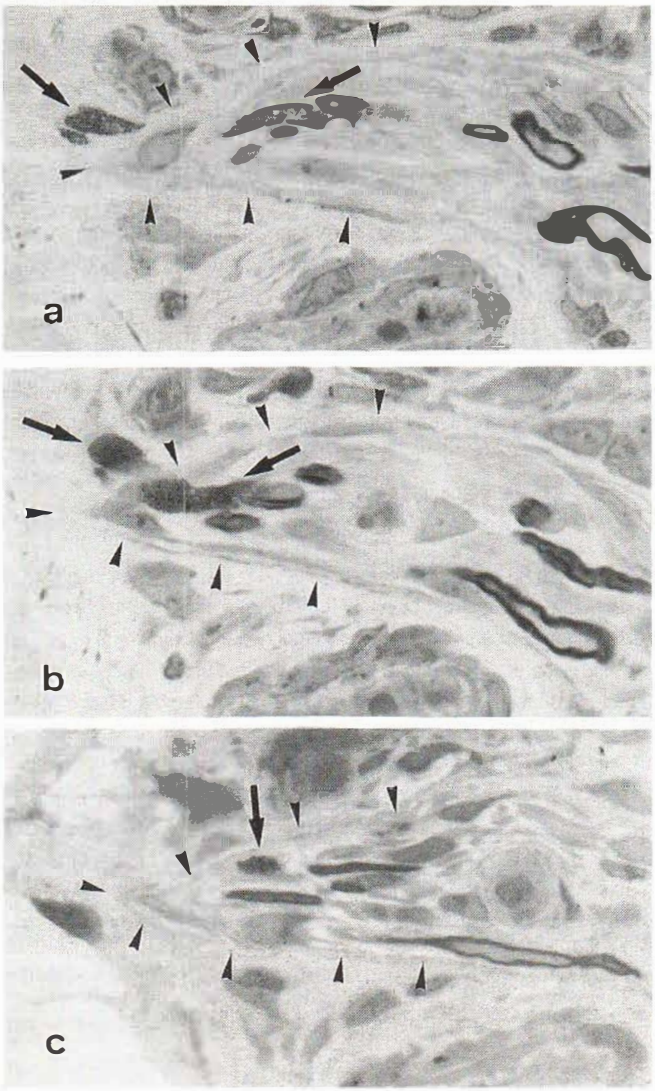

Fig. a–c. One micron-thick stepped semi-thin sections of Fig. 2. In Fig. 3a and 3b, cytoplasm (*arrows*) of a mast cell is divided by the perineurium (*arrowheads*). However, in Fig. 3c, the cytoplasm (*arrow*) of a mast cell is distributed within the perineurial nerve sheath.

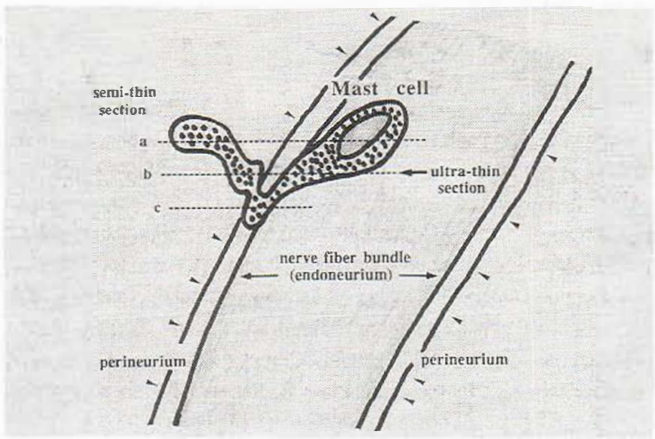

Fig. 4. This picture represents the morphological relation of the mast cell and the nerve fiber bundle as observed in the serial semi-thin sections (Fig. 3a–c) and the ultra-thin section (Fig. 2). A mast cell invading the nerve fiber bundle is shown.

be that we investigated dermal nerves in a more expanded area than that of the previous studies (1, 2).

Although the true pathological role of mast cells invading dermal nerves in AD lesions is not clear, the mast cell invasion of dermal nerves with edematous changes of the nerve fiber bundles might be related to provoking or aggravating the itchiness of atopic dermatitis.

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