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SHORT REPORTS

Electron Microscopic Observation of Infiltrating Neutrophils in Aphthous Ulceration in Behçet's Disease

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Abstract. Neutrophils infiltrating the site of aphthous ulceration of the oral mucosa of patients with Behçet's disease were studied in the electron microscope. Infiltrating neutrophils without degeneration in the lamina propria are frequently phagocytosed by large mononuclear cells.

Key words: Behçet's disease; Phagocytosed neutrophil; Electron microscopy

Histopathological examination of the oral mucosa at the site of aphthous ulceration in patients with Behçet's disease has revealed a transient, intense, exsudative inflammation with marked infiltration of neutrophils, followed by spontaneous dissipation without abscess formation (1, 2).

In Behçet's disease, mobilization of neutrophils to the site of involvement in various organs throughout the body has been emphasized frequently with reference to the etiology of Behçet's disease.

We observed that, in the very early pre-ulcerative stage of the aphthous lesions of the oral mucosa of patients with Behçet's disease, there was no neutrophilic infiltration of the epithelium (3) or of the lamina propria (4). It was not until the ulcerative stage that a marked neutrophilic infiltration was noted in the lamina propria (5).

In order to clarify the fate of neutrophils which infiltrated the tissue, neutrophils infiltrating the site of aphthous ulceration of the oral mucosa of patients with Behçet's disease were studied in the electron microscope, with the following findings.

MATERIALS AND METHODS

Biopsies were taken from 4 patients with the complete type of Behçet's disease. The specimens were excised from the lingual and labial mucosa during the ulcerative stage. (Sloughing of blanched membrane. A dusky red inflammatory halo rises, with red rampart-like margins) (2). The specimens were divided immediately: one-half was fixed in 10% formalin, stained with hematoxylin and eosin, and examined in the light microscope. The other half was fixed in a cold 2% solution of gutaraldehyde in phosphate buffer (pH 7.4) for 1 hour, divided into fragments less than 1 mm, followed by 120 min of post-fixation in 1% osmium tetroxide Veronal buffer solution (pH 7.4).

Dehydration was accomplished with graded concentrations of ethanol. The specimens were then embedded in Epon 812. Ultrathin sections were made with a LKB microtome. These were stained with uranyl acetate and lead citrate and examined in a Hitachi HU 11-DS electron microscope.

RESULTS

Light microscopy

The epithelial margins of the ulcer are undermined and there is a diffuse chronic inflammatory infiltra-

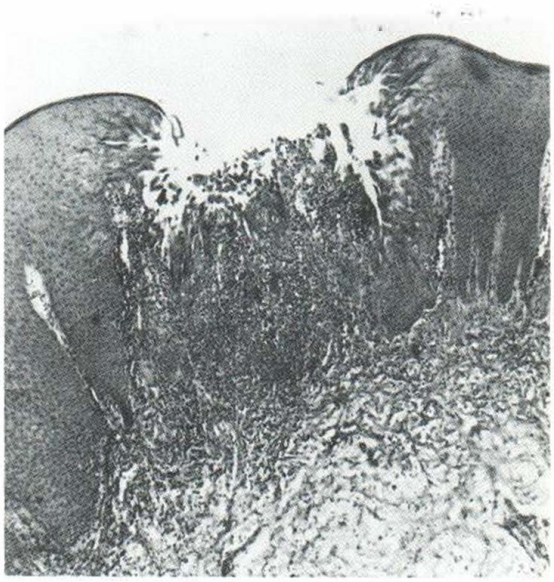

Fig. 1. An aphthous ulcer of the lingual mucosa. A breach has occurred in the epithelium, and is being filled by neutrophils. ×32.

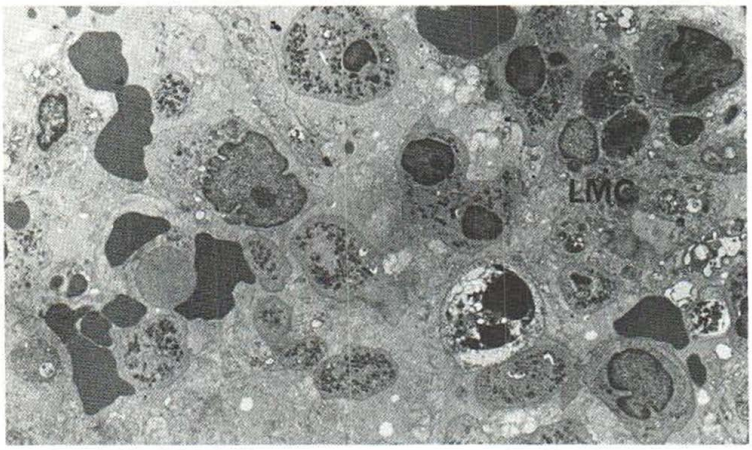

Fig. 2. Electron micrograph showing a sheet of neutrophils, with some large mononuclear cells (LMC). Infiltrated neutrophils are intact. ×960.

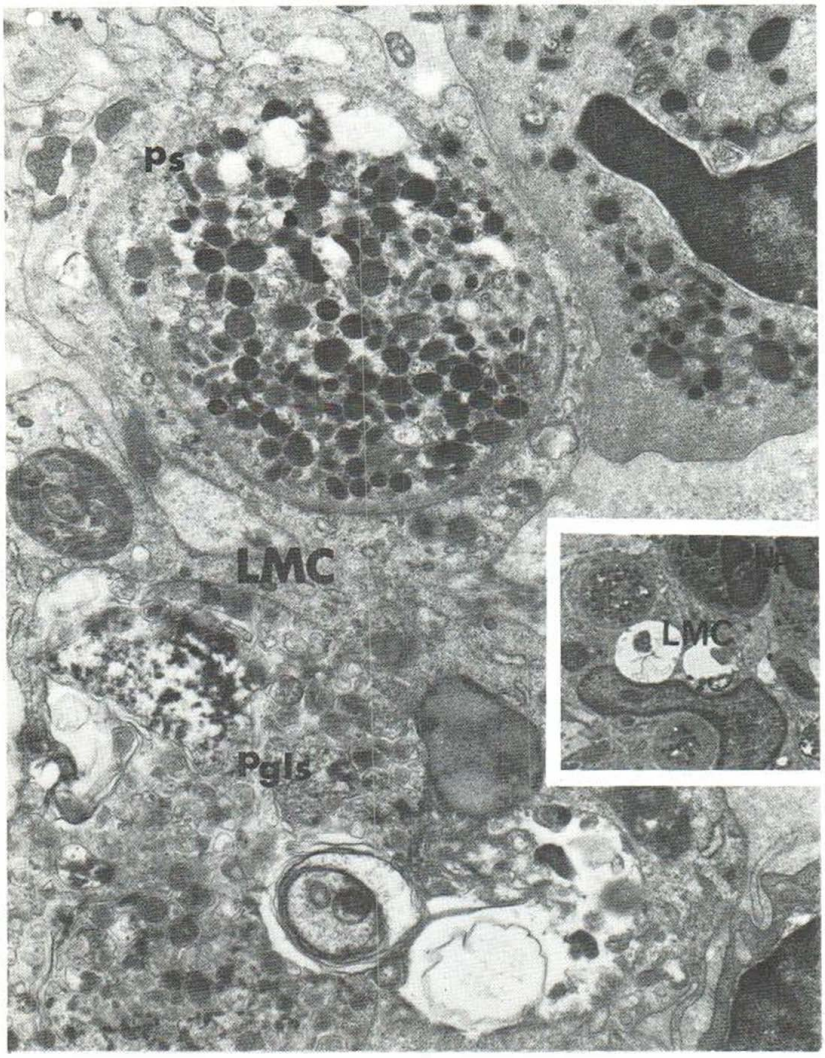

Fig. 3. Electron micrograph showing large mononuclear cell (LMC) containing an intact neutrophil in the cytoplasmic phagosome (Ps) and neutrophil debris in the cytoplasmic phagolysosome (Pgls). ×10625. *Inset:* Phagocytosis of intact neutrophil (Np) by a large mononuclear cell (LMC). ×3060.

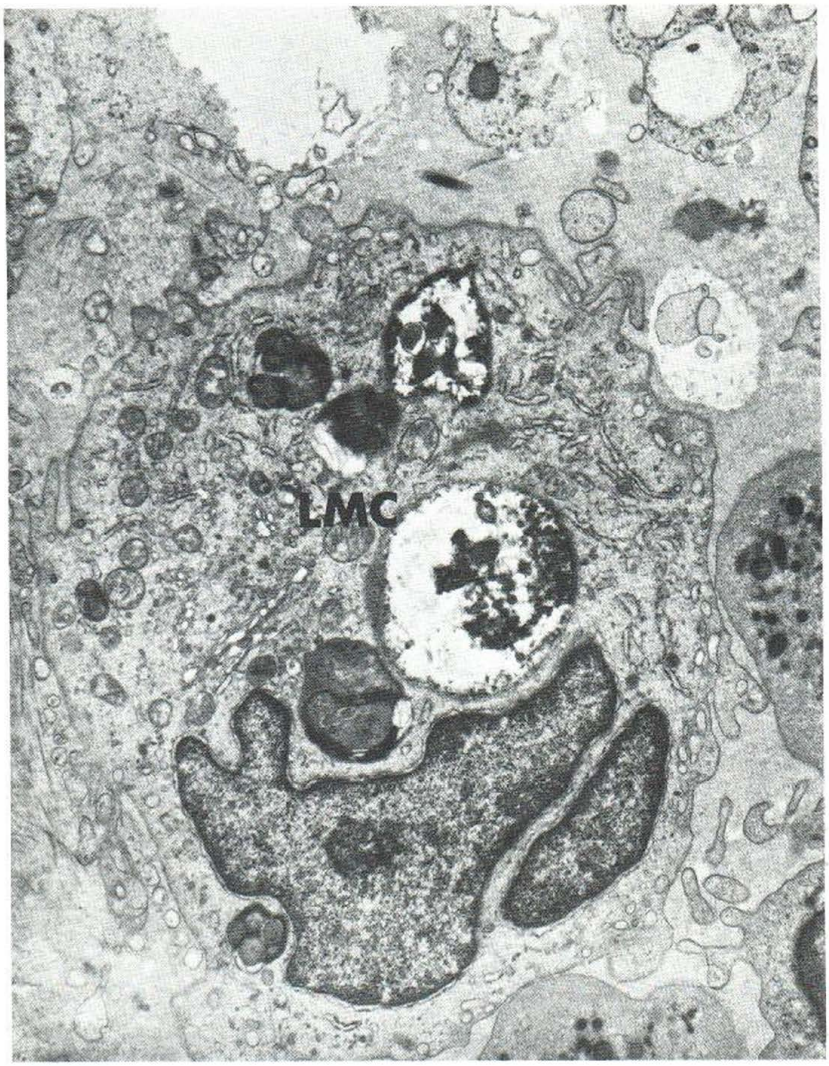

Fig. 4. Electron micrograph showing large mononuclear cell (LMC) with a lobulated nucleus, profiles of rough endoplasmic reticulum, well-developed Golgi zones, mitochondria, numerous primary lysosomes and phagolysosome. ×8 075.

tion in the lamina propria. An infiltration is seen consisting mainly of neutrophils, with some mononuclear cells (Fig. 1).

Electron microscopy

Marked edema was found in the lamina propria at the site of ulceration on account of the stimulus with numerous infiltrating cells. Among the infiltrating neutrophils which form a sheet, large mononuclear cells (LMC) are noted (Fig. 2). The morphology of neutrophils is entirely normal, with some phagosomes within the cytoplasm. Such neutrophils are frequently found to have been phagocytosed by LMC. Within the phagosomes in the cytoplasm of LMC, neutrophils are noted in various stages of digestion (Fig. 3). In view of the variety of findings of neutrophils with scarcely any degeneration in the cytoplasm and huge phagolysosomes formed by fusion between phagosomes and lysosomes containing evident remnants of nuclei or cytoplasm or neutrophilic granules, LMC appear to phagocytose neutrophils.

The nucleus of LMC occasionally shows deep indentations, giving it a lobulated appearance (Fig. 4). Among the intracellular organelles, the Golgi apparatus and rough surfaced endoplasmic reticulum are well developed. One LMC may phagocytose several neutrophils, but the destruc-

tion of neutrophils with release of granules is rarely found.

DISCUSSION

Neutrophils infiltrating the site of aphthous ulceration of the oral mucosa of patients with Behçet's disease without degeneration are frequently phagocytosed by LMC. In Behçet's disease, the presence of mononuclear cells with phagocytosed neutrophils was demonstrated electron microscopically in the synovial fluid by Abdou et al. (6). It is noteworthy here that neutrophils with almost normal ultrastructure (7) are phagocytosed by LMC. This phenomenon indicates the recognition of the infiltrating neutrophils as a foreign body, probably because of some non-specific damage sustained by the neutrophils (8) and/or some specific antigenicity against neutrophils acquired by LMC. According to the findings of the authors, epithelial prickle cells are phagocytosed by mononuclear cells (macrophages) in the pre-ulcerative stage without neutrophilic infiltration (9, 10). These macrophages invading intra-epithelially may be in intimate relationship with LMC bearing phagocytosed neutrophils, thus possibly playing an important role in the etiology of Behçet's disease.

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Immunoglobulin-bearing Cells in Liver Biopsies from Patients with Psoriasis

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Abstract. Sections of liver tissue from 41 patients with psoriasis were examined histologically and by immunofluorescence microscopy to detect cells bearing the immunoglobulins IgG, IgA or IgM. Two patients with non-specific, reactive hepatitis and two with cirrhosis had more numerous immunoglobulin-bearing cells, while no correlation was found between the number of immunoglobulin-bearing cells and 1) other types of abnormal liver histology, 2) lymphocytic infiltrates in the liver, or 3) methotrexate therapy.

Key words: Immunofluorescence microscopy; Immunoglobulin-bearing cells; Liver biopsy; Methotrexate; Psoriasis

Systemic disease associated with psoriasis has been reported (5), and abnormal liver morphology has been seen in psoriatics, particularly those receiving Methotrexate (MTX) treatment (3). It is not known whether psoriasis itself is associated with liver disease (4, 6).

The study reported was undertaken to determine whether the deposition of immunoglobulin-bearing cells in the liver of a patient with psoriasis is an