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LYMPHOMATOID PAPULOSIS

An Electron Microscope Study of the Acute and Healing Stages with Demonstration of Paramyxovirus-like Particles

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Abstract. An electron microscopic study was performed on biopsies from recent and old lesions of lymphomatoid papulosis. In recent lesions pleomorphic cellular infiltration was seen. Within the cytoplasm of these cells groups of microtubular formations were found, resembling paramyxovirus-like structures. In old lesions phagocytosis of collagen fibers and of nuclear debris were seen. The viral etiology of lymphomatoid papulosis has been discussed.

In previous reports of lymphomatoid papulosis the discrepancy between the benign clinical course and the apparent malignant histological findings was emphasized (1, 5, 14). The etiology of the disease remains obscure. The present communication describes the finding of paramyxovirus-like filaments within the cytoplasm of the cells infiltrating the dermis, by electron microscope study.

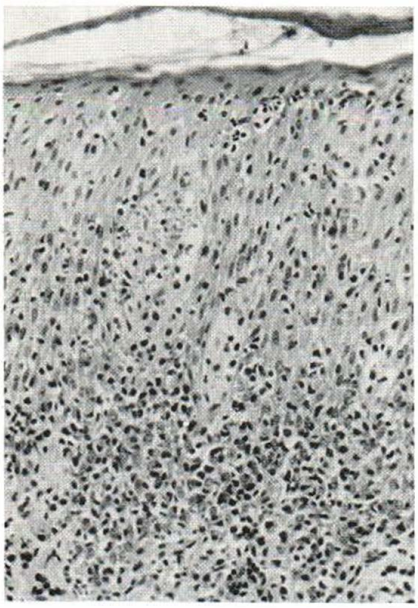

Fig. 1. Dense pleomorphic cellular infiltration of upper dermis with few cells penetrating the epidermis. Hematoxylin eosin, × 93.

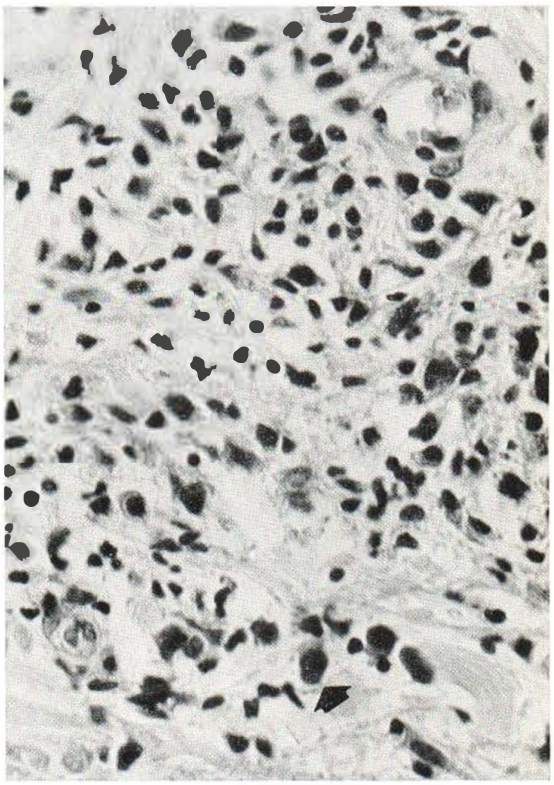

Fig. 2. Cellular detail of Fig. 1 showing the great variety of cell type with many large hyperchromatic round to oval-shaped nuclei (arrow). Hematoxylin eosin, × 320.

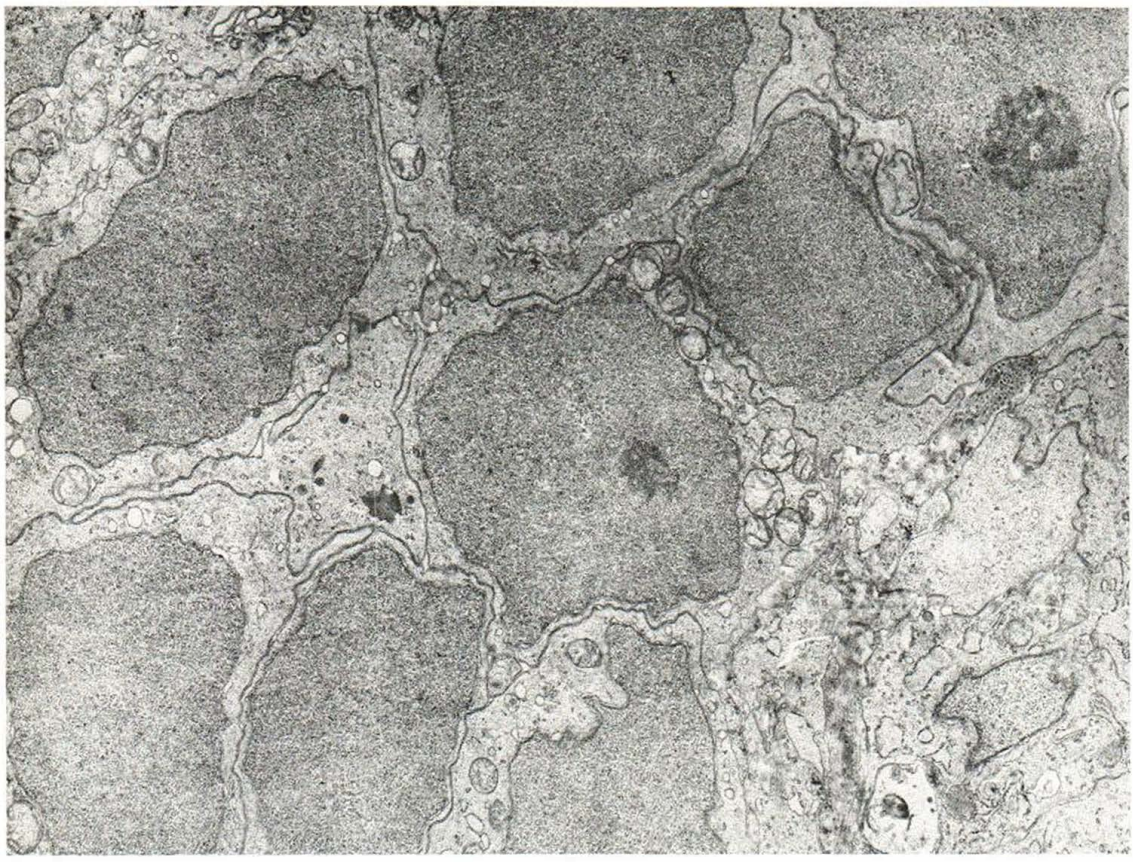

Fig. 3. Recent lesion showing dense cellular infiltration in dermis. Nuclei with dispersed chromatin network. Few intracytoplasmatic organelles. × 3 600 (original magnification).

Viral etiology of lymphomatoid papulosis has been suggested.

REPORT OF A CASE

The clinical and histological data of this case were reported recently (5) and will therefore only be summarized: A 53-year-old man suffered during the last 6 years from an asymptomatic eruption over the groins, lower abdomen, axillae and arms. Solitary groups of papules appeared, and became necrotic at their center with the formation of a shallow ulceration. The ulcers healed with a crust formation and developed into a small discolored scar. The life cycle of these papules was 2 to 4 weeks.

Histological examination

In the dermis a dense pleomorphic cellular infiltrate was seen (Fig. 1). The cells had round, oval, lobular or kidney-shaped hyperchromatic nuclei (Fig. 2). Sparse basophilic cytoplasm surrounded the nuclei. Few mitotic figures were seen. Lymphocytes, plasma cells, granulocytes and eosinophilic granulocytes were dispersed within the cellular infiltration. The dermis and epidermis were edematous. Clusters of the cells invaded the epidermis.

In an older lesion the epidermis was absent and replaced by an eosinophilic crust. The cellular infiltration was of the same character as in the recent lesion.

Electron microscope study

Punch biopsy specimens approximately 0.5 cm in diameter were fixed by immersion in 2% chilled glutaraldehyde in phosphate buffer for 2 hours. The specimens were afterwards cut into small pieces, washed three times in distilled water and post-fixed in 2% osmic acid. The blocks were embedded in Epon 812. Ultrathin sections were stained with lead citrate and uranyl acetate.

Biopsies were examined from recent lesions which developed during 3 to 4 days, and from old lesions with crust formation, aged 3 to 4 weeks.

(*a*) *Cell types.* The pleomorphism of the infiltrating cells, as seen by light microscopy, was similarly found in the electron micrographs. Cells of different shape and size were seen. The nuclei had a dispersed chromatin network, a few showing one or two large nucleoli: the cytoplasm was abundant with few round mitochondria;

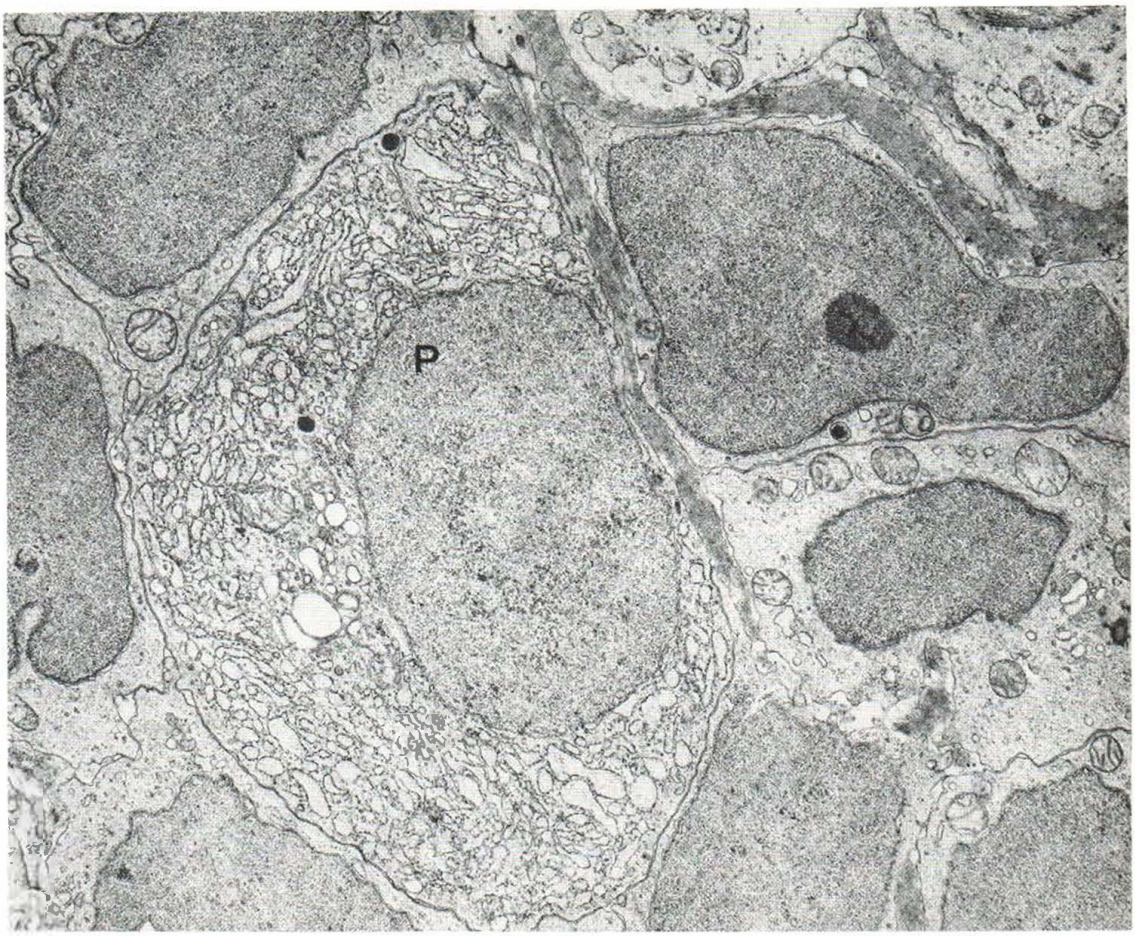

Fig. 4. A plasma cell (*P*) between the cells infiltrating the dermis. × 3 800.

and a small quantity of rough endoplasmic reticulum (Fig. 3). Few dense bodies were seen. A few typical plasma cells with abundant endoplasmic reticulum (Fig. 4) and bundles of filaments approx. 100 A° in diameter were found in the cytoplasm of few cells (Fig. 5). Polymorphonuclear leukocytes and mast cells were dispersed in between the cells.

(*b*) *Virus-like filaments.* Within the cytoplasm of several of the infiltrating cells an interwoven network of curved filaments measuring 160–180 A° in width were seen. None of these filaments were found within nuclei. In cross sections these filaments showed a microtubular appearance with a central electron-lucent core (Fig. 6). In one cell, a Langerhans granule was found near a cluster of the microtubules (Fig. 7).

Old lesion

The most prominent feature of the older lesions was the extensive phagocytotic activity of the infiltrating cells.

(*a*) *Phagocytosis of nuclei.* Large cells were observed with spindle-shaped or kidney-shaped nuclei, and an abundant cytoplasm, containing many dense bodies and clusters of disintegrated nuclei. The phagocytized nuclei were partly shrunken, appearing like pyknotic nuclei, whereas other parts showed fragmented irregular chromatin, appearing like karyolitic nuclei (Fig. 8).

(*b*) *Phagocytosis of collagen.* Collagen fibers were engulfed by cells and phagocytized. Within the cytoplasm, collagen fibers were seen surrounded by a membrane (Fig. 9). In many instances two collagen fibers were surrounded by one membrane thus forming pairs of phagocytosed collagen fibers. In the cytoplasm of many cells abundant myelin figures were seen (Fig. 10).

Four biopsies of old lesions were taken, 10 blocks were cut from each, but no virus-like filaments were found.

DISCUSSION

Recent communications report the presence of a paramyxovirus-like inclusion within cytoplasm of

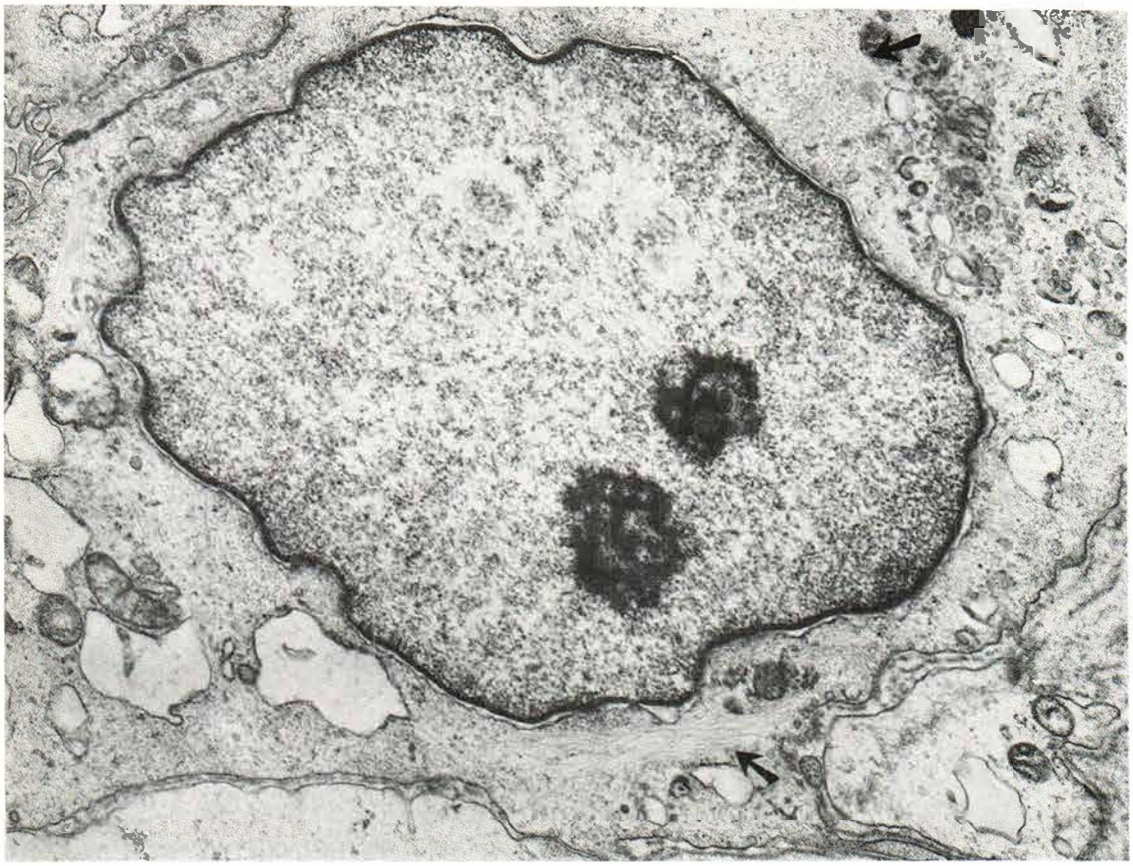

Fig. 5. Cell with large nucleus, two nucleoli, bundles of intracytoplasmic filaments (arrow), few dense bodies and empty vacuoles. × 6 550.

cells in cases of autoimmune diseases or the so-called collagen diseases. These tubular formations were found in disseminated lupus erythematosus (6, 7, 8, 9, 13, 15, 16), discoid lupus erythematosus (10), polymyositis (2, 3, 4, 21) and dermatomyositis (11, 16). Similar findings were reported in Sjögren's syndrome (23). In the present case the tubular intracytoplasmic formations were the same as those found in the above-mentioned reports. An interesting finding was their presence in new lesions, whereas they were absent in old ones. Hashimoto et al. (11) noted the presence of the inclusions in active skin lesions of dermatomyositis. Norton (16) also reported a correlation between the activity of the disease and the proportion of the inclusion in polymyositis. Hashimoto et al. (11) put forward recently the hypothesis that a slow infection by an incomplete and defective "paramyxovirus" causes malignancies. The same slow infection affecting the reticulo-endothelial system may elicit a chronic autoimmune response (12). Lymphomatoid papulosis is histologically a malignant proliferation of histiocytes thus tallying with the above-mentioned hypothesis. The presence of collagen fibers encircled by a membrane within macrophages was interpreted as constituting collagen phagocytosis. This interpretation, however, should be accepted very cautiously as the figures could be the result of invagination of extracellular collagen into cellular membrane. Phagocytosis of collagen fibers by macrophages was found in the tadpole tail during its atrophy (24), in mouse and rat involuting uterus (18, 22). These authors reported the presence in the cytoplasm of several vacuoles of various size containing collagen fibers. The macrophages afterwards became loaded with numerous large membrane-bound myelin figures. These

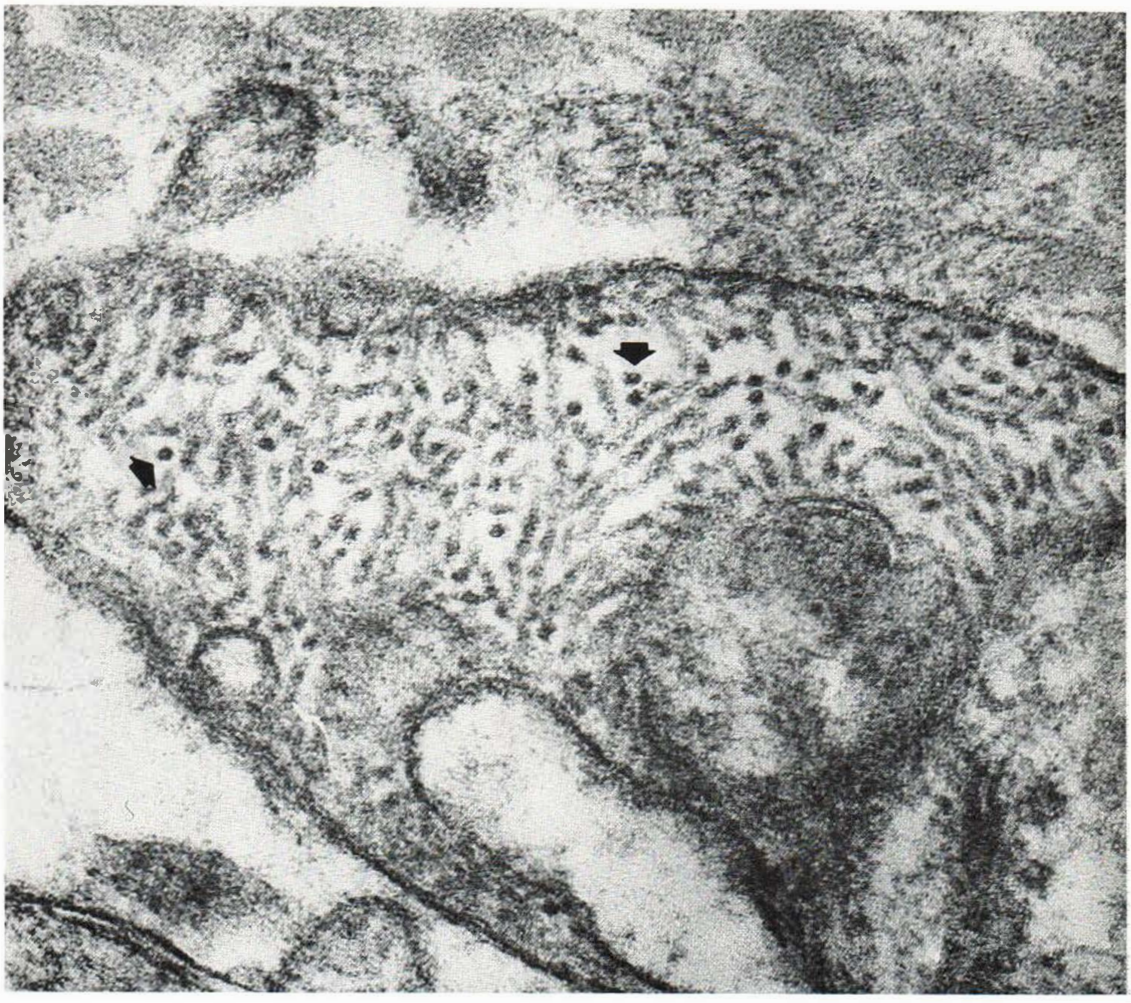

Fig. 6. Cytoplasmic projection with a group of elongated microtubules. On cross sectioning, ring-like formations (arrow) are seen. × 118 300.

myelin figures were thought to represent undigested end-products of collagen breakdown stored by the cell (22). Myelin figures have also been reported in monocytes of healing wounds (20). Similar myelin figures were found in the present case. According to Pérez-Tamayo (19) in Carrageenin granuloma, fibroblasts showed collagen phagocytosis. Welsh (25, 26) described human tumors and inflammatory conditions in which collagen fibers were found within fibroblasts. He interpreted this finding as collagen formation and not as collagen phagocytosis.

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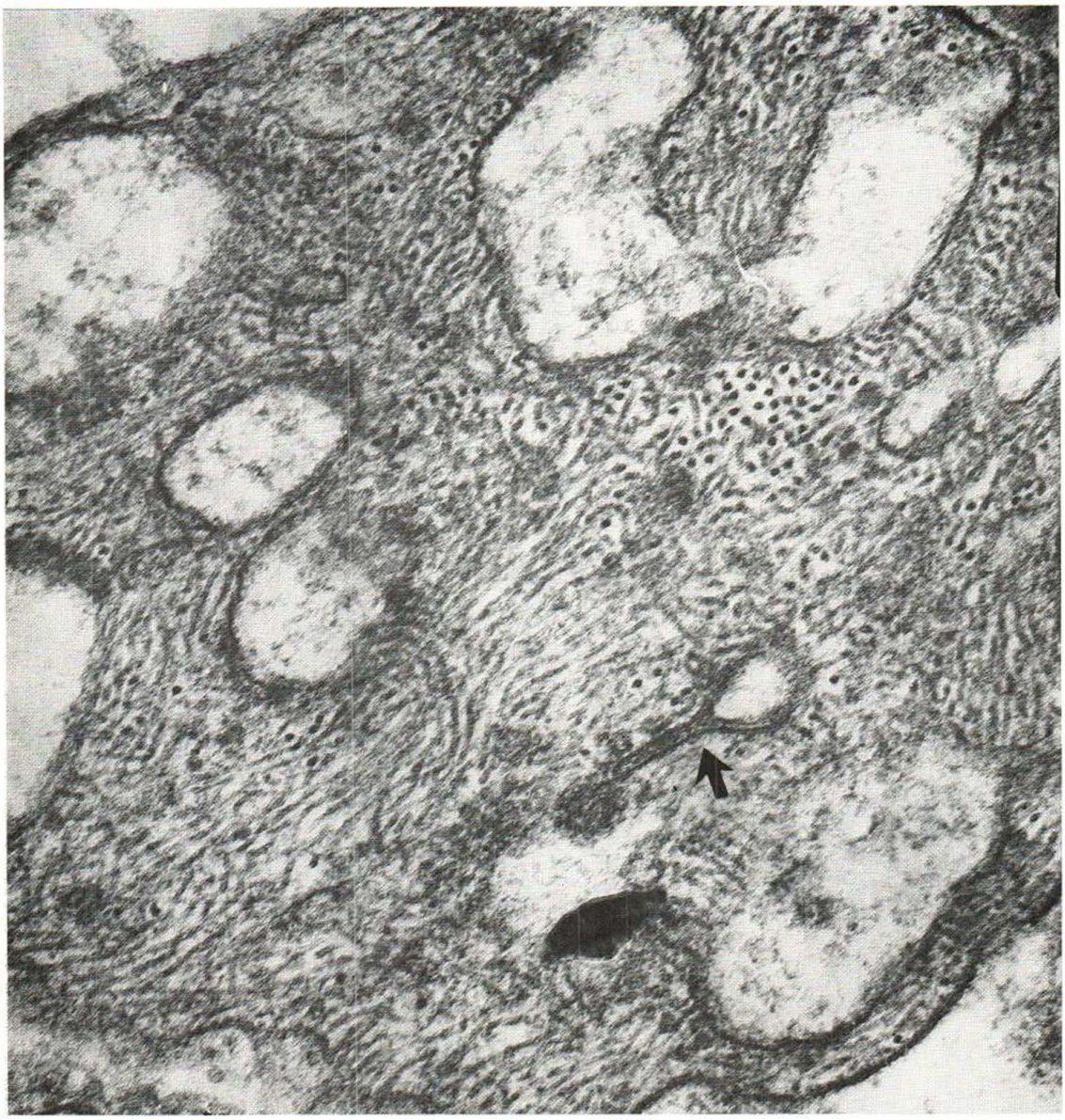

Fig. 7. A cluster of microtubules surrounding a Langerhans granule (arrow). ×88 600.

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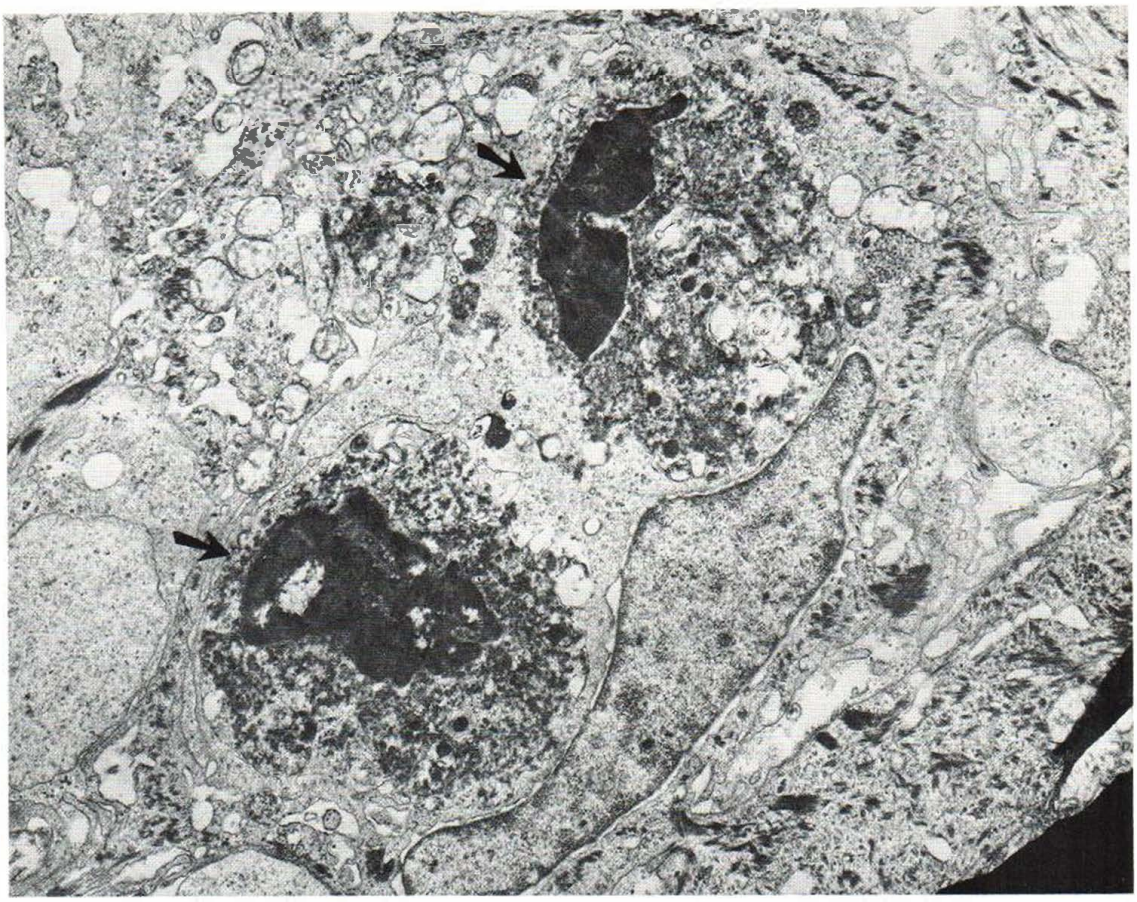

Fig. 8. Phagocytic cell. Elongated nucleus, within cytoplasm two nuclear debris (arrow), multiple dense bodies, vacuoles and few mitochondria. × 4 800.

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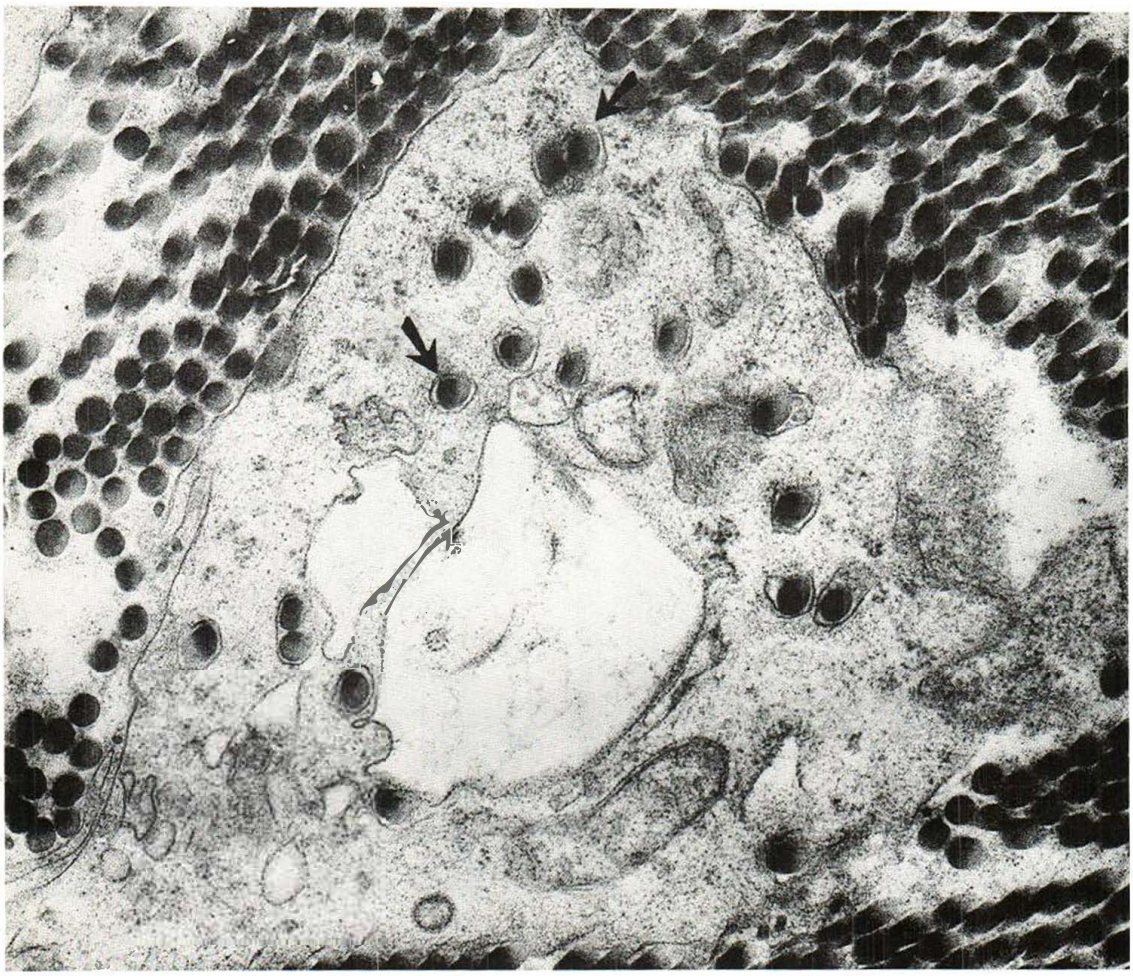

Fig. 9. Single or pairs of membrane-bound collagen fibers (arrow) within cytoplasm. Dilated vacuoles and mitochondria are seen. × 15 250.

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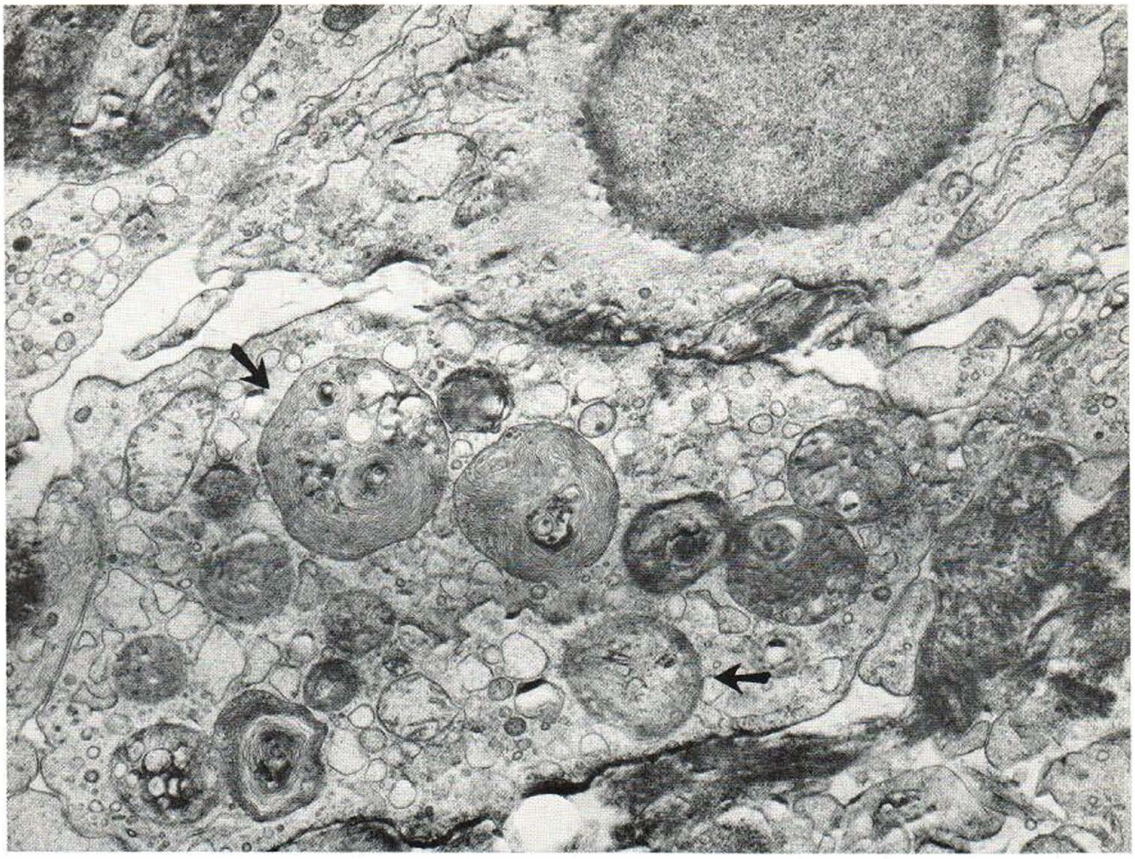

Fig. 10. Group of myelin figures (arrow) in different stages of development, shape and size. Numerous membrane-bound vacuoles, few mitochondria. × 6 850.