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The Ultrastructure of Lymphadenosis benigna cutis (pseudolymphoma cutis) *

Christian Schmoeckel, Günter Burg, Helmut H. Wolf, and Otto Braun-Falco**

Dermatologische Klinik und Poliklinik der Universität München
(Direktor: Prof. Dr. O. Braun-Falco), Frauenlobstr. 9, D-8000 München 2

Summary. In an ultrastructural study supplementing previous histological, cytochemical and immunocytological investigations of lymphadenosis benigna cutis, the tumor is shown to consist mainly of two cell types: Lymphocytes and macrophagocytic (reticulum?) cells. The tendency to spontaneous regression is manifested on the ultrastructural level by pronounced degenerative alterations.

Zusammenfassung. Bisherige histologische, cytochemische und immuncytologische Untersuchungen der Lymphadenosis benigna cutis wurden durch eine ultrastrukturelle Studie ergänzt. Elektronenmikroskopisch zeigen sich hauptsächlich zwei Zellarten: Lymphocyten und makrophagocytische (Reticulum?) Zellen. Die spontane Regressionsneigung manifestiert sich ultrastrukturell durch häufige degenerative Veränderungen.

In previous studies it was shown that lymphadenosis benigna cutis (LABC) consists predominantly of two different cell types [2, 5] with occasional development of follicular structures [6]. Large nonspecific esterases and acid phosphatase positive macrophagocytic ("starry sky") cells were scattered within the enzyme-cytochemically negative lymphocytic infiltrate [2, 7]. Further immunocytological studies of cells extracted from LABC led to the characterization of B (bone marrow derived) and T (thymus derived) lymphocytes in a 2:1 ratio [2–4]. Thus it became evident that the cellular composition in LABC is very similar to that of lymph nodes. From ultrastructural studies it is known that among the different cell types found in the follicular lymphoreticular tissue of lymph nodes [10] and of tonsils [11] the "dentritic reticulum cell" is specific for B-lymphocyte areas, whereas the "interdigitating reticulum cell" is specific for T-lymphocyte areas. Furthermore, a fibroblastic and a macrophagocytic reticulum cell type has been described. The term "reticulum cell" by itself is a morphological one generally designating various cells with abundant cytoplasm,

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cytoplasmic dendrites and large nuclei. It does not designate any specific cell in normal or pathological skin tissue unless further specified.

It is the purpose of this paper to study the cellular infiltrate in LABC on an ultrastructural level with special emphasis on these different types of reticulum cells.

Materials and Methods

Using local anaesthesia (Scandicain 1%) biopsies were taken from 6 patients with LABC. Small cubes of this tissue were fixed immediately after excision for 3 h in ice-could OsO_4 buffered in 0.1 M phosphate buffer at a pH of 7.4, dehydrated in ethanol and propylene oxide, embedded in epon, and cut with diamond knives on the Reichert OmU2 ultramicrotome. The sections were stained with uranyl acetate and lead citrate and studied with a Philips EM 300 electron microscope.

Results

Light Microscopy. In semi-thin sections of LABC two main cell classes were seen in the dermis: small lymphoid cells with dark nuclei, and scattered larger cells with the nuclei less stained and with dark vesicles sometimes present in the cytoplasm.

Electron Microscopy. On the ultrastructural level predominantly lymphoid cells and scattered large cells with abundant cytoplasm and large nuclei were found infiltrating the spaces of collagenous fibers of the dermis. The *lymphoid cells* has a round-to-oval nucleus with a mostly heterochromatic karyoplasm and no nucleolus. The cytoplasm

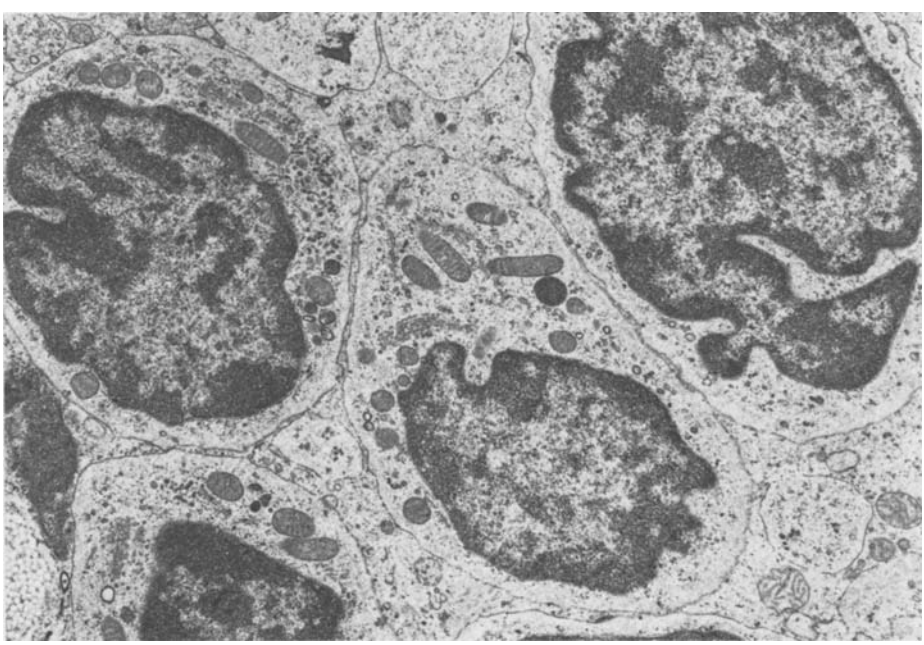

Fig. 1. Lymphadenosis benigna cutis. Normal lymphocytes. ×11200

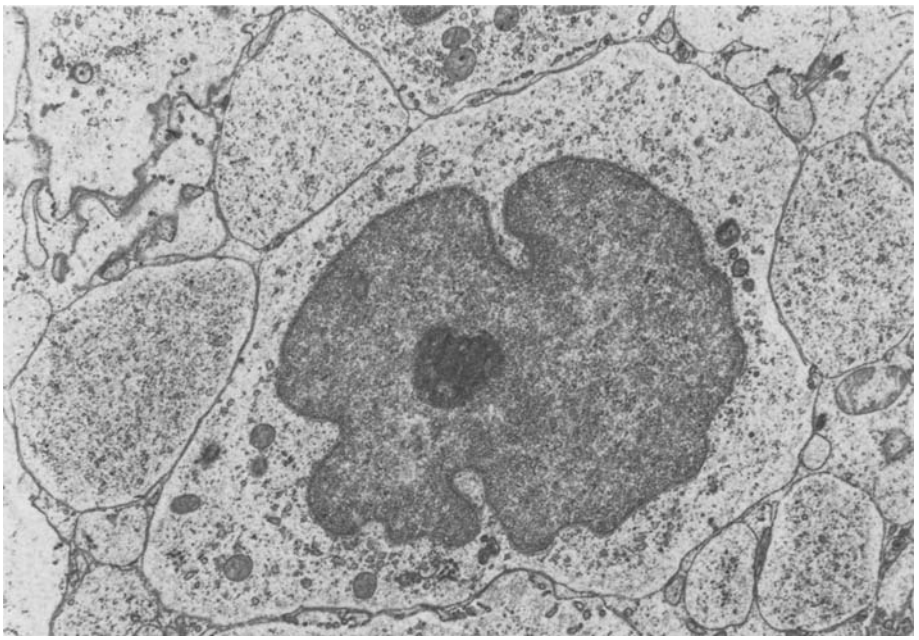

Fig. 2. Lymphadenosis benigna cutis. Centroblast. Note the distinct nucleolus and the chromatin being less dense than in lymphocytes. The size of the cell is clearly larger. ×8800

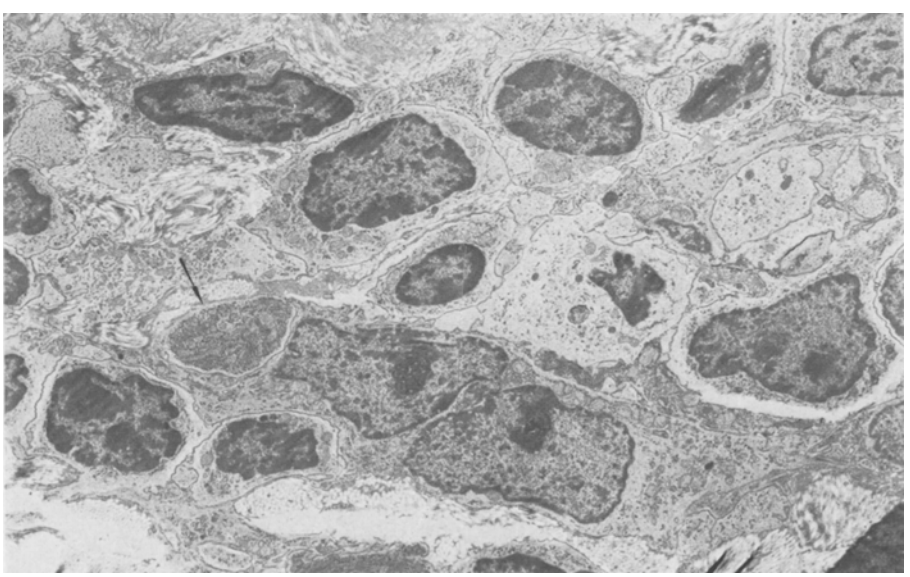

Fig. 3. Lymphadenosis benigna cutis. Large "reticulum cell" between lymphocytes. A large and lobulated nucleus can be seen, but no phagosomes. A tangential cut of a plasma cell is shown (→). ×4690

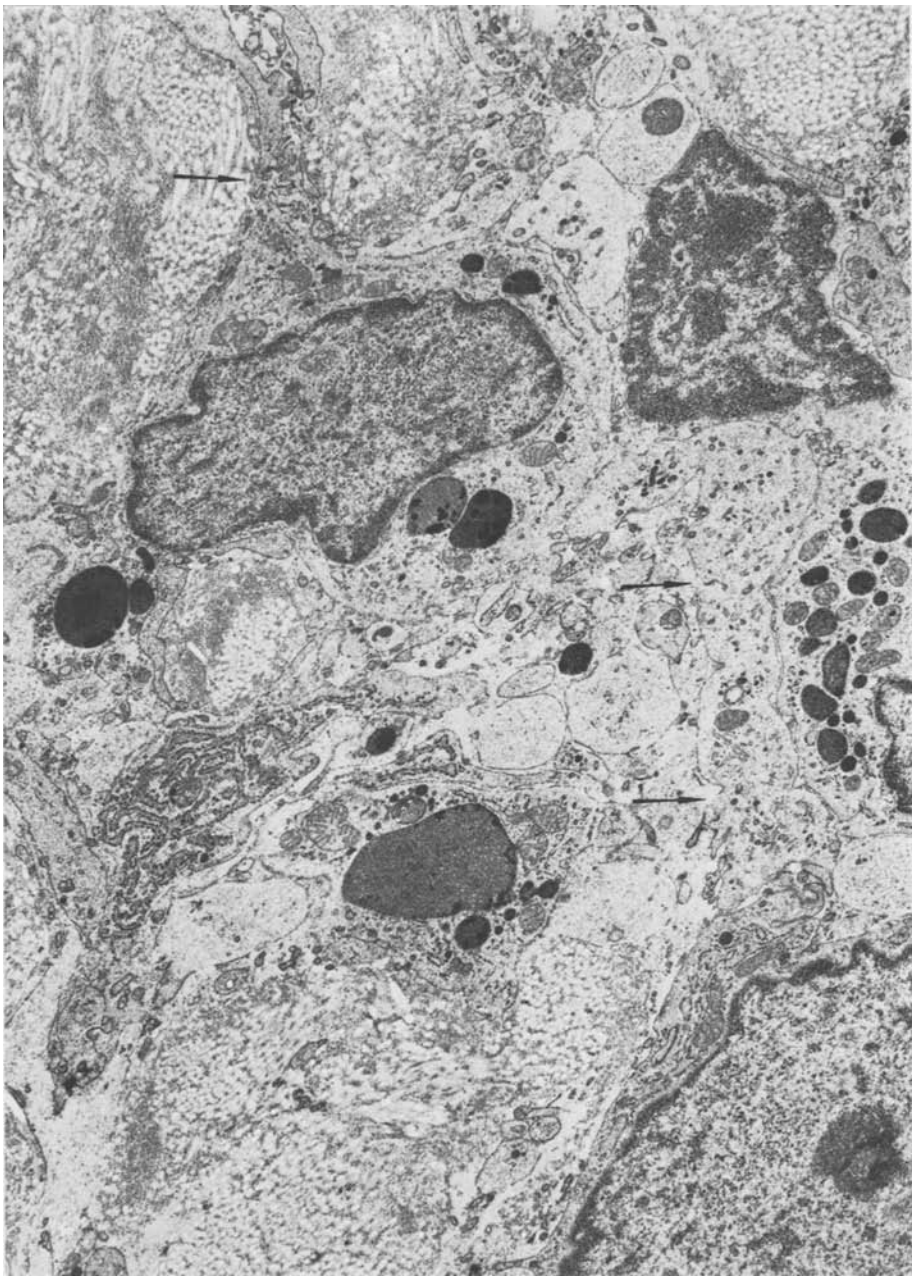

Fig. 4. Lymphadenosis benigna cutis. Macrophage with phagosomes and long cytoplasmic dendrites (→). ×8300

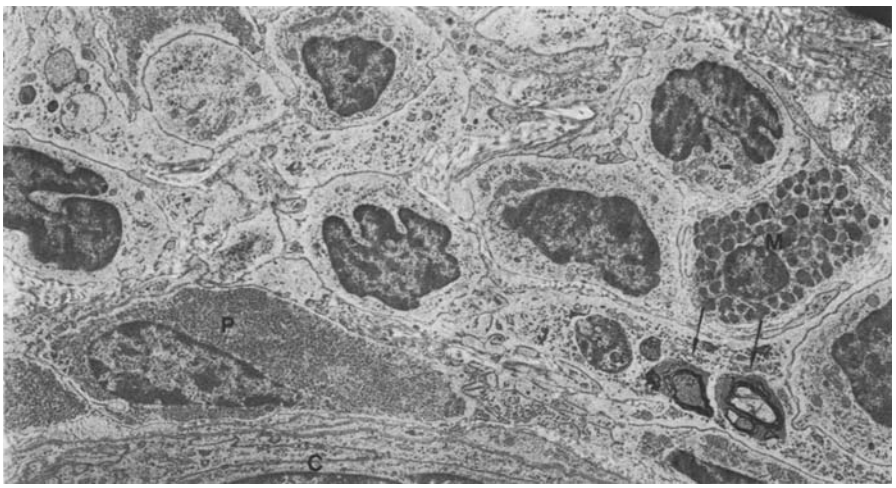

Fig. 5. Lymphadenosis benigna cutis. Close to a capillary (*C*) a plasma cell (*P*), lymphocytes, a mast cell (*M*), and a macrophage with residual bodies (→) are seen. ×4690

appeared as a narrow band around the nucleus with only a few organelles or as a more abundant mass. It regularly contained mitochondria, single ribosomes, and small vesicles. Many of these cells had a few dense bodies, and occassionally a Golgi apparatus or a centriole was present. The cytoplasmic membranes were smooth, and no microvilli were seen. Thus the morphology of the described cells corresponds to lymphocytes, whereas similar cells with pronounced nuclear clefts correspond to centrocytes (Fig. 1). A few lymphoid cells, however, showed a lightly stained and larger nucleus with small cytoplasmic invaginations and occasionally with a single nucleolus; they correspond morphologically to centroblasts (Fig. 2). It was notable that many of the lymphoid cells showed morphological signs of cellular degeneration such as nuclear pycnosis, alteration of organelles, and fragmentation of cell membranes.

The *second cell type* found in LABC lesions was characterized by its large size and by a lightly stained nucleus with the chromatin condensed only along the nuclear membranes. Some of these cells had large and lobulated nuclei, and one or two nucleoli were usually present (Fig. 3). The cells in most cases have an abundant cytoplasm filled with a rough endoplasmatic reticulum, polysomes, vesicles, a few mitochondria, and a Golgi apparatus. More characteristic and predominant were long cytoplasmic dendrites projecting deep into the tissue. Conspicuous in most of these cells, though not in all (Fig. 3), were phagosomes of different sizes containing electron dense material (Fig. 4). Occasional residual bodies were present (Fig. 5). In addition to these two main cell types, plasma cells, mast cells, neutrophils and eosinophils were present (Fig. 5).

Discussion

The cellular infiltrate in LABC consists predominantly of B-lymphocytes with some T-lymphocytes [2–4] and large macrophagocytic cells. Lymphocytes at the ultrastruc-

tural level are charaterized by dense and small nuclei and by sparse cytoplasm with almost no lysosomes and phagosomes. This explains their negative nonspecific esterases and acid phosphates enzymes-cytochemical reactions. A morphological differentiation between B- and T-lymphocytes, however, cannot be made by transmission electron microscopy. Some of the lymphoid cells with lightly stained nuclei and prominant nucleoli appear to be centroblasts (Fig. 2). In addition to normal lymphocytes, centrocytes and centroblasts, signs of degenerative alterations (pycnosis, fragmentation of cell membranes) can be found. These findings are in accordance with the tendency of the lesions to show spontaneous regression [1].

The non-lymphocytic cells in LABC lesions are difficult to classify. They correspond morphologically to reticulum cells, a term which includes at least four different specific cell types [8].

Dendritic reticulum cells have been demonstrated in B-cell areas of lymphatic tissue [11]. They are thought to be found in LABC, since in these skin lesions B-lymphocytes have been shown to predominate [2–4]. However, desmosomes and characteristic cytoplasmic membrane interdigitations, typical of dendritic reticulum cells, were not found in "reticulum cells" in LABC and therefore preclude their presence in these skin lesions.

For the same reasons *"interdigitating reticulum cells"* found in T-cell areas in lymphatic tissue [8] could not be identified.

Collagen-associated or fibroblastic reticulum cells could easily be ruled out, as "reticulum cells" in LABC were usually devoid of surrounding collagen fibers.

Phagocytic reticulum cells (macrophages) are characterized by phagosomes and lysosomes containing hydrolytic enzymes. It is very probable that most, if not all, "reticulum cells" in LABC are phagocytic reticulum cells. Some of these cells were seen in active phagocytosis ingesting degenerating lymphocytes, and many showed phagosomes of different sizes (Fig. 4). These cells can easily be determined cytochemically due to their high content of hydrolytic enzymes, especially nonspecific esterases and acid phosphatase; they show scattered and "starry sky" arrangement among the more numerous enzymecytochemically negative lymphocytes. Some of the cells are devoid of any apparent phagosomes, and their nuclear size and shape (Fig. 3) is unlike those of macrophages. A differentiation between reticulum cells and macrophages was also made by Mach (1966). However, it cannot be ruled out that these "reticulum cells" would exhibit phagosomes at different section planes, which would demonstrate their phagocytic nature.

Summerizing our findings, it can be said that our ultrastructural examinations of this type of cutaneous pseudolymphoma reveal a cellular infiltrate made up of lymphocytes, centrocytes and centroblasts, as well as of phagocytic reticulum cells. Morphological indications of a B-cell microenvironment such as in lymphatic tissue could not be found.

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