

The Ultrastructural Observation of a Case of Lymphomatoid Papulosis

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Electron microscopic studies of biopsy specimens from a patient with lymphomatoid papulosis were performed. In the epidermis, infiltrating lymphoid cells, many of which had highly convoluted nuclei, were revealed to come into close contact to increased Langerhans' cells but did not accumulate to form microabscesses. In the dermis, Langerhans' cells with rather small numbers of Birbeck granules were scattered among the thick infiltration of mononuclear cells showing close apposition with lymphoid cells. Some macrophages contacted the Langerhans' cells and lymphoid cells were also observed. On one occasion, a Langerhans' cell clinged by a lymphoid cell in the uppermost dermis was revealed to expand the cytoplasm through the ruptured basal lamina touching another lymphoid cell in the epidermis. *Key words: Langerhans' cells; Apposition of mononuclear cells to Langerhans' cells.* (Received October 29, 1983.)

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Since Macaulay (1) described a clinically benign but histologically malignant self-healing papular eruption which he called "lymphomatoid papulosis", many such cases have been reported on under this term, and several investigators have studied this skin disorder to clarify the nature of its infiltrating cells (2-7). The primary pathogenic factor is still obscure, and it has not been made clear whether the proliferating atypical cells, especially the cerebriform mononuclear cells, are essentially neoplastic or merely blastic, being stimulated by unknown mitogenic factors. Nevertheless, it is well known that some of the patients with lymphomatoid papulosis developed lymphoreticular malignant neoplasm during the course (2, 3, 5, 6, 8-10).

Recently, based on immunological, cytochemical and ultrastructural observations, Willemze et al. (7) reported that the cellular composition of one of two types of lymphomatoid papulosis, characterized by a predominance of variously-sized cerebriform mononuclear cells with the phenotype of activated T-helper cells and numerous OKT 6-positive cells, was similar to that observed in the early stage of mycosis fungoides.

In the present study, the epidermal and dermal infiltrates of this skin disorder were investigated with an electron microscope, and the apposition of Langerhans cells to mononuclear cells was disclosed in each of them.

PATIENT AND METHODS

The patient was a 71-year-old man with papular skin eruptions developed in flocks on the lower extremities, abdomen and back since March 1982. The individual eruptions were asymptomatic red papules, 1-5 mm in diameter, which disappeared several weeks later leaving brownish shallow scars with a slight scale (Fig. 1). The appearance of the eruptions was not affected by topical corticosteroid ointment but slightly decreased with the systemic administration of 1.5 mg of betamethasone. No remarkable findings were revealed in the laboratory blood tests, and no abnormal findings were noted in the physical examinations.

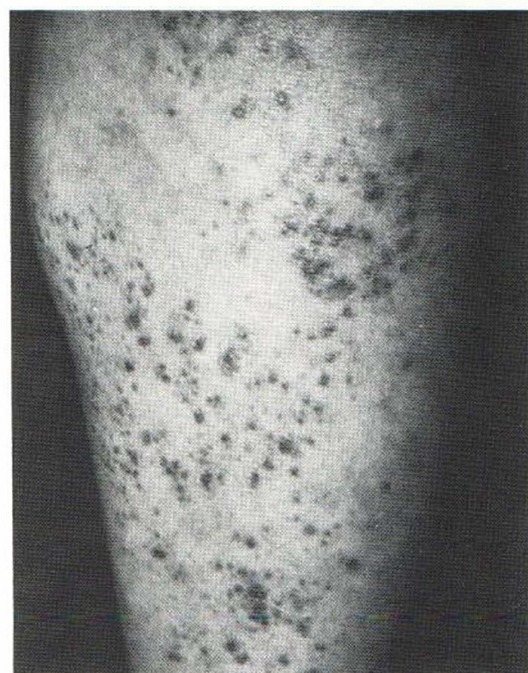


Fig. 1. Red papules and small plaques on the extensor side of the lower left leg. Similar eruptions are distributed on the flexor side, the other leg, abdomen, lower and upper back.

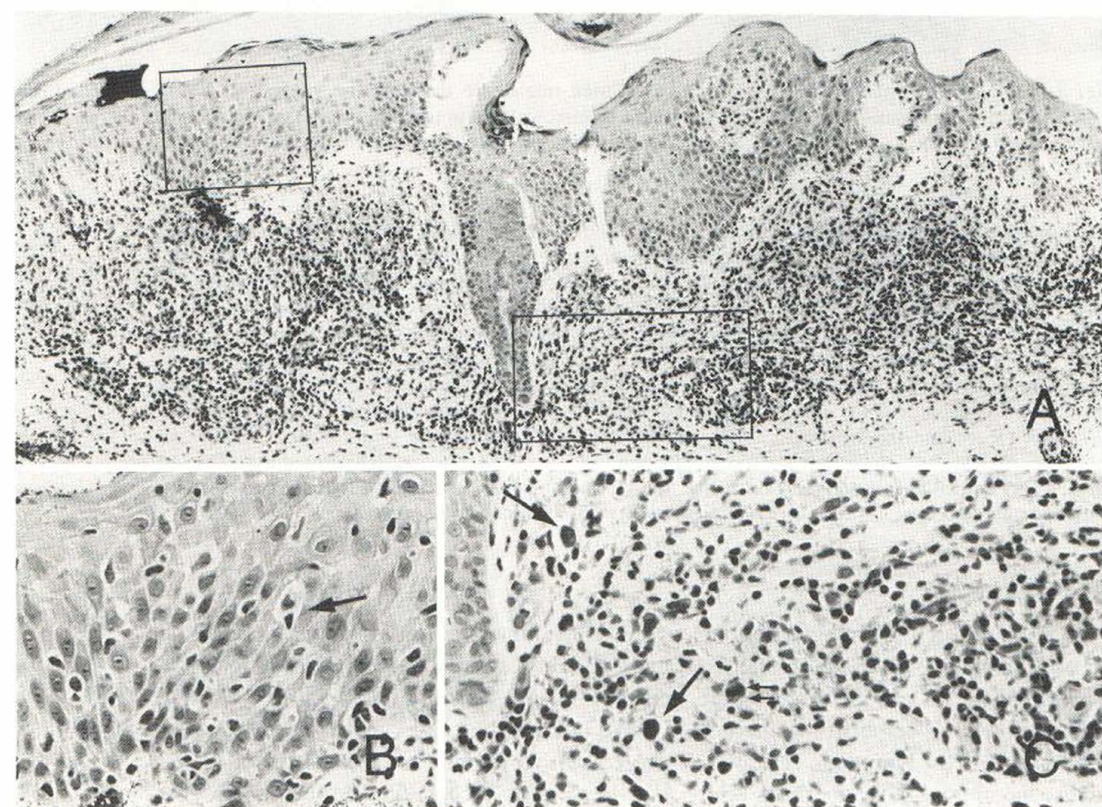


Fig. 2. Light microscopic photographs of a fully developed papule. (A) Rather diffuse dermal infiltration of mononuclear cells. (B) Some exocytotic mononuclear cells are close to clear cells in the epidermis (arrows). (C) Large hyperchromatinated cells (arrows) and mitotic cells (double arrows) are among the dermal infiltrates.

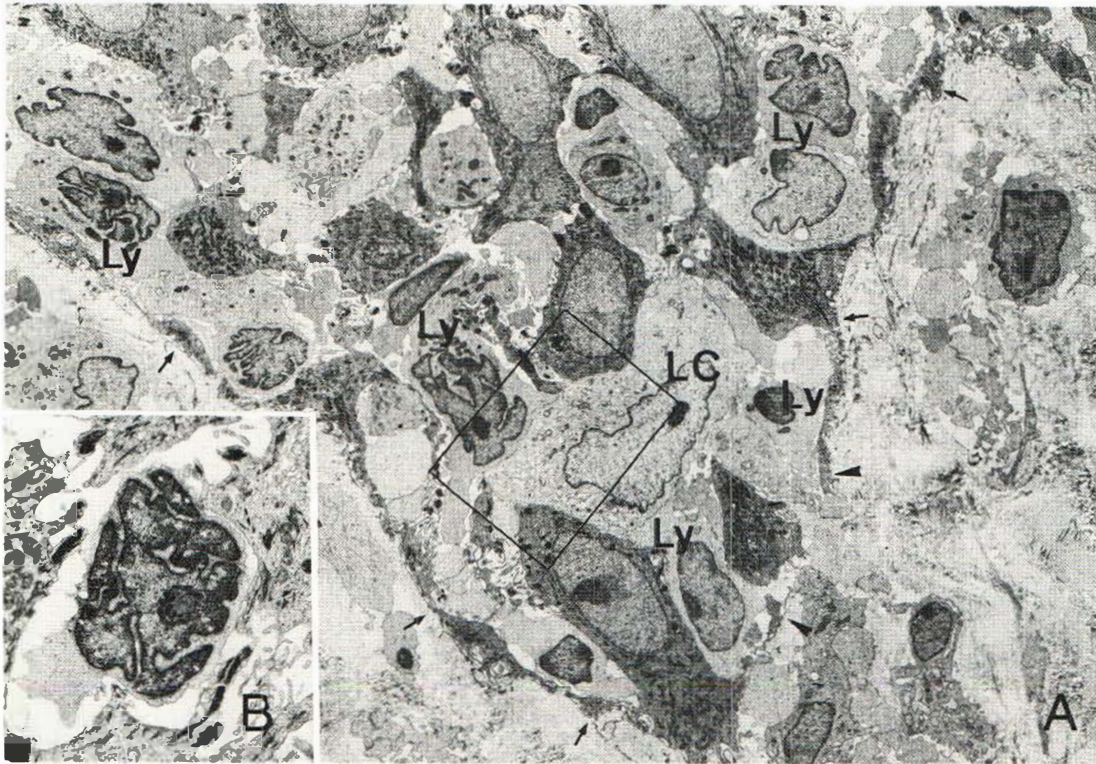


Fig. 3. (A) Many lymphoid cells (Ly) with convoluted nuclei are invading the epidermis. Some of them form apposition to Langerhans' cells (LC). Basal lamina (arrows) is ruptured by some invading mononuclear cells (between arrow heads). $\times 2000$. (B) Some lymphoid cells have highly convoluted cerebriform nuclei. $\times 6200$.

Histological findings of early red papules were mild but epidermotropic infiltrations of mononuclear cells without any atypism and extravasation of erythrocytes into the uppermost dermis. In the fully developed papules, the dermal infiltration was rather thick and diffuse, and many mononuclear cells were noted in the epidermis (Fig. 2 A). Some exocytotic mononuclear cells were close to clear cells in the epidermis (Fig. 2 B). In the dermal infiltration, some large mononuclear cells with hyperchromatized, pleomorphic nuclei and mitotic cells were scattered (Fig. 2 C). A band-like, mild infiltration of normal mononuclear cells in the uppermost dermis was found in a late guttate parapsoriatic scaly lesion. Biopsy specimens for electron microscopy were taken from fully developed red papules, cut into small pieces and fixed in a 2.5% phosphate-buffered glutaraldehyde solution (pH 7.4) for two hours, postfixed in 1% phosphate-buffered osmium tetroxide for 1.5 hours, dehydrated in a series of ethanol and embedded in epoxy resin using Spurr's method (11). Ultrathin sections, stained with uranyl acetate and lead citrate, were examined with a H-300 electron microscope.

RESULTS

A larger part of infiltrating mononuclear cells invading the epidermis had irregularly convoluted nuclei, 4 to 6 μm in diameter, and relatively large cytoplasm containing only a few mitochondria, granules and free ribosomes (Fig. 3 A). Some of the lymphoid cells had highly convoluted cerebriform nuclei (Fig. 3 B). Langerhans' cells, increased in number, were attended by lymphoid cells which projected cytoplasmic micropods to touch the plasma membrane of Langerhans' cells, but they did not accumulate to form microabscesses. Some Langerhans' cells were abundant in Birbeck granules (Fig. 4), but many of

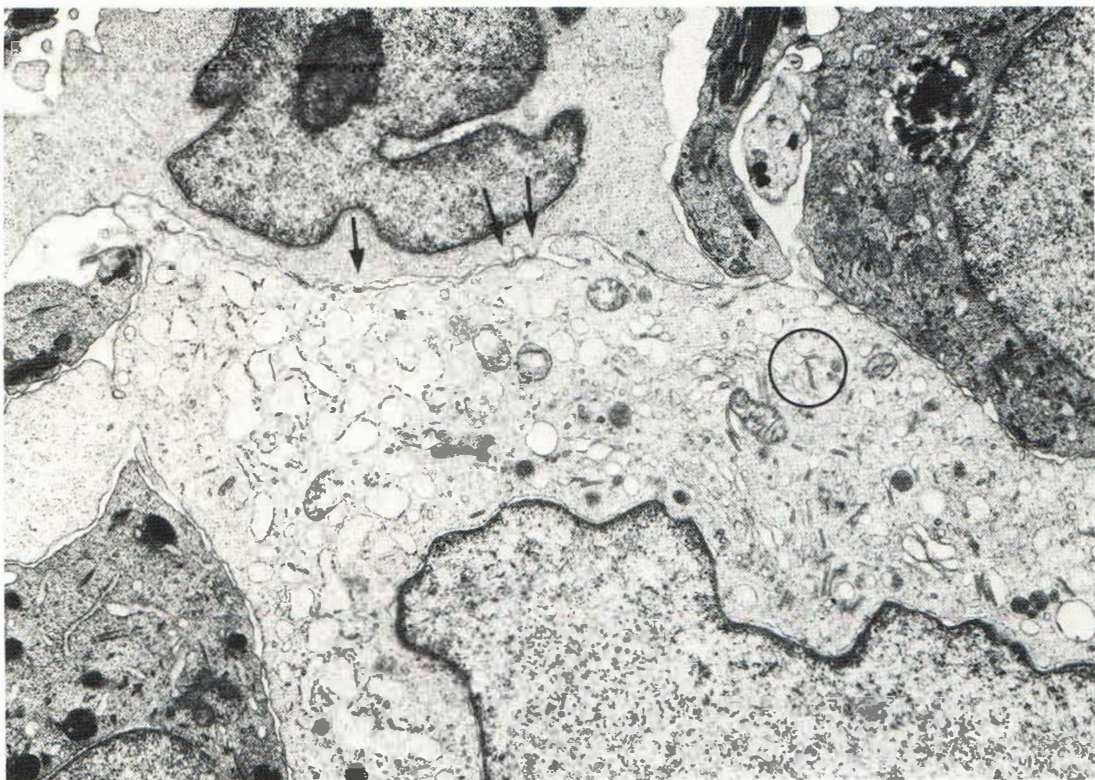


Fig. 4. Enlargement of the circled area of Fig. 3. Numerous Birbeck granules including typical racket-shaped ones (as encircled) are in the Langerhans' cell. An adjacent lymphoid cell protrudes micro-pods (arrows) to touch the Langerhans' cell. $\times 12\ 500$.

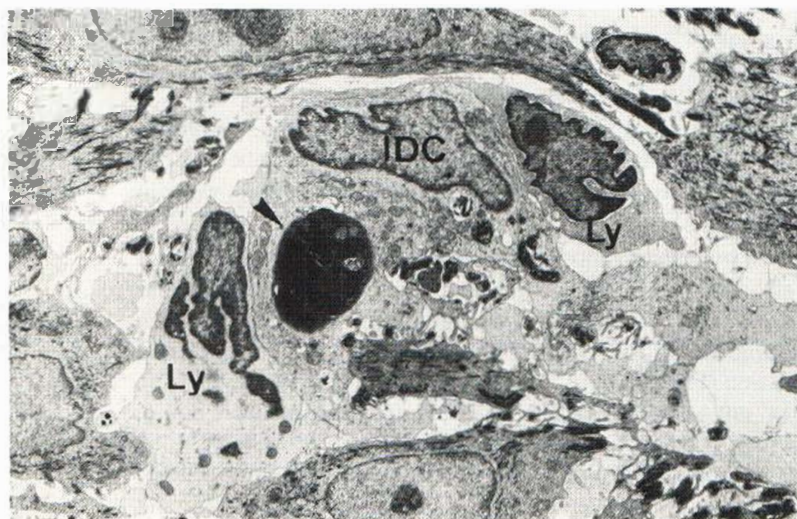


Fig. 5. Two lymphoid cells (Ly) are in contact with an indeterminate cell (IDC) containing a phagocytized lymphoid cell in the cytoplasm (arrow head). $\times 4\ 300$.



Fig. 6. A chain-like cellular apposition over the dermo-epidermal junction. A Langerhans' cell (LC) clinged by a lymphoid cell (Ly 1) extending cytoplasm through ruptured basal lamina (between arrow heads) to connect with an epidermal lymphoid cell (Ly 2). An indetermined mononuclear cell (IDMC) forms contact with the lymphoid cell (Ly 1). $\times 2700$. Inset: A small number of Birbeck granules (as encircled) are seen in the cytoplasm of the Langerhans' cell. $\times 12000$.

them had only a few such granules and rather poor Golgi apparatus. Furthermore, indeterminate cells, morphologically indistinguishable from Langerhans' cells except for the lack of Birbeck granules, were also in contact with the lymphoid cells. On one occasion, an indeterminate cell which was attended by lymphoid cells contained a phagocytized lymphoid cell in its cytoplasm (Fig. 5). There were no figures that indicated cell damage or degeneration of Langerhans' cells and indeterminate cells which were in apposition with lymphoid cells.

The basal lamina was ruptured by invading mononuclear cells in places. A Langerhans' cell, clinged by a lymphoid cell which had a connection with an indetermined mononuclear cell in the dermis, elongated its cytoplasm through the ruptured basal lamina to touch another lymphoid cell in the epidermis. They looked as a chain-like cellular apposition over the dermo-epidermal junction (Fig. 6).

Among the dermal infiltrates, not a few Langerhans' cells and macrophages were noted. Most Langerhans' cells were in contact with two or three lymphoid and/or indetermined mononuclear cells, and some were touched only by some cytoplasm of unknown cells. Many Langerhans' cells were abundant in organelles such as mitochondria, vesicles and

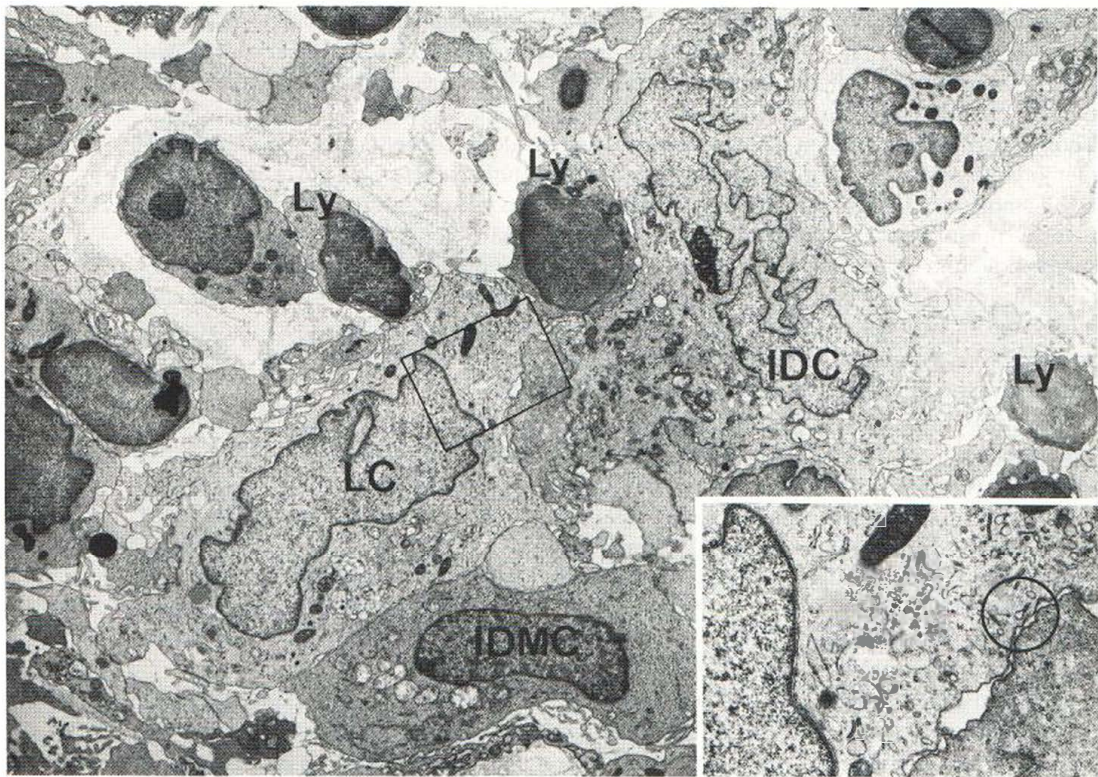


Fig. 7. Two similar large non-lymphoid cells in the dermal infiltrates. The left one, a Langerhans' cell (LC), contains several Birbeck granules as shown in inset, but the right one with multi-lobulated nucleus, an indeterminate cell (IDC), reveals no Birbeck granules even in several serial sections. Some lymphoid cells (Ly) and indetermined mononuclear cells (IDMC) are in contact with them. $\times 3\ 500$. Inset: Several Birbeck granules (as encircled) are seen in the cytoplasm of the Langerhans cell. $\times 11\ 000$.

endoplasmic reticulum but showed only a few Birbeck granules in a section. Generally, they showed no prominent Golgi complexes. Furthermore, there were non-lymphoid mononuclear cells which should be called "Langerhans'" cells without Birbeck granules" or "dermal indeterminate cells". Some of them were revealed to have Birbeck granules in other serial sections, but some showed no Birbeck granules at all even when several serial sections were observed (Fig. 7).

DISCUSSION

It is well known that Langerhans' cells are electron microscopically present in the dermis under several pathologic conditions, such as histiocytosis X (12, 13), contact hypersensitivity (14–16), granulomatous syphilis (17), actinic reticuloid (18), adult T-cell leukemia (19) and mycosis fungoides (20). Willemze et al. (7) demonstrated the presence of OKT-6-positive cells not only in the epidermis but also in the dermal infiltrate of patients with a type of lymphomatoid papulosis. However, they found no Birbeck granules in such infiltrating cells with the electron microscope.

Though the meaning of the dermal appearance of Langerhans' cells in lymphomatoid papulosis is obscure, it should be discussed along with that of mycosis fungoides, as there

are unnegligible occasions of malignant transformation in lymphomatoid papulosis (2, 3, 5, 6, 8–10). Jimbow et al. (20) with the electron microscope and McMillan et al. (2) with OKT-6 monoclonal antibody demonstrated the presence of Langerhans' cells and/or related cells in the dermal infiltrate in mycosis fungoides as well as in the epidermis. Thomas et al. (22), based on the observation using the double-labelling immunofluorescent methods, found that Ia-like antigen-positive non-lymphoid cells formed close contact with OKT-4-positive, OKT-8-negative T-lymphocytes in the dermal infiltrate of early stage of mycosis fungoides. Considering the previous findings that activated human T-lymphocytes secreted factors which induced the synthesis of Ia-like antigen in monocyte/macrophages (23), they pointed out a "vicious circle" of immunoregulatory cells in mycosis fungoides during the early stage of the disease. Namely, T-cells may cause a local accumulation of interdigitating type cells with increased Ia-like antigen synthesis which, in turn, prolong the survival and increase the proliferation of T-cells (22).

Willemze et al. (5) clinically and histologically studied sixteen cases of lymphomatoid papulosis and reported that two histological types could be distinguished in this disease. Furthermore, as previously described, they investigated the distribution of subset of T-lymphocytes and Langerhans' cells and/or related cells with monoclonal antibodies, OKT series, showing immunohistochemical differences between these two types of lymphomatoid papulosis (7). Though, it could not be easily determined to which type our case belonged, the appearance of Langerhans' cells in the dermal infiltrates of our case may indicate the same cellularity as one of the two types of their classification in which they demonstrated the OKT-6-positive cells in the dermal infiltrates.

In conclusion, Langerhans' cells and related cells seem to play an important role in the development of at least one type of lymphomatoid papulosis. Further investigations will clarify the meaning and the generally agreed expectation that some cases of this chronic skin disorder takes a middle position between a reactive benign condition and a malignant neoplasm.

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