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LYMPHOMATOID PAPULOSIS: A CUTANEOUS T-CELL PSEUDOLYMPHOMA

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Abstract. It was the purpose of this study to further define the nature of the dermal infiltrates in lymphomatoid papulosis (LP) by means of enzyme cytochemistry (acid phosphatase and esterase), immunology (rosetting techniques, immunoperoxidase technique on cryostat sections), and by semithin and ultrathin sections. The studies performed on biopsy samples with clinically and histologically typical LP indicated that most lymphoid cells display markers for T-lymphocytes, which were helper T-cells in the one case studied with monoclonal antibodies. Regarding the typical benign self-involutive clinical course, LP is considered to be a cutaneous pseudolymphoma of T-cell type.

Key words: Lymphomatoid papulosis; T-lymphocytes; Pseudolymphoma

The first description of the disease designated lymphomatoid papulosis by Macauly in 1968 (15) was given by Dupont (7) and Verallo & Haserich (24). Since then, more than 120 cases have been reported (18, 19).

Clinically, LP may simulate pityriasis lichenoides et varioliformis acuta (PLEVA). The diagnosis is based on the typical histopathological features suggestive of malignant lymphoma, due to the presence of a polymorphous lymphoid infiltrate consisting of small lymphocytes intermingled with conspicuous large blast cells.

It was the purpose of our studies to further identify the infiltrating cells in patients with clearly defined LP by means of enzyme cytochemical and immunocytological studies using various methods.

MATERIAL AND METHODS

In the 3 patients studied (Table I), soft papules measuring up to 1 cm in diameter developed and partly regressed spontaneously.

From each of the patients, multiple biopsies were taken. Besides routine histology, the fine structure was investigated in semithin and ultrathin sections of Epon-embedded material. In addition, the following specific techniques were applied to some of the material.

Enzyme cytochemical tests included demonstration of a variety of hydrolytic enzymes (acid phosphatase, acid and neutral α-naphthylacetate esterase, naphthol-AS-D-acetate esterase, naphthol-AS-D-chloracetate) and peroxidase for cell typing (4).

Immunocytological typing of the infiltrating cells was performed by the following methods. Rosetting techniques: Evaluation of E and EAC rosette-forming cells (E-RFC, EAC-RFC) was performed on cell suspensions from a skin biopsy in one patient (Z. A.). In 2 patients (H. G., Z. A.) cryostat sections were tested for receptors for erythrocyte–antibody (IgM) complement (EAC) complexes (16, 22).

Immunohistochemical identification of cells was performed on cryostat sections with anti-human T cell globulin (AHTG), anti-IgG, anti-IgM, anti-IgA, anti-kappa, anti-lambda serum (Dakopatts) and monoclonal anti-T (OKT3, T28[1]), anti-helper (OKT4) and anti-suppressor (OKT5, 8) (Ortho) using the unlabelled antibody enzyme method (PAP technique of Sternberger et al. (23)) described elsewhere in detail (9, 11).

RESULTS

Histology (Figs. 1 *a, b*)

In all lesions there is a perivascular infiltrate in the upper and mid-dermis consisting of small lymphocytes, large lympho-blast-like cells with folded or convoluted hyperchromatic nuclei, and large histiocyte-like hyperchromatic cells. In addition, swelling of vascular endothelial cells and varying numbers of eosinophils are found. The epidermis

Abbreviations: E-RFC=cells forming spontaneous rosettes with sheep red blood cells; EAC-RFC=cells forming rosettes with antibody (IgM) and complement-coated sheep red blood cells; AHTG=anti-human-T-cell globulin (Courtesy of H. Rodt, M.D., Institut für Hämatologie, Abteilung Immunologie, GSF, München).

[1] Courtesy of P. R. L. Beverly, M.D., London.

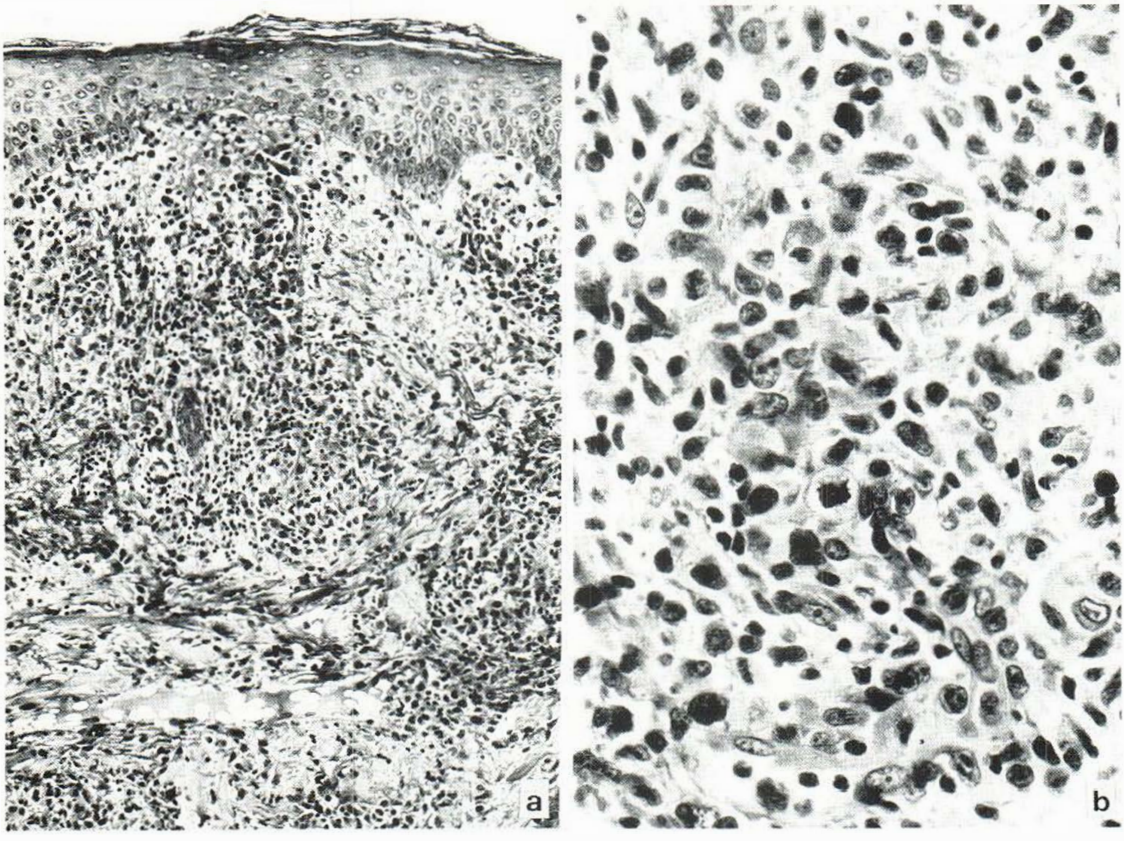

Fig. 1. (*a*) Lymphomatoid papulosis. Polymorphous infiltrate in the upper dermis, infiltrating the epidermis. HE. ×125. (*b*) Large atypical lymphoid cells of various sizes and shapes. HE. ×455.

may be normal or may show eczematous changes of varying degrees with invasion of lymphoid cells.

Enzyme cytochemistry

In cryostat sections the lymphoid cells of varying sizes and shapes show a focal paranuclear acid phosphatase reaction. A dot-like paranuclear intracytoplasmic reaction is also seen with acid α-naphthylacetate esterase in some of the cells from single-cell suspensions of homogenates from cutaneous tumorous infiltrates.

Table I. *Data on the 3 patients with lymphomatoid papulosis*

	Age (y.)	Localization of papules	Follow-up (y.)
1. K. R. ♂	5	Extremities	1
2. H. G. ♂	50	Extremities	2
3. Z. A. ♂	41	Face and trunk	7

Immunocytological typing (Table II)

In one of the patients (Z. A.) cells were freed from a cutaneous infiltrate. Ninety-five percent of the lymphoid cells evidenced spontaneous rosette formation with sheep red blood cells. With erythrocyte-antibody (IgM)-complement (EAC) complexes, neither rosette formation in cell suspensions nor fixation on cryostat sections could be found.

Immunohistochemical findings

In tissue sections, most of the perivascular infiltrating cells in the upper and mid-dermis were labelled by anti-T-cell globulin (AHTG) whereas the cells infiltrating the corium scattered between the small vessels were only partly stained by AHTG. The cells infiltrating the epidermis consisted almost entirely of T-lymphocytes, many of them found in lower areas of rete ridges or arranged in cell clusters. B-lymphocytes labelled by anti-IgM and anti-kappa or -lambda are very rare. When using mono-

Table 11. *Immunocytological typing of cells in lymphomatoid papulosis*

Patient	Fixation of EAC on cryostat sections	Tissue homogenate		Peroxidase-anti-peroxidase-technique[a]			
				Anti-human T-cell globulin[b]		Surface-Ig IgG, A, M, kappa, lambda	Intracytoplasmic IgG
		E-RFC	EAC-RFC	Upper dermis	Mid and deep dermis		
1. K.R.	Negative	Not done		>50%	>75%	Few cells	Occasional cells
2. H.G.	Negative	Not done		Rare cells	>75%	Few cells	Not done
3. Z.A.	Negative	95%	ø	>50%	>75%	Few cells	Occasional cells

[a] Demonstration of lymphoid cells.
[b] Courtesy of H. Rodt, M.D., GSF, Munich.

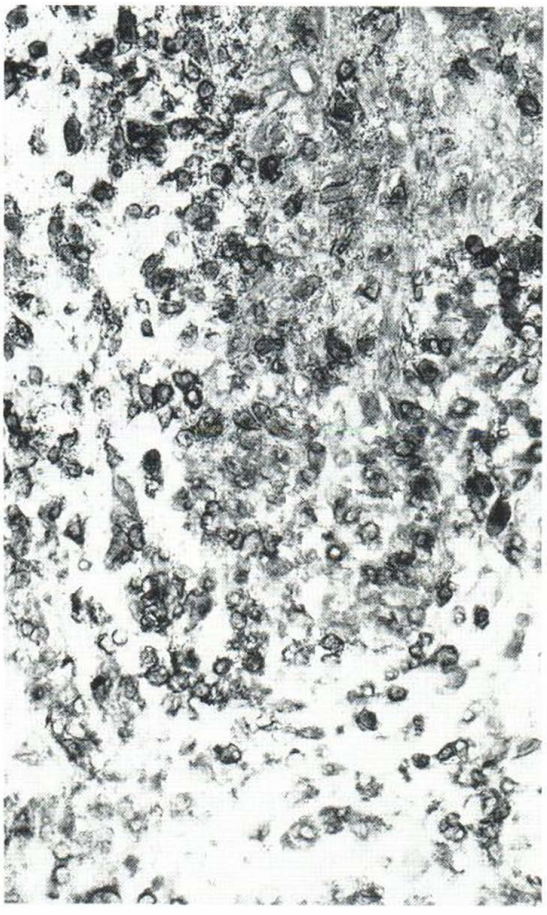

Fig. 2. Lymphomatoid papulosis. Labelling of most of the mononuclear round cells in the dermis by use of anti-T-cell globulin in the peroxidase–antiperoxidase technique. ×250.

clonal antibodies in one case (Z. A.) the lymphoid cells were labelled with anti-pan T-antibodies (T28[1], OKT3) and with an anti-helper T-cell antibody (OKT4) but were negative with suppressor T-cell antibodies (OKT5 and OKT8) (Fig. 2).

Findings on semithin and thin sections

On semithin sections (Fig. 3) in addition to small and medium-sized lymphocytes numerous blast-like cells were seen with large clear nuclei containing one to three prominent nucleoli. Typical Sézary-like cells were rarely observed.

On thin sections (Fig. 4) the large cells revealed a morphology consistent with immunoblasts. Their size varied between 11 and 17 μm; the nuclei were euchromatic, the nucleoli were generally centrally located. In the cytoplasm, numerous vesicles, some microvesicular bodies, free ribosomes and a moderate ergastoplasmic reticulum, and occasionally dense bodies were noted.

DISCUSSION

Lymphomatoid papulosis (LP) is a strange disease—clinically benign, histologically malignant. However, fatal outcomes have been reported in some cases in recent reviews (1, 2, 7, 14, 18, 19). Typical cases of LP show a clear distinction, both clinically and histologically, from pityriasis lichenoides et varioliformis acuta (PLEVA) (18, 20).

[1] Courtesy of P. C. L. Beverly, M.D., London.

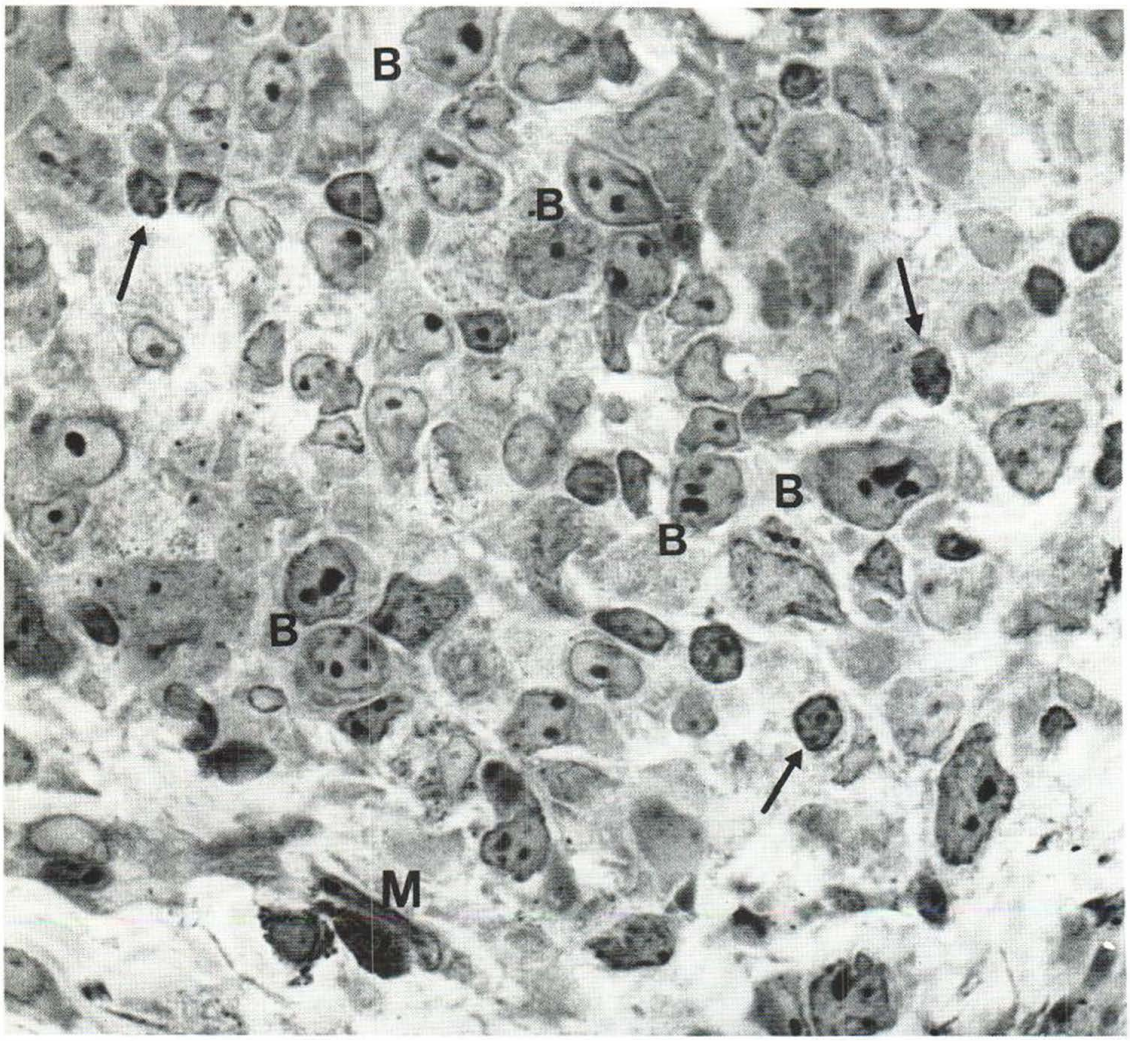

Fig. 3. Lymphomatoid papulosis, semithin section. Within the dermal infiltrate numerous blast cells (*B*) are seen; in addition, small lymphocytes (→) and occasional mast cells (*M*). ×1200.

However, in borderline cases a differentiation between the two disease entities may be difficult.

From immunohistochemical and electron microscopic studies in one patient with LP it has recently been suggested, that the infiltrating cells in lymphomatoid papulosis are primarily derived from variants of T-lymphocytes (13).

We have tried to further characterize the lymphoid cells in 3 patients with LP by means of more specific enzyme cytochemical and immunological tests.

The diagnosis in the 3 cases studied was based on the following criteria: 1) recurrent episodes of papular skin eruptions, 2) spontaneous regression, 3) follow-up of up to 7 years, 4) presence of atypical large lymphoblastoid cells within the dermal infiltrates.

T-lymphocytes are characterized by their focal paranuclear reaction with acid-phosphatase and acid α-naphthylacetate esterase (3, 12, 17). Most of the lymphoid cells in infiltrates of LP show a positive reaction for acid phosphatase.

In cryostat sections, subpopulations of lymphocytes can be differentiated according to their surface antigens, by using the unlabelled antibody enzyme method (4, 5, 8, 9, 10, 11, 23). Most of the

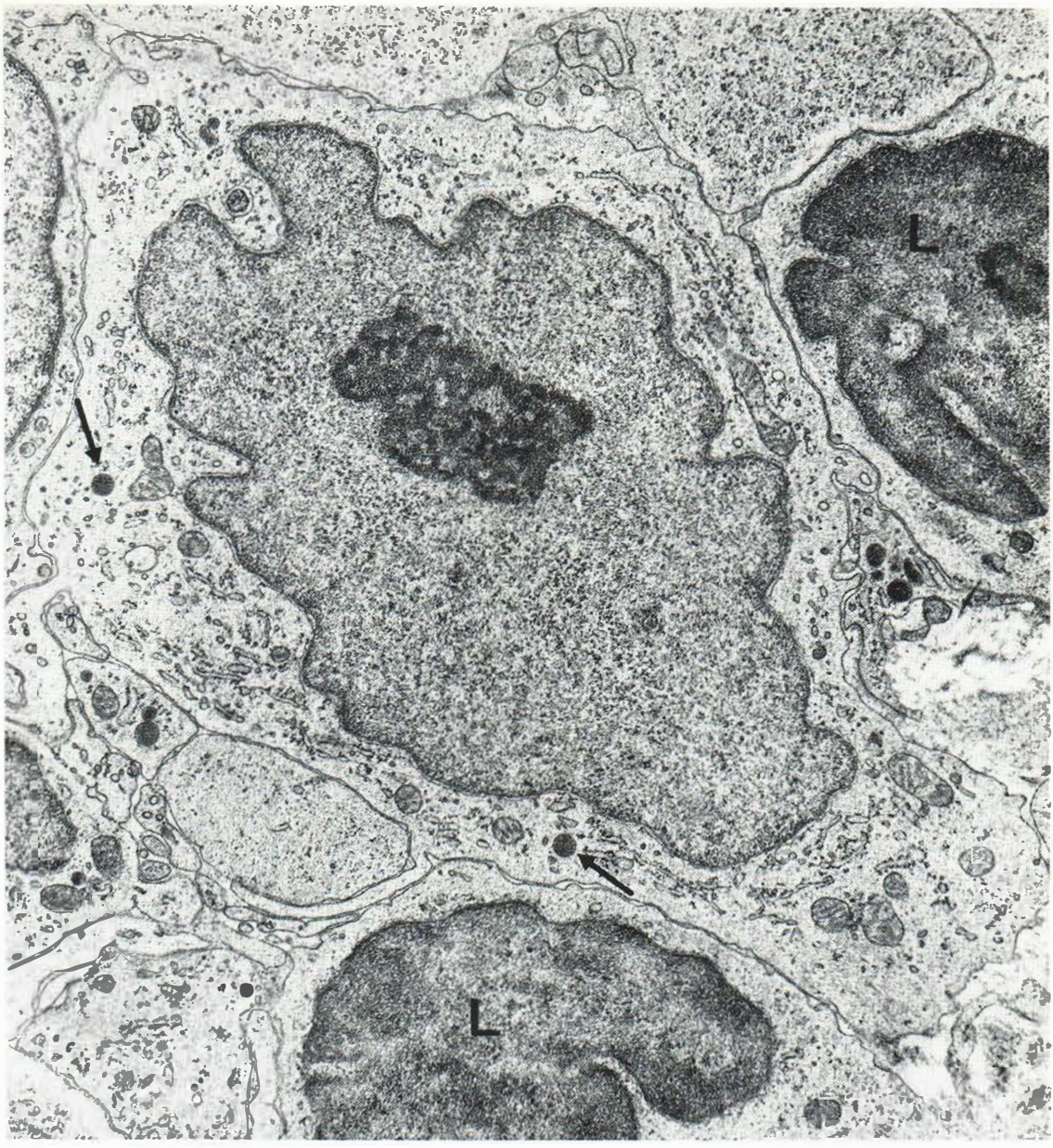

Fig. 4. Lymphomatoid papulosis, thin section. Next to two small lymphocytes (*L*) an immunoblast is shown, characterized by a large and euchromatic nucleus with a prominent and centrally located nucleolus. The cytoplasm is more abundant and contains mitochondria, some ergastoplasmic reticulum and a few dense bodies (→). ×13300.

lymphoid cells in LP could be demonstrated to be stained by a specific anti-human T-cell globulin (21). In one patient (Z. A.) the lymphoid cells showed helper T-cell-specific antigen as shown by a monoclonal antibody (OKT4) but only a few cells were positive with monoclonal anti-suppressor T-cell antibodies (OKT5, 8). Receptors for C_3 (EAC rosettes) and for antibodies against human kappa and lambda light chains and heavy chains of IgM, IgG and IgA were lacking.

Our results indicate that most of the lymphoid cells in the LP show markers of T-lymphocytes which were T-helper cells in the one case studied with monoclonal antibodies. Taking into account the benign clinical course showing self-involutive papules (rhythmic paradoxic eruptions), LP is classified as pseudolymphoma simulating cutaneous T-cell lymphoma.

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