

## CUTANEOUS LYMPHOCYTOMAS: CLINICAL AND HISTOLOGICAL ASPECTS

Gunhild Lange Wantzin, Klaus Hou-Jensen, Mads Nielsen,  
Jens Petri and Kristian Thomsen

*Department of Dermatology and Department of Pathology,  
The Finsen Institute, Copenhagen, Denmark*

**Abstract.** 25 cases of cutaneous lymphocytoma were reviewed, of which 13 were benign lymphocytoma of the skin and 15 lymphocytic infiltration of the skin (Jessner). The clinical diagnosis benign lymphocytoma of the skin was in agreement with the histology, except in 2 patients where lymphocytic infiltration of the skin (Jessner) was the most likely clinical diagnosis. Of the 15 patients treated, 8 went into complete remission and 5 into partial remission. Eight patients suffered a relapse after partial and complete remission. The duration of the follow-up period varied between 2 months and 22 years. The histological diagnosis lymphocytic infiltration of the skin (Jessner) tallied in 9 patients with the clinical diagnosis, whereas in 6 patients the clinical diagnosis was benign lymphocytoma or pseudolymphoma. None of the patients developed systemic malignancy within the lymphoreticular system. A suspicious-looking skin lesion should always require further examination in order to exclude cutaneous manifestations of a systemic malignant lymphoreticular disease. The present histologic review demonstrates some uncertainty in diagnosing cutaneous lymphocytomas.

**Key words:** Lymphocytic infiltrates (Jessner); Lymphocytoma cutis benigna

The differentiation between benign and malignant lymphocytic infiltration of the skin can clinically as well as histologically be very difficult. This problem has recently been considered by Evans et al. (5) by reviewing 57 cases on suspicion, of malignant lymphoma. Of these cases 19 were histologically regarded as benign lymphoid hyperplasia. But also in distinguishing between the different types of benign cutaneous lymphocytic infiltrates great difficulties may arise clinically and to some extent also histologically. Histologically and clinically the picture is complex and indistinct terminology adds to the confusion. Patients with lymphocytic infiltration of the skin (Jessner) were included in the investigation in order to study the interrelation between benign lymphocytoma of the skin and Jessner and to

compare the clinical aspects with the histological diagnosis.

The aim of the present investigation was to ascertain whether patients with benign lymphocytomas had an invariably benign course and to compare the clinical findings with the histological changes.

### MATERIALS AND METHODS

The file of the dermatological department of the Finsen Institute were searched for cases under the diagnoses benign lymphocytoma of the skin, pseudolymphoma, and lymphocytic infiltration of the skin (Jessner) over the last 10 years (1970-80).

Twenty-five patients were reviewed, of whom 13 had benign lymphocytoma of the skin, 15 lymphocytic infiltration of the skin (Jessner) and 3 had both diagnoses but on different areas of the skin. In none of the patients could insect bites be blamed. Clinical follow-up was done by re-examination of all patients, of whom 19 of 25 turned up. The biopsies were reviewed and new biopsies taken if any skin lesions were present. Histologically the cases were classified according to Clark et al. (3) as modified by From (6).

*Type 1:* superficial perivascular infiltrate with focal epithelial involvement.

*Type 2:* deep perivascular infiltrate without epithelial involvement.

*Type 3:* a dermal, predominantly lymphocytic infiltrate which appears patchy due to its perivascular and sometimes periappendicular distribution. There are always degenerative changes in the collagen (mucinosis), however of varying and mostly slight degree. The epidermis is unaffected. This type corresponds clinically to Jessner's lymphocytic infiltration of the skin.

*Type 4:* a dense cellular infiltration of the dermis mostly sparing the papillary dermis. The cell infiltrate consists of a mixture of lymphocytes, histiocytes, plasma cells, mast cells and eosinophils with a predominance of lymphocytes, some of which may be immature. In the infiltrate, which is nodular often imitating germinal centres, many newly formed small vessels with prominent plump endothelial cells can be seen. Usually the epidermis is unaffected, but slight reactive hyperplasia may be seen.

*Type 5:* similar to type 4 with the exception that the infiltrate is diffuse without any nodularity. Clinically, types 4 and 5 correspond to benign lymphocytoma of the skin.

*Type 6:* characterized histologically by atypical mononuclear cell infiltrates.

## RESULTS

### *Benign lymphocytoma of the skin*

Thirteen patients were histologically diagnosed as having benign lymphocytoma of the skin. There were 5 women and 8 men. The age of the patients varied between 26 and 78 years with a median of 50.

The lesions were asymptomatic, red to red-purple papules or nodules. Six patients had solitary lesions and 7 patients had multiple lesions. In 9 patients the lesions were localized to the trunk and/or extremities, whereas in 4 patients the lesions were located to the face and thus always solitary.

The clinical diagnosis was in agreement with the histology, except in 2 patients where lymphocytic infiltration of the skin (Jessner) was the most likely clinical diagnosis. In all patients laboratory investigations were normal including antinuclear antibody test and LE cells. The treatment consisted of topical steroids, systemic antibiotics, local radiotherapy, hydroxychloroquine and excision. Of the 13 patients, 8 went into complete remission and 4 into partial remission followed by relapse in 8 patients. The duration of the initial lesions varied between 1 month and 5 years. The follow-up period varied between 1 month and 22 years (Table I). None of the patients developed systemic malignancy within the lymphoreticular system.

### *Histology*

In 9 cases the histologic picture was consistent with the diagnosis of lymphocytoma benignum (type 4/5). In fourteen biopsies from 6 cases the histologic picture aroused suspicion of malignancy due to some degree of aggressive growth pattern, immaturity or even atypical mononuclear cells participating in the cell infiltrate and/or mitotic activity.

### *Lymphocytic infiltration of the skin (Jessner)*

Fifteen patients were histologically diagnosed as having lymphocytic infiltration of the skin (Jessner). There were 9 women and 6 men. The age of the patients varied between 19 and 74 years, with a

Table I. Duration of follow-up period in 12 patients with benign lymphocytoma of the skin

	Follow-up period		
	<1 yr	1-3 yrs	>8 yrs
Number of patients	2	7	3

median of 42. The lesions were asymptomatic, dull red, deeply located papules or plaques, in 5 cases solitary and in 10 cases, multiple. Lesions were seen on the face in 8 patients, on the trunk in 7, on the extremities in 3 patients and on the scrotum in 1 patient.

The histological diagnosis was in 9 patients in agreement with the clinical diagnosis, whereas in 6 patients the clinical diagnosis was benign lymphocytoma or pseudolymphoma. In all patients laboratory investigations were normal, including antinuclear antibody test and LE cells. The treatment given had been topical steroids, penicillin, hydroxychloroquine, excision and local radiotherapy. Of the 15 patients treated, 8 went into complete remission, and 5 into partial remission. Eight patients showed relapse after partial and complete remission. The duration of the follow-up period varied between 2 months and 22 years (Table II). None of the patients developed systemic malignancy within the lymphoreticular system.

### *Histology*

The biopsies from the Jessner-cases showed a distinct histologic picture. Three biopsies, however, showed a slightly atrophic epidermis with follicular plugging and a slight hydropic degeneration of the basal layer, indicating a conceivable diagnosis of lupus erythematosus. In two biopsies exocytosis and confinement of the perivascular lymphocytic infiltrate to the upper dermis brought a type 1 (superficial perivascular infiltrate with focal epithelial

Table II. Duration of follow-up period in 13 patients with lymphocytic infiltration of the skin (Jessner)

	Follow-up period		
	<1½ yrs	2-4 yrs	>10 yrs
Number of patients	5	5	3

involvement as seen in erythema annulare centrifugum) into consideration. In one biopsy the perivascular infiltrates were so sparse that no specific histologic diagnosis could be established.

#### *Histological transition to malignancy*

Five patients had sequential biopsies taken due to clinical and/or histological suspicion of malignancy. The 2 following patients illustrate this diagnostic problem. In one patient three successive biopsies in 2 years were taken from the same lesion from the left leg (Fig. 1). In the first biopsy perivascular lymphocytic infiltrates were seen. In the next biopsy, the infiltrate was dense, with an admixture of plasma cells and some vascular proliferation. In the last biopsy the infiltrate had become even more dense and eosinophils had appeared. Furthermore the histologic picture in the last biopsy aroused a suspicion of malignancy due to some mitotic activity, single filing of cells between collagen bundles and the presence of histiocytic cells with prominent nucleoli and vesicular nuclei (Fig. 2).

In another patient eight biopsies within 8 years were taken from a skin lesion on the right hip (Fig. 3). Only the fifth biopsy revealed a histologic picture which was evidently benign (Fig. 4). The remaining seven biopsies showed various features of malignancy due to mitotic activity, dominance of immature looking lymphocytic cells, presence of atypical reticular cells and single filing of cells between collagen bundles (aggressive growth patterns) (Fig. 5). The clinical course, however, was completely benign over an observation period of 8 years.

## DISCUSSION

### *Benign lymphocytoma of the skin*

The term benign lymphocytoma of the skin covers the disease also known as Spiegler-Fendt sarcoid, lymphadenosis benignum cutis (Bäfverstedt) and pseudolymphoma (1, 10). Clinically benign lymphocytomas of the skin are characterized by single or multiple purple papules or nodules which may disappear and recur with or without treatment. None of our patients developed systemic malignancy within the lymphoreticular system during the follow-up period, which in 10 patients was more than 1 year.

Malignant degeneration has been claimed not to

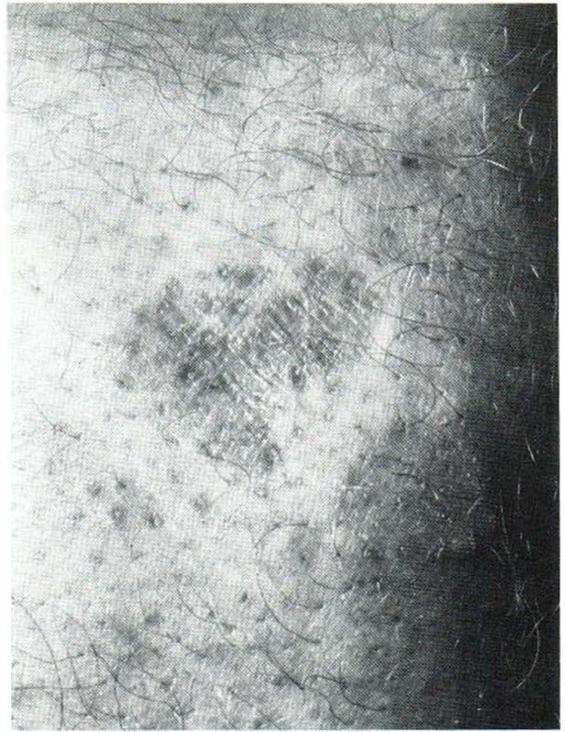


Fig. 1. Single dull red plaque on leg.

occur (11) whereas other authors have reported transformation of lymphocytoma into malignant lymphoma (7, 8). Also an association of lymphocytoma with other malignant tumours such as carcinoma and dermatofibrosarcoma has been reported (2, 4). In the present study it was not possible to demonstrate malignant transformation in any of the patients. In one patient (Fig. 5) the histology, however, was suspect for malignancy because of atypical reticular cells and mitosis which varied in appearance over the observation period of 8 years with only one of the biopsies being completely benign (Fig. 4). The clinical course in this patient has so far been benign, with spontaneous remission and successive relapses. The histological picture of the biopsies that aroused suspicion of malignancy in this patient has a considerable resemblance to the large-cell lymphocytoma described by Duncan et al. (4) with the exception that these authors affirm the nodularity of the infiltrate as a characteristic feature of the histologic pattern, whereas the infiltrate in the biopsies of our patient was diffuse.

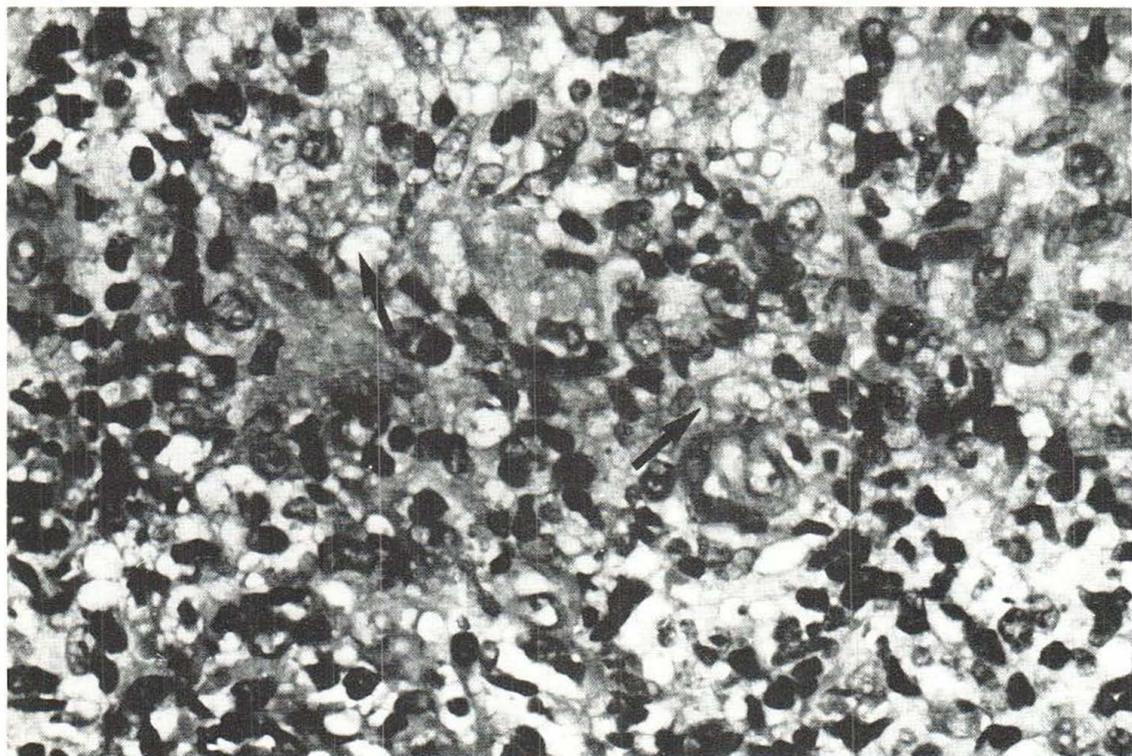


Fig. 2. Photomicrograph showing dense infiltrate with atypical lymphoreticular cells (arrows)  $\times 400$ .

*Lymphocytic infiltration of the skin (Jessner)*

The lesions are characterized by erythematous papules or plaques, often with central clearing. The lesions may disappear and reappear. Histologically, lymphocytic infiltration of the skin (Jessner) is classified as type 3 by From (6) as a patchy, perivascular, sparse to moderate lymphocytic infiltrate. In the present study of lymphocytic infiltration of the skin (Jessner) the histological diagnosis was evident in all cases, although in a few biopsies focal epithelial involvement was seen, indicating a type 1 lesion (superficial perivascular infiltrate with focal epithelial involvement) (6). One patient (Figs. 1 and 2) with a histologically diagnosed lymphocytic infiltration of the skin (Jessner) later showed transformation to benign lymphocytoma of the skin but with histological features of malignancy.

In conclusion, a suspicious looking skin lesion should always warrant further examination in order to exclude cutaneous manifestations of a systemic malignant lymphoreticular disease. The histological suspicion of malignancy alone should not indicate

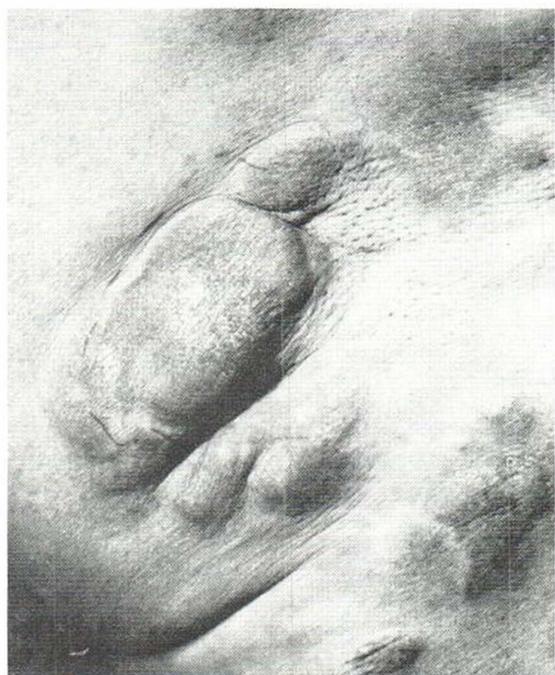


Fig. 3. Red-purple plaques and nodules on right hip.



Fig. 4. Photomicrograph showing nodular infiltrate with a mixture of mononuclear inflammatory cells.  $\times 250$ .

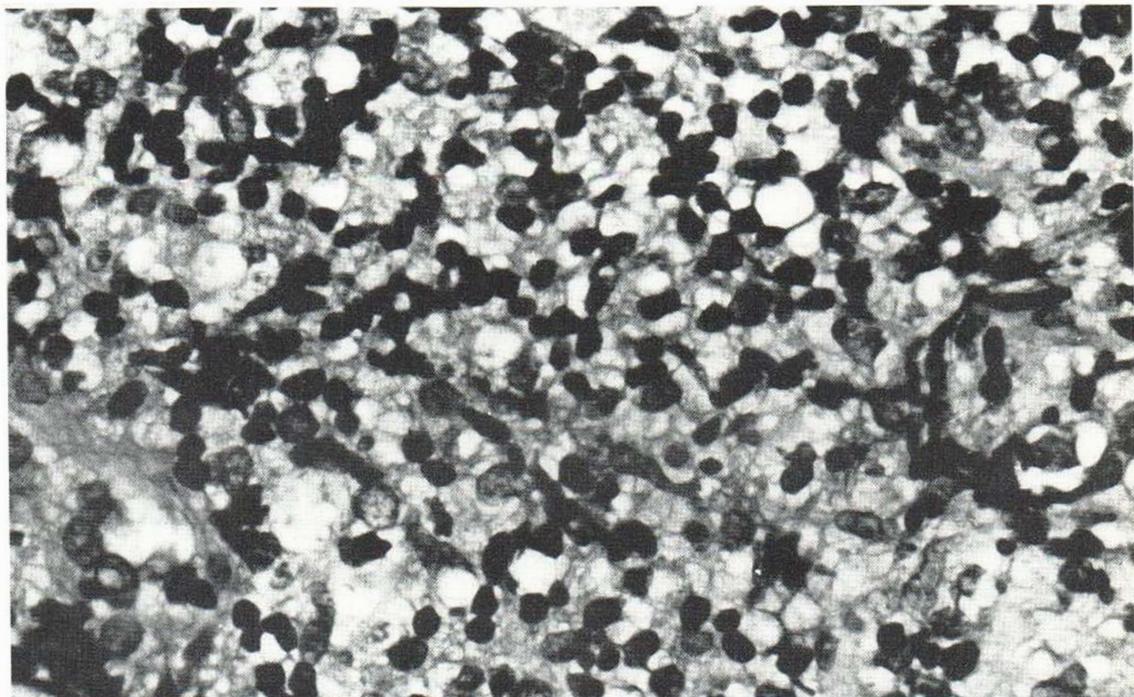


Fig. 5. Photomicrograph demonstrating immature lymphocytes and atypical reticular cells.  $\times 400$ .

antineoplastic treatment when the clinical course and other investigations favour a benign disorder. Large excision biopsies should whenever possible be performed to facilitate and improve histologic evaluation.

The present histologic review demonstrates some uncertainty in diagnosing cutaneous lymphocytomas. However, flow-cytometric DNA studies of the infiltrates may prove a useful diagnostic way of distinguishing between benign and malignant disorders. Further studies comparing flow-cytometric DNA measurements and histology are in progress.

#### ACKNOWLEDGEMENT

We thank B. Bruun-Rasmussen, M. D., Department of Pathology, The Finsen Institute, for performing the photomicrography.

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Received June 24, 1981

G. Lange Wantzin  
Department of Dermatology  
The Finsen Institute  
49, Strandboulevarden  
DK-2100 Copenhagen Ø, Denmark