Lymphomatoid Papulosis: A Follow-up Study

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A follow-up study has been performed on 16 patients with lymphomatoid papulosis diagnosed at the Finsen Institute during the years 1970–81. In none of the patients did malignant lymphoma develop during the observation period (7 months to 22 years). During this period the nature of the lesions and the tendency to recurrence were unchanged in 11 patients, spontaneous remission took place in 4, and 1 patient went into complete remission after PUVA treatment (8-methoxsalen followed by UVA). The histological material (32 punch biopsies) could be divided into two major groups diagnosed as either typical (16 biopsies) or consistent with lymphomatoid papulosis (16 biopsies). Based on our present knowledge, we suggest the following classification of lymphomatoid papulosis: 1) "classical" lymphomatoid papulosis, 2) lymphomatoid papulosis associated with parapsoriasis en plaque or mycosis fungoides and 3) primary cutaneous T-cell lymphoma. *Key words: Lymphomatoid papulosis; Malignant lymphoma.* (Received April 18, 1983.)

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Lymphomatoid papulosis, originally described by Macaulay (1) in 1968, is a clinically benign, papular skin disorder with an alarmingly lymphoma-like histology (2, 3, 4). Difficulties have arisen in trying more precisely to define this paradoxical rhythmic disorder—or, perhaps, group of disorders. Lymphomatoid papulosis has been considered by some as a variant of pityriasis lichenoides (5, 6) and by others grouped with mycosis fungoides and Sézary syndrome as a cutaneous T-cell lymphoma. Moreover, the results of studies on the clinical course have been controversial, with reports of an invariably benign course (2, 7), contrasting with reports of a malignant outcome (5, 8, 9, 10, 11, 12).

A clinical study has been made of 16 patients with lymphomatoid papulosis, in order to try to clarify the clinical picture and the long-term course, with particular emphasis on the development of malignant lymphoma. Further, we reviewed our biopsy material in order to re-evaluate the histological criteria.

MATERIAL AND METHODS

Sixteen patients from the dermatological department of the Finsen Institute, diagnosed as having lymphomatoid papulosis during the years 1970–81 have comprised the subject of a thorough clinical examination (Table I) supplemented by haematological studies, urinanalysis and X-ray of the lungs. In 4 cases a bone-marrow examination was performed, as well as bipedal lymphangiography. All the skin biopsies sampled over the years of follow-up were re-examined by one of us (K. H. J.). A follow-up study of all patients has been successful, with observation periods ranging between 7 months and 22 years. It should be noted that cases 8, 9, 10, 11, and 12 (Table I) have been published previously (7) as also cases 1, 2, 3, 14, and 15 (13, 14).

RESULTS

Clinical (Table I)

Skin lesions. Lesions were recurrent dark-red papules and nodules, but one patient (case 1) also presented 1–2 cm recurring tumours. In 9 patients, ulceration of the lesions was

observed and in 10 patients the lesions left white, atrophic scars. The course of a typical papular lesion is demonstrated in Fig. 1.

Clinical course. During the observation period the nature of the lesions and the tendency to recur were unchanged in 11 patients. In 5 patients, lesions ceased to develop, in

Table I. *Clinical data of 16 patients with lymphomatoid papulosis*

Patient	Sex	Age at onset	Duration month(s)	Type of lesion	Average no. of lesions	Sites of lesions	Life-cycle of lesions (weeks)	Follow-up (months)	Other manifestations	Comment
1	M	26	120	Nodules Tumours	60	Face Trunk Extremities	4–6	35	Splenectomy 12 years earlier	PUVA
2	F	43	30	Papules	12	Face Trunk Extremities	4–6	92	Adenocarcinoma of the breast Parapsoriasis en plaque	PUVA
3	F	30	3	Papules	35	Extremities	3–6	20		CR after PUVA
4	M	58	1	Papules Nodules	10	Extremities	4–6	23	Rheumatoid arthritis Parapsoriasis en plaque	
5	M	63	24	Papules	<10	Trunk Extremities	4–6	38	Parapsoriasis en plaque	
6	M	36	96	Papules	<10	Trunk Extremities	4–6	12	Parapsoriasis en plaque	
7	M	60	12	Papules	<10	Extremities	4–6	7		CR after biopsy
8	F	59	12	Papules	20	Face Extremities	4–8	264		CR spontaneous
9	F	53	36	Nodules	20	Extremities	4	96	Contact Dermatitis	CR spontaneous
10	F	49	300	Papules	<10	Face Palms	3	121	Carcinoma of the tongue	
11	F	27	120	Papules	15	Extremities	4	192		
12	F	20	36	Nodules	<10	Extremities	4	144		
13	M	32	12	Papules	15	Trunk Extremities	4–6	10		CR spontaneous
14	M	57	1	Papules	<10	Trunk Extremities	4–6	144	Erythroderma	PUVA
15	F	47	60	Papules	15	Trunk Extremities	4–6	13		PUVA
16	M	49	24	Papules Nodules	10	Extremities	4–6	14	Malignant melanoma of the chorioidea	

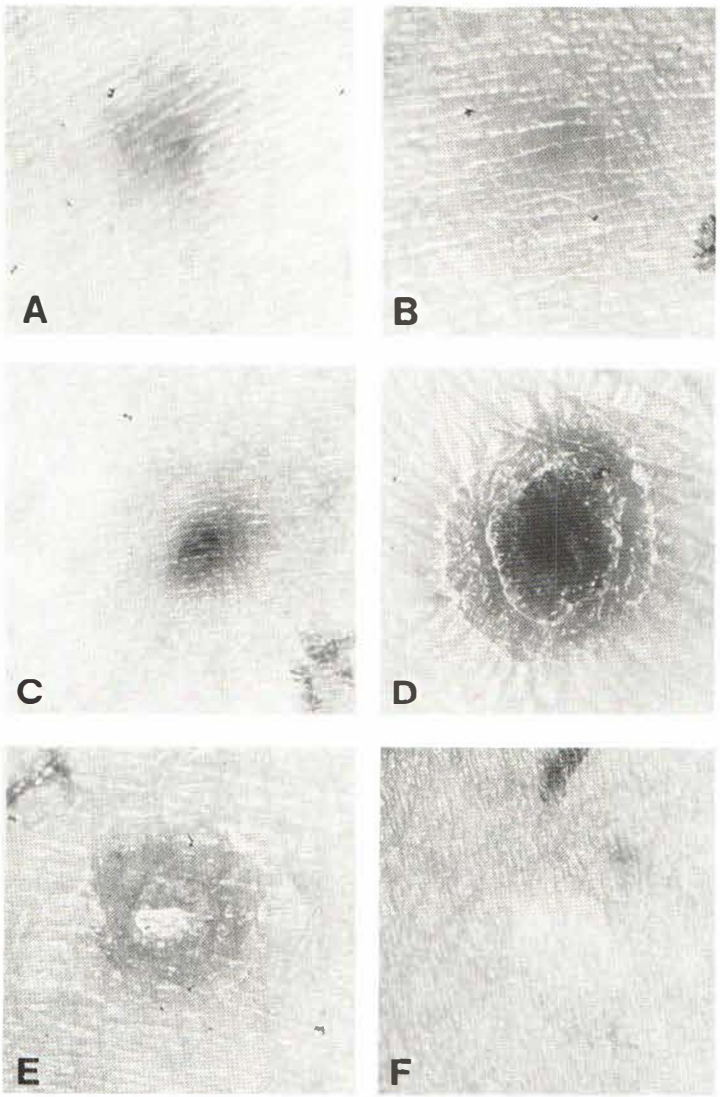

Fig. 1. An example of the course of a typical lesion: pink papule (3 A), formation of a central vesicle (3 B), which turns into a pustule (3 C); the lesion becomes inflamed, covered with a crust (3 D), it subsequently flattens and is covered by a scale (3 E) and finally a white atrophic scar is formed (3 F).

cases 8, 9 and 13 spontaneously, while remission in case 7 apparently occurred following biopsies.

In case 3, PUVA treatment (8-methoxsalen followed by UVA) resulted in complete remission which has now been maintained for 12 months. Neither cutaneous nor systemic lymphomatous disease was observed during the observation period in any of the 16 patients.

Concomitant disease. Parapsoriasis en plaque was diagnosed in 4 patients (cases 2, 4, 5, and 6), allergic contact dermatitis in 1 (case 9) and exfoliative erythroderma in 1 patient (case 14). Before the appearance of lymphomatoid papulosis, 3 patients (cases 2, 10, and 16) had been treated successfully for internal cancers (Table 1). One patient (case 1) had been splenectomized 12 years before because of a traumatic spleen rupture.

Treatment. PUVA (oral 8-methoxsalen followed by UVA) treatment resulted in com-

plete remission in one patient (case 3), now maintained without further treatment for 12 months, and in partial remission in 4 other patients (cases 1, 2, 14, and 15) (13).

Histology. The biopsy material from 16 patients with lymphomatoid papulosis consisted of 32 punch biopsies; 4 patients had 1 biopsy, 8 patients 2 biopsies, and 4 patients 3 biopsies each. The paraffin sections were all stained with haematoxylin eosin.

The histological material could be divided into two equal groups diagnosed as either typical (16 biopsies) or consistent with lymphomatoid papulosis (16 biopsies).

Major changes were present in the epidermis in less than half of the biopsies (Table II). Obscure dermo-epidermal junction was present in 7 biopsies only and was not a dominant feature in this material. Many lymphoid cells are mandatory for the diagnosis of lymphomatoid papulosis and in the typical biopsies, large atypical lymphoid cells were usually noticed. Small-vessel vasculitis with discrete collections of neutrophils was a frequent finding in the typical biopsies as also was a modest quantity of eosinophils. Nuclear dust as found in allergic vasculitis was rare. Large binucleate cells were found in 9 biopsies, but none of these were typical Reed-Sternberg cells with large nucleoli surrounded by a light halo.

DISCUSSION

This study presents the clinical and histological features of 16 patients with the remittent, eruptive papular disease lymphomatoid papulosis. These findings are identical with those reported in other studies (3, 4) except for the sex distribution, which has previously been found to be dominated by women, whereas we found an equal female–male ratio.

In 6 patients a concomitant cutaneous disorder was found, a phenomenon also observed by others (14, 15, 16), and it has been proposed (14) that the simultaneous presence of another skin disease such as parapsoriasis en plaque or erythroderma might herald the later development of malignancy. Perhaps this is not true, as normal DNA histograms by flow cytophotometry (17) were found in one of these patients, whereas one would expect that an abnormal DNA histogram would be present in latent malignancy.

Table II. *Histologic findings in 32 punch biopsies from 16 patients with lymphomatoid papulosis*

	Number of biopsies		Number of biopsies
Epidermis		*Dermis*	
Spongiosis	12	Inflammatory infiltrate located	
Parakeratosis	2	Superficial perivascular	30
Ulceration	6	Deep perivascular	27
Pautrier abscess	1	Interstitial	27
		Type of inflammatory cell	
		Many lymphocytes	32
		Abnormal lymphocytes	17
		Scattered neutrophils	16
		Scattered eosinophils	13
		Few nucleated cells	9
		Nuclear dust	0
		Papillary fibrosis	7
		Small-vessel vasculitis	21
		Large-vessel vasculitis	3
		Prominent endothelial cells	17

It is remarkable that none of the 16 patients in this study demonstrated an evolution into a malignant lymphoma during an observation period as long as 22 years. One of the patients (case 1) is, however, at present under close observation because of intense disease activity and large, tumour-like lesions in the skin. In a recent study by Sanchez et al. (11), 6 out of 31 patients eventually developed a lymphoproliferative disorder during an observation period of up to 18 years and others have found that malignant lymphoma developed in about 10% of the cases.

PUVA treatment of 5 patients has so far shown promising results, with complete remission in one patient and partial remission in 4 (Table I). Christophers (18) treated 4 cases of lymphomatoid papulosis with similar good results.

Histopathologically, the typical lymphomatoid papulosis lesion has been characterized by a superficial and deep, often wedge-shaped cellular infiltrate, most dense in the papillary dermis where it tends to obscure the dermo-epidermal junction (4). In our material we were not surprised to find that only 50% (16 biopsies) were typical of lymphomatoid papulosis, while the remaining biopsies were consistent with lymphomatoid papulosis as developing lesions change in histologic appearance (2, 4, 19). Some biopsies showed a similarity to pityriasis lichenoides, but no cases were diagnostic for or clinically suspect of this disease, even if lymphomatoid papulosis has been considered by some to be a variant of pityriasis lichenoides (3); as recently shown by Hood & Mark (20) the histological picture of pityriasis lichenoides can also be found in a wide variety of diseases, such as pityriasis rosea, insect bites and eczema.

Due to the presence of large atypical lymphoid cells in the dermal infiltrate, lymphomatoid papulosis has been related to malignant lymphoreticular neoplasms and, together with mycosis fungoides and Sézary syndrome, classified as a T-cell lymphoma. Cell membrane characteristics and electron microscopy (16) as well as reports of the disease culminating in malignant lymphoma support this concept. However, lack of lymph node- and bone marrow involvement as well as the clinical course in our material suggest that lymphomatoid papulosis also includes a distinctive, completely benign skin disorder. This benign biological nature of lymphomatoid papulosis is reflected by the demonstration of normal DNA histograms in 4 patients with lymphomatoid papulosis (17). However, one patient (case 1 of this study) showed abnormal DNA histograms. This patient had a somewhat diverging clinical picture, with tumours, nodules and papules and he always presented a far greater number of lesions than the remaining patients. We suspect that this patient has a primary cutaneous lymphoma.

Based on the literature and the present study of lymphomatoid papulosis, we suggest the following classification: 1) "classical" benign lymphomatoid papulosis, 2) lymphomatoid papulosis associated with parapsoriasis en plaque or mycosis fungoides, and 3) a primary cutaneous T-cell lymphoma.

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