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LICHEN PLANUS: A DISTINCT ENTITY FROM LUPUS ERYTHEMATOSUS

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Abstract. Thirty-five patients with classical lichen planus (LP) were extensively investigated with special reference to immunohistological changes and histocompatibility (HLA) typing. There was no evidence of lupus erythematosus (LE) in any patient, although one patient with LP and eczema had an elevated titre of antinuclear factor. There was no increased incidence of any HLA type—in particular HLA-B7 and HLA-B8—known to be associated with LE. The results suggest that LE and LP are separate disorders.

Key words: Lichen planus; Lupus erythematosus

It has been proposed that there is a relationship between LP and LE in view of certain clinical, immunological and histological similarities (7). The coexistence of the two conditions is relatively rare, as illustrated by the fact that in recent years there have been only isolated case reports (Table I).

In order to test this proposal, we investigated 35 unselected patients presenting with LP, for evidence of LE.

MATERIALS AND METHODS

Thirty-five patients with classical LP were investigated, 19 females and 16 males, whose ages ranged from 11 to 71 years. A clinical history, with particular reference to precipitating causes, associated conditions and family history, was taken and a full general examination was carried out.

The following haematological and serological investigations were performed: blood count, erythrocyte sedimentation rate (ESR), direct Coombs test, blood grouping, blood urea and electrolytes, liver function tests, serum IgG, IgA, IgM, complement C3 and C4. HLA typing was done by a modification of the micro lymphocytotoxic technique of Terasaki & McClelland (17) on lymphocytes separated from heparinized blood by the Ficoll-Triosil density gradient method (4). Antisera obtained from local antenatal patients, the National Tissue Typing Reference Laboratory, Bristol, and from the National Institute of Health, Bethesda, Maryland, identified 21 HLA antigens. The frequency of HLA antigens in the normal population was determined in 229 subjects. Skin biopsies, taken from lesions, were examined histologically with haematoxylin and eosin stain. Biopsies from both lesions and clinically uninvolved skin from light-exposed flexor aspects of the forearm were examined under immunofluorescence. The biopsies were quick frozen, using a bench-mounted CO_2 freezing unit. Sections were then cut from the block in a cryostat and washed in phosphate-buffered saline before being fixed in 95% ethyl alcohol. These sections were reacted in direct staining experiments with fluorescein isothiocyanate labelled gammaglobulin fractions and monovalent antiserum against human IgG, IgA, IgM, C1q, C3 and fibrinogen (15).

RESULTS

When compared with a random group of 35 patients attending the Skin Department but not known to have any connective tissue disease or LP, matched for age and sex, the only significantly associated factor appeared to be stress (Table II). The ESR, blood count, direct Coombs test, urea and electrolytes, liver function tests, immunoglobulins, serum complement and Paul-Bunell test, were all normal or negative. There was no rise in antibody titre to mycoplasma, herpes virus hominis, cytomegalovirus or Epstein Barr virus. Only one patient had an elevated titre of antinuclear factor (1 in 50 of the homogeneous pattern). The incidence of the antibodies listed in Table III is no higher than expected in a random sample of a normal population.

Table I. *Previous reports of cases showing overlap between lichen planus and lupus erythematosus*

	No. of patients
P. W. M. Copeman et al. (1970)	4
J. Thorman (1974)	1
M. G. Davies et al. (1977)	3
R. W. Romero et al. (1977)	11
T. H. Jamison et al (1978)	1
T. Piamphongsant et al. (1978)	2
Nagy & Szakaly (1978)	1

Table II. *Associated features in lichen planus*

	Patients	Controls	P^a
Number	35	35	
Stress	22	10	<0.01
Clinical diabetes	1	0	>0.05
Family history of diabetes	5	5	>0.05
Clinical thyroid disease	2	0	>0.05
Family history of thyroid disease	5	2	>0.05
Clinical atopy	7	4	>0.05

[a] Fisher's exact test.

Table III. *Circulating autoantibodies in lichen planus in 35 patients*

A.N.F.	1
Thyroid	4
Gastric parietal	1
Smooth muscle	1
Pemphigoid	1
Rheumatoid factor	2

Table IV. *HLA antigens in lichen planus*

HLA antigen	Phenotype Frequency: Patients (n=31)	Phenotype Frequency: Controls (n=229)	p corrected for 21 antigens
A3	0.35	0.30	>0.05[a]
A28	0.03	0.08	>0.05[b]
B5	0.16	0.07	>0.05[b]
B7	0.19	0.34	>0.05[a]
B8	0.32	0.21	>0.05[a]

[a] χ^2 with Yates correction.
[b] Fisher's exact test.

Table V. *HLA B7 in lupus erythematosus and lichen planus*
Males and females, onset 15–39 years

Lupus erythematosus	25/39
Lichen planus	2/6

P (Fisher's exact test) >0.05.

Table VI. *Histology of lesional skin in 34 patients with lichen planus*

	No. of patients
Basal cell damage	34
Colloid bodies	25
Melanophages	16
Dermal infiltrate	32

Table VII. *Immunohistology of lesional skin in 34 patients with lichen planus*

	No. of patients
Fibrin at basement membrane zone	30
Colloid bodies	30
Changes in blood vessels	9
Dermal band of IgG or C_3	0

Table VIII. *Immunohistology of uninvolved light-exposed skin in 31 patients with lichen planus*

	No. of patients
Normal	24
Colloid bodies	5
Fibrin	1
IgM at dermo-epidermal junction	2

HLA typing was carried out to 21 antigens. No significant association was demonstrated with any antigen. Table IV gives the data for A3 and B5 because of their previously reported association with LP, and B7 and B8 because of the known association with LE. An increased incidence of B7 has been shown in patients who develop discoid LE between the ages of 15 and 39 years (11) and Table V compares the incidence of B7 in patients with LP and LE of this age at onset group. A28 has been associated with LP in non-diabetics but there was no evidence of this in the present series.

All the skin biopsies of lesional skin were histologically, and on immunofluorescence, consistent with LP and not with LE. The features are summarized in Tables VI and VII. The immunohistological findings in uninvolved light-exposed skin are shown in Table VIII.

DISCUSSION

The relationship between LP and LE has aroused much interest in recent years. As previously mentioned, there have been cases reported in which a definite diagnosis could not be established due to clinical, histopathological and immunofluorescence overlap.

The present series of 35 consecutive patients with LP showed no clinical, immunological serological or pathological evidence of LE. Only one patient

constituted a clinical problem in diagnosis. This was a 71 year-old man with an elevated titre of homogeneous antinuclear factor. The distribution of his eruption on the backs of the hands, extensor aspects of the forearms and on the lips, raised the possibility of photosensitivity. Biopsy of lesional skin showed changes consistent with LP and not with LE. Uninvolved light-exposed skin showed no abnormality on immunofluorescence.

Histologically, LP and LE can be usually distinguished by the character of the lymphocytic infiltration in the areas of basal cell damage. In the former there is a heavy lymphocytic infiltration at the dermo-epidermal junction, whereas in the latter, the infiltration is patchy. Colloid or hyaline bodies can be seen in both LP and LE but are more numerous and more compactly aggregated in LP. Both conditions show erosive changes of the basal layer.

The immunofluorescent changes in LP are described in detail by Baart de la Faille-Kuyper & Baart de la Faille (1). Fluorescent ovoid bodies occur at the dermo-epidermal junction and in the dermis in association with fibrin and immunoglobulins, predominantly IgM and complement. The pattern of fibrin deposition is usually a linear broad band, although this may vary according to the age of the lesion. In LE the lesions show a granular band of IgG and C3 at the dermo-epidermal junction. This dermal band test was negative in all our cases. Some LE lesions may show ovoid bodies in conjunction with the linear basement membrane fluorescence. Immunohistology of light-exposed uninvolved skin in our patients with LP showed no evidence of LE. Five out of these 31 biopsies showed colloid bodies, which are not usually present in normal skin (2) but have been found in 3 out of 5 biopsies from clinically uninvolved sites of predilection in LP (1). The significance of IgM at the dermo-epidermal junction in 2 of our cases is not known, but Baart de la Faille-Kuyper et al. (2) found granular deposits of IgM in the basement membrane zone in 5 out of 23 biopsies from the skin of normal individuals.

The aetiology of both LP and LE is not known. Viruslike particles have been demonstrated by electron microscopy in both conditions (16, 19). Viruses have been suggested as a causative factor in certain exanthematic dermatoses, including LP (3). In the present series of LP we have found no evidence of a significant rise in antibody titre to a variety of viral antigens. Many textbooks suggest that stress may be a triggering factor and we have found a history of mental or physical stress preceding the onset of the rash significantly more frequently than in other patients of similar age and sex attending the Skin Department with other conditions.

Although it is likely that some individuals are genetically predisposed to LP, we have found no evidence of an association with any HLA type. This is in agreement with the work of Veien et al. (20) although other workers have shown an association with HLA-A3 and B5 in LP (10), B7 in familial LP (6) and A28 in non-diabetic patients with LP (8). In particular, there is no increased incidence of B7 or B8 types associated with certain groups of discoid and systemic LE patients (11).

Our evidence suggests that LP and LE are different diseases and that the occasional patient with clinical, histological and immunohistological overlap, probably has both diseases. LP is a common disorder and may coexist with other skin conditions.

Obsessive investigation, therefore, for evidence of LE in patients with classical LP is not required and patients should not be alarmed unnecessarily.

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