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HLA-DR and DQ Antigens in Lichen planus

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A study on HLA-DR and DQ typing in 40 patients with lichen planus (26 males and 14 females) and in 92 normal blood donors of both sexes was performed. Twenty-seven patients had cutaneous lesions, 11 cutaneous and mucosal involvement and 2 patients had oral erosive lesions. Serological typing revealed a highly significant increase of HLA-DR1 antigen in the patient group. No difference has been observed on the prevalence of DR1 antigen among the different clinical status of the disease. (Received May 8, 1987.)

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Lichen planus (LP) is a chronic papulosquamous disease that can affect skin and mucous membrane. The current literature about the pathogenesis of LP reflects a growing acceptance of a T-cell mediated immune mechanism (1–8). LP has been reported in patients with lupus erythematosus, myastenia gravis, alopecia areata and vitiligo, bullous pemphigoid and primary biliary cirrhosis. The detection of immune reactans at the basement membrane zone using direct immunofluorescence technique (9) and the recent demonstration of circulating antibodies reactive with epidermal antigens in patients with LP (10) are consistent with a proposed autoimmune pathogenesis.

Familial LP has been described (11–12) and an early HLA-study of LP patients showed HLA-A3 antigen to be significantly increased (13), but subsequent studies did not demonstrate statistically significant differences from normal controls (14–15).

Table I. *Results of serological HLA-DR and DQ typing in LP patients and controls*

Anti-gen	Patients (n=40) Pres-ent	%	Ab-sent	Controls (n=92) Pres-ent	%	Ab-sent	χ^2 with Yates' correction	p	Corrected p	RR	EF
DR1	26	65	14	15	16.3	77	28.64	3.35×10^{-7}	3.68×10^{-6}	9.53	0.58
DR2	11	27.5	29	21	22.8	71	0.12	0.72	7.92	1.28	0.06
DR3	4	10	36	21	22.8	71	2.21	0.14	1.54	0.37	−0.16
DR4	6	15	34	14	15.2	76	0.03	0.85	9.35	0.95	−0.006
DR5	8	20	32	39	42.4	53	5.16	0.02	0.22	0.33	−0.38
DR6	4	10	36	3	4.3	89	1.36	0.24	2.64	3.29	0.06
DR7	10	25	30	20	26.0	72	0.034	0.85	9.35	1.20	0.04
DR8	1	2.5	39	7	7.6	85	0.54	0.46	5.06	0.31	−0.05
DQ1	32	80	8	57	61.9	35	3.35	0.07	0.77	2.45	0.47
DQ2	13	32.5	27	41	44.6	51	1.22	0.27	2.97	0.59	−0.21
DQ3	15	37.5	25	46	50	46	1.28	0.26	2.86	0.60	−0.25

Because it is known that DR antigens can control the susceptibility and the expression of some immunologic disorders, we performed HLA-DR typing on patients with LP.

DQ antigens, which are class II antigens closely related to DR, were also typed during the study.

MATERIALS AND METHODS

Forty LP patients seen in our department, from October 1985 to October 1986, had HLA-DR and DQ typing carried out. There were 14 females and 26 males ranging in age from 30 to 60 years. Twenty-seven patients had cutaneous lesions, 11 cutaneous and mucosal involvement and 2 patients had oral erosive LP. No patient was suspected of having drug-induced LP. Ninety-two normal blood donors of both sexes were studied during the same time period, using the same methods and antisera. None had a personal and family history of LP. All of the subjects lived in the same geographic area as the patients and HLA testing was carried out without knowledge of the clinical status of the patients. HLA-DR and DQ typing was performed by the microlymphocytotoxicity test of Terasaki & McClelland for the following specificities: DR1, DR2, DR3, DR4, DR5, DR6, DR7, DQ1, DQ2, DQ3.

The significance of possible deviations between the frequencies observed in the patients and in the control subjects has been evaluated by means of χ^2 analysis with the correction of Yates for discontinuities. p values were then corrected by the number of antigens tested. The value of the strength and rank of association was obtained by calculating the relative risk (RR). We have also evaluated the etiological fraction (EF); EF value indicates how much of a disease is "due to" the disease-associated factor. It is computed from RR value and the frequency of the antigen in patients.

RESULTS

The results of HLA-DR and DQ typing are summarized in Table I, together with the calculated χ^2, p, corrected p values, RR and EF. HLA-DR1 was found to be significantly increased in LP patients with p and corrected p values of 3.35×10^{-7} and 3.68×10^{-6} respectively. The RR for patients with DR1 of developing LP was 9.53 and the EF value was 0.58. No difference has been observed on the prevalence of DR1 antigen among the different LP clinical status.

DISCUSSION

Our study on HLA-DR and DQ typing shows a striking statistically significant increase in the frequency of DR1 antigen in LP patients. These data are in partial agreement with a

concomitant study (16), where the serological typing for HLA Class II antigens in LP revealed a highly significant increase of HLA-DR1 and MT1 (DQ1) antigens. In our study, in fact, we have obtained furthermore a significantly high frequency of HLA-DR1. The frequency of DQ1 antigen is higher in the group of patients. The difference, however, with respect to the control subjects is not statistically significant, but near to the significance level.

Our results really are apparently conflicting with the Mayo Clinic report, and this fact may be due, at least in part, to the different number of patients studied.

The frequency of HLA-DQ1 antigen in patients and in controls is similar in the two studies, showing that the two populations are genetically comparable. Moreover, the linkage disequilibrium between DR1 and DQ1 antigens is very frequent, but not absolute.

On the other hand our and Powell's results (16) support the hypothesis that LP is probably linked more with DR1 antigen rather than with DQ1. We also must remember that the locus-DR is frequently associated with most of HLA-linked immune diseases.

Previous HLA studies of patients with LP have shown an increased frequency of HLA-A3. This antigen, controlled by the correspondent gene of Locus A, is known to be in linkage disequilibrium with DR1 (17). So we can suggest that an increased frequency of A3 may reflect a stronger association with a Class II antigen.

During the last two years DR1 antigen has been linked with reduced serological response to Epstein-Barr viral antigen (18) and MT3 (DRW53) has been shown to be involved in the presentation of mumps viral antigen to T-cell (19). These last data suggest that different Class II antigens may be involved in the afferent limb of the immune response to alloantigens.

Ir genes are thought to be associated to the DR locus and are expressed through Ia antigens on different cells (endothelial cells, macrophages, T-lymphocytes and Langerhans' cells of the epidermis). Some of these Ia-like antigen-carrying cells are involved in LP. Variations in the relative number of T-cell subsets with the age of LP lesions have been described (2, 3, 5), thus suggesting an antigen specific education of inducer T-cells in early LP lesions, whereas in late lesions cytotoxic T-cell could destroy keratinocytes (3, 5, 7, 8).

Our study has shown that in LP patients there is a statistically significant increase of HLA-DR1 antigen; this result could support the hypothesis that, in some predisposed subjects, epithelial Langerhans' cells may process a foreign antigen (virus, drug, allogeneic cells, chemical substances) in a particellar way and induce a local immune response.

The antigen activated lymphocytes in the dermis may secrete the recombinant human gamma interferon, which causes some changes: expression of HLA-DR by keratinocytes and an increased rate of differentiation of these cells with formation of a thickened granular cell layer.

Moreover, the observed destruction of basal cell layer in LP could be explained in terms of keratinocytes expressing a foreign HLA-DR on their surface as in graft-versus-host disease, or presenting an alloantigen with autologous HLA-DR. As a consequence the keratinocytes are recognized as foreign by the immunocompetent cells and become targets for cytotoxic T-cells.

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Ultrastructure of Angiokeratoma Vulvae

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A case of vulvar angiokeratoma studied by electron microscopy is described. The patient, a 51-year-old woman, had noticed eruptions for the last 15 years, though without symptoms. Osmiophilic bodies with myelin-like figures were found in the vascular endothelial cells. The findings support previous opinion that vulvar angiokeratoma is a variant of scrotal angiokeratoma. (Received July 14, 1987.)

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Angiokeratoma vulvae is probably a variant of scrotal angiokeratoma Fordyce (1). Few papers have described the condition, though it seems to be more common than generally