Epithelial response to the immunitary aggression in oral lichen planus

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Summary

Oral lichen planus is an inflammatory disease with mucous and cutaneous affects caused by cellular immune reaction. Basal cell vacuolation degeneration is the result of T-cell aggression. As the clinical and histopathological alterations of OLP range from epithelial hyperplasia to epithelial atrophy and erosion, it could be that different forms of OLP finally express differences in the intensity of immune attack. The aim of the present study was to analyse the relationship between the clinical and histopathological behaviour and the intensity of the immune response to OLP by means of basal cell vacuolation and inflammatory infiltrate intensity measurement. We analysed 47 patients with OLP. Requirements for inclusion were histopathological diagnosis of OLP from an oral biopsy. Clinical and histopathological correlations were made. OLP's with an intense inflammatory infiltrate were correlated with a high grade of basal cell vacuolations ($p<0.01$). A positive statistical correlation between basal cell vacuolation and epithelial atrophy ($p<0.01$), and between inflammatory infiltrate intensity and epithelial atrophy ($p<0.01$) were observed. An inverse statistical correlation was found when the inflammatory infiltrate intensity and the degree of basal cell vacuolation were compared with epithelial hyperplasia ($p<0.05$ and $p<0.01$ respectively). In the present study, OLPs with intense immune aggression frequently show epithelial atrophy and erosion on microscopic examination and viceversa.

KEY WORDS

Oral Lichen Planus, Immunity.

INTRODUCTION

Oral Lichen Planus (OLP) is an inflammatory disease with mucous and cutaneous affects [12, 13]. Today it is accepted that the initial alterations in OLP are located in the basal cell layer in the oral epithelium [2] and that subepithelial inflammatory infiltrate is a secondary event involved in T-cell immune response development [4]. The result of T-cell aggression is the vaculation

degeneration of basal cells. As the clinical and the histopathological alterations of OLP range from epithelial hyperplasia to epithelial atrophy and erosion, it could be that different forms of OLP are finally expressing differences in the immune attack intensity. In this way, the aim of the present study was to analyse the relationship between the clinical and histopathological behaviour, and the immune response intensity of OLP by means of basal celle vacuolation and inflammatory infiltrate intensity measurement.

PATIENTS AND METHODS

In the present study, the authors analysed 47 patients (27 males and 20 females, mean age= 52 yr, range= 25-87) with OLP who were attended in the Oral Medicine Department of the University of Granada, Spain. Requirements for inclusion were the histopathological diagnosis of lichen planus from an oral biopsy (formalin fixed-paraffin embedded; hematoxilin-eosin stain). When atrophic and erosive lesions were present, they were always included in the biopsy. In all cases the following data was recorded: age, sex, oral location, clinical appearence (reticular, atrophic, erosive, bullous, papular, plaque like lesions), and histopathological parameters (epithelial hyperplasia, acanthosis, hiperquerathosis, ephithelial atrophy and erosion, papillomathosis, dysplasia, Max-Joseph spaces). Also a semiquantitive grading of the inflammatory infiltrate intensity (grade I, II, III) and the vacuolation degeneration of basal cell layer (grade I, II, III), together with counts of Civatte bodies – 8 fields – 40X (0-1, 2-4, >4) and the number of the intraepithelial leukocytes – 8 fields – 40X (1-10, 11-25, >25) were made.

Descriptive statistics for the variables analysed were calculated. In the statistical analysis the Chi square test and spearman correlation coefficient were used. Analyses were performed using SPSS-PC+, 4.0-199-(SPSS Inc. Chicago, Illinois).

RESULTS

Clinical results

Reticular (91.5%, 43 cases) and atrophic forms (31.9%, 15 cases) were the most frequently found, whereas bullous forms were never observed (table 1). 40.4% (19 cases) of the patients were affected by more than one type of OLP. Buccal mucosa (97.9%, 46 cases) and gingiva (68.15, 32 cases) were the most frequent intraoral location (table 2), and in 34 patients (72.3%) the disease affected more than one intraoral location.

TABLE 1
Percentages of clinical types of OLP.

Clinical type	No	Yes
	n (%)	n (%)
Reticular	4 (8.5%)	43 (91.5%)
Atrophic	32 (68.1%)	15 (31.9%)
Erosive	41 (87.2%)	6 (12.8%)
Bullous	47 (100%)	0 (0.0%)
Papillose	45 (95.7%)	2 (4.3%)
Plaque-like	42 (89.4%)	5 (10.6%)

TABLE 2
Intraoral locations of OLP.

Location	No	Yes
	n (%)	n (%)
Buccal	1 (2.1%)	46 (97.9%)
Tongue	35 (74.5%)	12 (25.5%)
Gingiva	15 (31.9%)	32 (68.1%)
Lips	44 (93.6%)	3 (6.4%)
Palate	42 (89.4%)	5 (10.6%)
FM	45 (95.7%)	2 (4.3%)

FM: Floor of the mouth.

HISTOPATHOLOGICAL RESULTS

Table 3 shows the rate of epithelial histopathological alterations. Epithelial hyperplasia and acanthosis were the most frequent events found (both occurring at 80.9%, 38 cases). An intense inflammatory infiltrate was found in 53.2% (25 cases). Small number of Civatte bodies (72.3%, 34 cases) and intraepithelial leukocytes (63.8%, 30 cases) were observed, whereas 51.1% of the samples (24 cases) showed an intense basal layer vacuolation (table 4).

TABLE 3
Histopathological alterations in OLP analyzed.

	No	Yes
	n (%)	n (%)
Hyperplasia	9 (19.1%)	38 (80.9%)
Acanthosis	9 (19.1%)	38 (80.9%)
Papillomatosis	38 (80.9%)	9 (19.1%)
Hyperquerathosis	21 (44.7%)	26 (55.3%)
Paraquerathosis	20 (42.6%)	27 (57.4%)
Ortoquerathosis	35 (74.5%)	12 (25.5%)
Atrophy	34 (72.3%)	13 (27.7%)
Erosion	43 (91.5%)	4 (8.5%)
Dysplasia	44 (93.6%)	3 (6.4%)
Max-Joseph spaces	21 (44.7%)	26 (55.3%)

TABLE 4
Quantified histopathological alterations in OLP.

	n (%)
Inflammatory infiltration	
Grade I	12 (25.5%)
Grade II	10 (21.3%)
Grade III	25 (53.2%)
Civatte bodies	
0-1/8 fields/40x	34 (72.3%)
2-4/8 fields/40x	11 (23.4%)
>4/8 fields/40x	2 (4.3%)
Intraephitelial leukocytes	
1-10/8 fields/40x	30 (63.8%)
11-25/8 fields/40x	13 (27.7%)
>25/8 fields/40x	4 (8.5%)
Basal layer vacuolation	
Grade I	14 (29.8%)
Grade II	9 (19.1%)
Grade III	24 (51.1%)

STATISTICAL CORRELATIONS

Table 5 shows collected statistical correlations between histopathological variables observed in OLP. A statistical correlation between the inflammatory infiltration intensity and the degree of basal cell layer vacuolation was observed ($p<0.05$). Moreover, an intense inflammatory infiltrate was statistically correlated with epithelial atrophy ($p<0.01$) (figure 1) and erosion ($p<0.01$), whereas epithelial hyperplasia was inversely correlated with the intensity of the inflammatory infiltration ($p<0.05$) (figure 2) and the degree of basal cell vacuolation ($p<0.01$). In table 6 the statistical correlations between histopathological aspects and clinical types of OLP are reflected. A high correlation between the intensity of the inflammatory infiltrate, a high degree of basal celle layer vacuolation and the atrophic forms, was observed ($p<0.01$ respectively).

TABLE 5
Correlations between histopathological parameters of OLP.

	Hyperp.	Acant.	Papil.	Hyper.	Paraq.	Ortoq.	Atrof.	Erosion	Disp.	Max J.	Infil.	Civat.	Exoc.
Acanthosis	0.86**												
Papillomatosis	0.09	0.23											
Hyperquerathosis	0.10	0.10	0.00										
Paraquerathosis	0.01	-0.09	-0.01	0.35*									
Ortoquerathosis	-0.08	-0.08	-0.03	0.23	-048**								
Atrophy	-0.66**	-0.66**	-0.18	-0.11	-0.04	0.07							
Erosion	-0.04	-0.04	-0.14	0.12	-0.04	-0.00	0.49**						
Dysplasia	0.12	0.12	0.53**	0.05	0.04	0.04	-0.16	-0.07					
Max-Joseph spaces	-0.21	-0.32*	-0.32*	-0.11	0.09	0.03	0.26	0.27	0.05				
Inflammatory infiltration	-0.35*	-0.23	-0.19	-0.04	-0.18	0.11	0.41**	0.16	-0.01	0.25			
Civatte bodies	0.06	-0.07	0.16	-0.11	0.07	0.05	0.02	-0.02	0.20	0.16	0.11		
IEL	-0.08	0.01	0.14	-0.00	0.04	-0.34**	0.23	0.31*	0.13	-0.00	0.26	0.12	
Basal layer vacuolation	-0.45**	-0.37**	-0.05	-0.06	-0.19	0.08	0.40**	0.18	-0.07	0.22	0.73**	0.20	0.29*

The table shows the Spearman correlation coefficients.
* $p<0.05$; ** $p<0.01$. IEL: Intraepithelial leukocytes

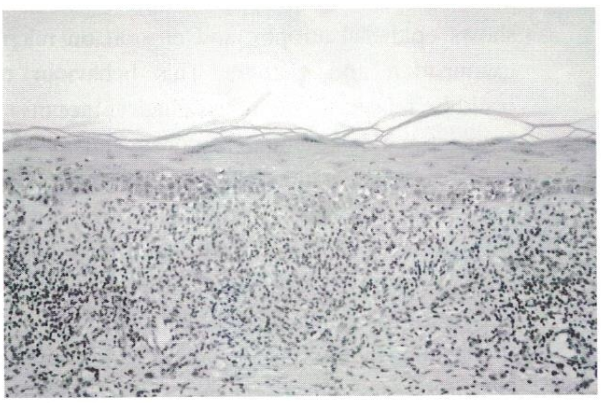

Fig. 1
Epithelial atrophy and grade III inflammatory infiltration in OLP (H&E, 40*)

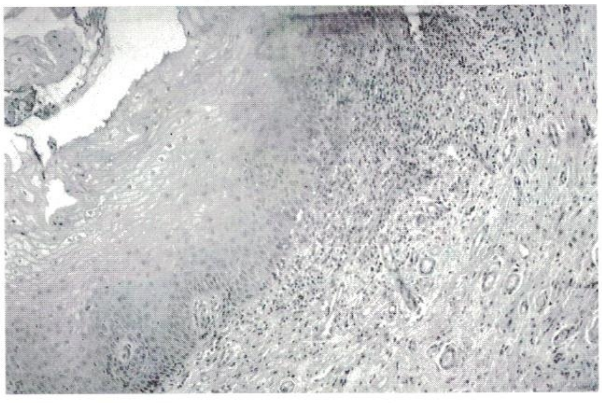

Fig. 2
Epithelial hyperplasia and grade I inflammatory infiltration in OLP (H&E, 40*).

TABLE 6
Histopathological aspects in relation to clinical types of OLP.

		Reticular - +	Atrophic - +	Erosive - +	Papular - +	Plake - +
Hyperplasia	No	3 6	1 8	8 1	9 0	9 0
	Yes	1 37*	31 7**	33 5	36 2	33 5
Acanthosis	No	4 5	1 8	8 1	8 1	8 1
	Yes	0 38**	31 7**	33 5	37 1	34 4
Papillomatosis	No	4 34	25 13	33 5	36 2	34 4
	Yes	0 9	7 2	8 1	9 0	8 1
Hyperquerathosis	No	3 18	15 6	20 1	20 1	19 2
	Yes	1 25	17 9	21 5	25 1	23 3
Paraquerathosis	No	2 18	13 7	17 3	20 0	17 3
	Yes	2 25	19 8	24 3	25 2	25 2
Ortoquerathosis	No	4 31	25 10	31 4	33 2	33 2
	Yes	0 12	7 5	10 2	12 0	9 3
Atrophy	No	1 33	31 3	32 2	32 2	29 5
	Yes	3 10	1 12**	9 4*	13 0	13 0
Erosion	No	4 39	32 11	40 3	41 2	38 5
	Yes	0 4	0 4**	1 3**	4 0	4 0
Dysplasia	No	4 40	31 13	39 5	42 2	39 5
	Yes	0 3	1 2	2 1	3 0	3 0
Max-Joseph spaces	No	1 20	18 3	20 1	20 1	18 3
	Yes	3 23	14 12*	21 5	25 1	24 2
Inflammatory infiltrate	Grade I	1 11	12 0	12 0	10 2	7 5
	Grade II	0 10	8 2	10 0	10 0	10 0
	Grade III	3 22	12 13**	19 6*	25 0*	25 0*
Civatte bodies	0-1/8 fields/40x	2 32	23 11	30 4	33 1	30 4
	2-4/8 fields/40x	1 10	7 4	9 2	11 0	11 0
	>4/8 fields/40x	1 1	2 0	2 0	1 1	1 1
IEL	1-10/8 fields/40x	2 28	23 7	29 1	28 2	25 5
	11-25/8 fields/40x	2 11	8 5	10 3	13 0	13 0
	>25/8 fields/40x	0 4	1 3	2 2**	4 0	4 0
Basal layer vacuolation	Grade I	0 14	13 1	14 0	13 1	11 3
	Grade II	1 8	8 1	8 1	8 1	8 1
	Grade III	3 21	11 13**	19 5	24 0	23 1

This table presents the number of lesion by clinical and histopathological type. IEL: Intraepithelial leukocytes
* $p<0.05$ ** $p<0.01$

DISCUSSION

As expressed above, an important correlation between the immune aggression intensity and some histopathological epithelial alterations was observed. Thus, OLPs with intense inflammatory infiltrate were correlated with the high degree if basal cell vacuolation ($p<0.01$). Moreover, a statistically positive correlation between basal cell vacuolation and epithelial atrophy ($p<0.01$), and between the inflammatory infiltration intensity and epithelial atrophy ($p<0.01$) was observed. An inverse statistical correlation was found when the inflammatory infiltration intensity and the degree of basal cell vacuolation was compared with epithelial hyperplasia ($p<0.05$ and $p<0.01$ respectively). In the present study, OLP with intense immunitary aggression frequently shows epithelial atrophy and erosion on microscopic examination and viceversa. This behaviour of OLP could be related to the immunological mecanism development in T-cell immune response. Thus, the first step is antigenic alteration of basal keratinocites (KC). Langerhans cells (LC) recognize, process and present an antigenic information to T-cells with subsequent T-cells activation and citokine liberation which sends a population of active T-cells towards altered KC [8, 9, 11]. Gamma interferon (INF) production by activated T-cells is an important event in the cellular immune response. INF induces a prominent HLA-DR and intercellular adhesion molecule 1 (ICAM-1) expression in KC.

HLA-DR expression is an important event in antigenic presentation [3, 4, 7, 10], whereas ICAM-1 expression is an outstanding phenomenon for T-cell aggression because it is essential in the T-cell-KC union. So, T-cell could be binded to LC and to KC. T-cell-KC union is unable to stimulate the proliferation of active T-cells, whereas T-cell-LC union can stimulate a population of activated T-cells with subsequent KC aggression by citokine production. In the cellular immune response epithelial growth factors are produced [6]. In this way, OLP with low immune aggression and scant basal cell degeneration may be hyperplasic as a result of basal cell response to epithelial growth factors. Intensively altered basal KCs have a low proliferative potential and so, OLP with intense immune aggression frequently present epithelial atrophy and erosion. The intensity of the immune response is probably related to the previously stated normal development events. Thus, depletion or abnormal function of LC may induce a predominant T-cell-KT union with a progressive decrease of immune response and epithelial hyperplasia. Moreover, other events may also occur as for example in the case reported by the authors where a decrease occurs in the ICAM-1 expression in hyperplasic OLP [5].

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