



Evaluating the Frequency of Histopathological Features of Oral and Cutaneous Lichen Planus Lesions: A Retrospective- Comparative Study

**Maryam Zamanzadeh^{1,2}, Fatemeh Montazer³, Atena Shiva^{1,2},
Mahmood Moosazadeh⁴, Taravat Sadeghi⁵
and Mohammad Koochak Dezfouli^{1,2*}**

¹*Department of Oral and Maxillofacial Pathology, School of Dentistry, Mazandaran University of Medical Sciences, Sari, Iran.*

²*Dental Research Center, Mazandaran University of Medical Sciences, Sari, Iran.*

³*Dermatopathologist, Department of Pathology, Iran University of Medical Sciences (IUMS), Tehran, Iran.*

⁴*Gastrointestinal Cancer Research Center, Non-communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*

⁵*Dentist, Sari, Iran.*

Authors' contributions

This work was carried out in collaboration among all authors. Author MZ, FM, MKD and AS designed the study, wrote the protocol and wrote the first draft of the manuscript. Author MM managed the analyses of the study. Author TS managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background and Aim: Lichen planus (LP) is an immunological disease of skin and mucous membranes. Cutaneous and oral LP (CLP and OLP) have almost similar histopathological changes determined microscopically with symptoms such as basal cell layer degeneration, hyperkeratosis,

*Corresponding author: E-mail: Mkoochek2000@yahoo.com;

band-like infiltration of lymphocytes, and saw tooth ridges. The present study aimed to determine the frequency and compare the histopathological features of OLP and CLP samples.

Materials and Methods: This was a descriptive-analytical, and cross-sectional research performed on 91 paraffin-embedded tissue blocks (41 OLP lesions and 50 CLP lesions). The frequency of histopathological features was determined by an optical microscope, and data analysis was performed in SPSS version 21 using descriptive statistics (frequency and percentage) and Chi-square.

Results: In this study, the frequency of LPs was higher in female subjects, compared to male participants. The frequency of histopathological features of hyperkeratosis, acanthosis, spongiosis, and epithelial hypertrophy was significantly higher in CLP samples, compared to OLP lesions ($P < 0.005$). Meanwhile, the frequency of saw tooth ridges was higher in OLP lesions, compared to CLP samples ($P < 0.008$).

Moreover, there was a severe frequency of basal cell layer degeneration and the presence of civatte bodies (CBs) in most CLP lesions while they were moderate in most OLP samples.

Conclusion: According to the results of the study, histopathological features of OLP and CLP lesions were not completely similar and had different frequencies in the two groups. It is recommended that more comprehensive studies be performed on these differences and their causes.

Keywords: Histopathology; cutaneous lichen planus; oral lichen planus.

1. INTRODUCTION

Lichen planus (LP) is a disease characterized by lesions of the skin, hair, nails, and mucous membranes [1,2]. The disease has an unknown etiology and a multifactorial pathogenesis. Many believe that TCD8+ cells, which are responsible for apoptosis at the epithelial level, play an important role in the pathogenesis of the disease [3,4]. Classic LP lesions commonly present with the four P's: purple, pruritus, polygonal, and papules/plaques, usually involving the flexor surfaces of the legs and arms. Cutaneous papules, often crossed by fine white lines (Wickham striae), are detected with a meticulous examination of the area. The cutaneous lichen planus (CLP) lesions are reported in 20-60% of patients with oral lichen planus (OLP) [1,5]. Lichen planus has varied clinical forms in the oral mucosa, the most common of which is reticular presenting as interlacing white keratotic lines that form a ring-like pattern. OLP has a multiple-site involvement, with the buccal mucosa being the most prevalent. Other forms of LP include erosive and bullous [6]. Although oral changes are relatively stable over time, similar cutaneous lesions tend to increase and decrease and spontaneously clear within one-two years after initial presentation [1]. OLP and CLP lesions have similar histopathological changes, which are microscopically determined by hyperkeratosis, basal cell degeneration, band-like infiltration of lymphocytes, and sawtooth ridges [2,5]. Given the lack of a research performed to compare the frequency of

histopathological features of OLP and CLP lesions, the present study aimed to evaluate and compare the histopathological features of OLP and CLP lesions.

2. MATERIALS AND METHODS

This was a descriptive, analytical and cross-sectional study conducted on paraffin-embedded tissue blocks of patients with OLP and CLP lesions. All samples had clinically and histologically diagnosed LP recorded in the lab. Four-micron sections of the paraffin-embedded blocks were prepared and stained with hematoxylin for diagnosis and entry into the study. After observing hematoxylin-eosin slides and confirming the diagnosis of paraffin-embedded blocks, slides with sufficient connective tissue depth and appropriate epithelial length were selected and the slides without these criteria were excluded from the research. Other exclusion criteria included a low quality, unfavorable fixation, or not agreed upon by the pathologists from a microscopic aspect. Ultimately, 91 samples (41 OLP and 50 CLP lesions) were evaluated in terms of the frequency of histopathological features, as presented below [2,5]:

1. Different surface patterns of lesions (e.g., ortho and superficial parakeratinization or ulcerative areas)
2. Max Joseph cleft under the epidermis (Max Joseph space)

3. Band-like infiltration of T-cells
4. Hydropic degeneration of the basal cell layer
5. Presence of Civatte bodies (CBs)
6. Sawtooth ridges

The histopathological features were assessed by two pathologists (oral pathologist and dermatopathologist) using an optical microscope (Nikon, Eclips E200, Tokyo, Japan) at 100x and 400x magnification. However, a mean of the features was considered in case of a lack of consensus between the two experts. Data analysis was performed in SPSS version 21 using descriptive statistics (percentage, mean and standard deviation) and Chi-square (to compare the frequency of histopathological features between OLP and CLP lesions). Moreover, a P-value of below 0.05 was considered statistically significant.

3. RESULTS

In the present study, 91 samples (41 OLP and 50 CLP lesions) were assessed to determine the presence or absence of the desired histopathological features.

According to Table 1, the frequency of LP lesions was higher in female subjects, compared to male participants. In addition, the frequency of CLP

lesions was higher in both genders, compared to OLP lesions; Nevertheless, this difference was statistically insignificant based on Chi-square test results (P= 0.285). According to the table, the frequency of LP lesions was higher in patients aged 43-52 years and lower in subjects aged 34-42 years, compared to the other age groups. Moreover, the frequency of CLP lesions was higher in the first and second age groups, compared to OLP lesions, whereas the frequency of the latter was higher in the third and fourth age groups, compared to the former. Nonetheless, this difference was not statistically significant (P =0.27).

Table 2 presents the frequency of histopathological features in OLP and CLP lesions. According to the table, the frequency of hyperkeratosis, acanthosis, spongiosis, and epithelial hypertrophy was higher in CLP lesions, compared to OLP lesions (P<0.005). Meanwhile, the frequency of saw tooth ridges was higher in OLP lesions, compared to CLP lesions (P< 0.008).

On the other hand, while the frequency of band-like infiltration of lymphocytes was higher in patients with CLP lesions, compared to those with OLP lesions, this difference was statistically insignificant.

Table 1. Frequency of OLP and CLP lesions based on age and gender of patients

		CLP Lesions	OLP Lesions	Total LPs
		Frequency (%)	Frequency (%)	Frequency (%)
Gender	Male	16 (64.0%)	9 (36.0%)	25 (27.5%)
	Female	34 (51.5%)	32 (48.5%)	66 (72.5%)
Age group	Group 1 (33> years)	17 (77.3%)	5 (22.7%)	22 (24.1%)
	Group 2 (34-42 years)	13 (65.0%)	7 (35.0%)	20 (22.0%)
	Group 3 (43-52 years)	10 (40.0%)	15 (60.0%)	25 (27.5%)
	Group 4 (53< years)	10 (41.7%)	14 (58.3%)	24 (26.4%)

Table 2. Frequency of histopathological features of OLP and CLP lesions

Frequency of histopathological features	CLP lesions	OLP lesions	Total LPs	P-value
	Frequency(%)	Frequency(%)	Frequency (%)	
Hyperkeratosis	30 (83.3%)	6 (16.7%)	36 (39.6%)	<0.001
Parakeratosis	36 (54.5%)	30 (45.5%)	66 (72.5%)	<0.661
Acanthosis	44 (93.6%)	3 (6.4%)	47 (51.6%)	<0.001
Epidermal atrophy	6 (60%)	4 (40%)	10 (11%)	<1
Spongiosis	29 (74.4%)	10 (25.6%)	39 (42.9%)	<0.001
Erosion	2 (22.2%)	7 (77.8%)	10 (9.9%)	<0.073
Epithelial hypertrophy	19 (79.2%)	5 (20.8%)	24 (26.4%)	<0.005
Max Joseph space	15 (60%)	10 (40%)	25 (27.5%)	<0.051
Band-like infiltration	39 (54.2%)	33 (45.8%)	72 (79.1%)	<0.771
Sawtooth ridge	19 (41.3%)	27 (58.7%)	46 (50.5%)	<0.008

According to the randomly examined slides, the presence of CBs and degeneration of the basal cell layer were classified into three groups of mild, moderate, and severe diffusion intensity. According to Table 3, severe CBs were detected in most CLP lesions (82.9%), whereas moderate CBs were observed in most OLP lesions (62.5%).

In addition, the frequency of CBs was mostly moderate (61.5%) in all LP lesions, and this difference was statistically significant according to the Chi-square test ($P < 0.001$). Furthermore, the degeneration of the basal cell layer was severe and moderate in most CLP (84.2%) and OLP (66%) lesions, respectively. In all LP lesions, the frequency of basal cell layer degeneration was moderate (58.2%), and this difference was statistically significant ($P < 0.001$).

4. DISCUSSION

LP is a relatively chronic cutaneous disease, which often affects the mucosa and its exact etiology is unknown. A higher prevalence of OLP was found in non-Asian countries, among women, and among people 40 years and older [2,5]. In the present study, the frequency of OLP and CLP lesions was higher in female subjects, compared to male participants, and most patients were in the age range of above 43 years. However, no significant difference was observed between patients in terms of the relationship between age and LP. Numerous previous studies have reported a higher frequency of LP lesions in women [2,7,8]. However, there were a few studies that reported a higher LP lesion frequency in men [9-11]. The age group of patients in most studies is similar to our study. In a research by Fernández-González et al., LP lesions were more observed in the fifth and sixth decades of life [12]. In other studies, estimated the mean age of patients with confirmed LP lesions to be 41 and 59 years [13,14]. According to Żychowska et al., the mean age of patients with LP lesions was 51.6 years, and 53.8 % of the subjects were female [15].

With the exception of CBs and basal cell layer degeneration, which were observed in all samples, three other common features in all LP lesions were band-like infiltration, parakeratosis and acanthosis. Moreover, the histopathological features of hyperkeratosis, acanthosis, spongiosis and epithelial hypertrophy were significantly higher in CLP lesions, compared to

OLP lesions. On the other hand, the frequency of saw tooth ridges was higher in CLP lesions.

The most common features observed in other studies had differences with each other due to differences in sample size and type of LP samples. In a research by Fernández-González conducted on 50 OLP samples, hydropic degeneration of the basal cell layer and infiltration of lymphocytes in the subepithelial layer were observed in 100% of cases. Other common histopathological symptoms included necrotic keratinocytes (92%), hyperkeratosis (66%), hyperplasia (54%), acanthosis (48%). Meanwhile, the lowest frequencies were related to serrated ridges (30%) and the presence of plasma cells (26%) [12].

In a research by Arora et al. performed on 38 LP samples, the most common histopathological features included the band-like infiltration of lymphocytes (100%), vacuolization of basal cells (100%), hyperkeratosis (92%), and hypergranulosis (82%). Moreover, band-like infiltration of lymphocytes was mild in 45% of the cases, whereas it was moderate and severe in 37% and 13% of the cases, respectively [16].

Studying OLP and lichenoid lesions, Aminzadeh et al. reported band-like infiltration of lymphocytes, hydropic degeneration of basal layers, sawtooth ridge degeneration, hyperparakeratosis, atrophic epithelium, hyperparakeratosis, Max Joseph space and hyperkeratosis to be 91.7%, 81.3%, 53.1%, 46.9%, 26%, 23.4%, 15.1%, and 7.8%, respectively [17].

In a study, Dixit et al. evaluated lichenoid tissue reaction/interface dermatitis (LTR/ID) lesions, reporting that 91.2% of lesions were of LP type and common features included basal cell vacuolation (100%), inflammatory cells in the upper dermis (98.6%), hyperkeratosis (97.9%), acanthosis (85.8%), Max Joseph space (77%), CBs (62.1%), atrophy (13.5%), and parakeratosis (12.1%) [11].

In a research by Rampal et al., the most common features included a saw tooth pattern of the rete ridges and irregular acanthosis (85%), basal cell layer degeneration (81.7%), band-like infiltration (71.7%), hyperkeratosis/orthokeratosis (63.3%), CBs (45%), Max Joseph space (16.7%), and atrophy (8.3%) [18]. In the Parihar study, all samples showed orthokeratosis, and irregular acanthosis, band-like infiltration, CBs, and Max

Table 3. Frequency of CBs and basal cell layer degeneration in CLP and OLP lesions

		CLP Lesions	OLP Lesions	Total LPs
		Frequency (%)	Frequency (%)	Frequency (%)
Presence of CBs	Mild	0 (0%)	0 (0%)	0 (0%)
	Moderate	21 (37.5%)	35 (62.5%)	56 (61.5%)
	Severe	29 (82.9%)	6 (17.1%)	35 (38.5%)
Basal cell layer degeneration	Mild	0 (0%)	0 (0%)	0 (0%)
	Moderate	18 (34%)	35 (66%)	53 (58.2%)
	Severe	32 (84.2%)	6 (15.8%)	38 (41.8%)

Joseph cleft were reported at 94%, 94%, 82%, and 29.5%, respectively [19].

In the present study, signs of atypia and dysplasia were observed in none of the samples, which is consistent with the results obtained by Arora [16]. Nevertheless, atypical symptoms were observed in 4% of the samples in the research by Fernández-González, performed on 50 OLP lesions. However, symptoms of dysplasia were observed in none of the samples in the aforementioned research [12]. In the study by Dixit et al., dysplasia was observed in 15.5% of cases, all of which were at a low grade [11]. Among 21 OLP samples assessed by Werneck et al., cytopathological examination showed epithelial dysplasia in 11 samples, 10 of which were mild and one was moderate [20]. In a study by Mozafari et al., dysplasia was detected in 15.5% of the cases, and the frequency of this symptom was higher in subjects aged above 50 years, compared to those below the age of 50 [21].

In the present study, CBs were observed in all samples and their presence was severe in most CLP lesions but moderate in most OLP lesions. The CBs represent necrotic keratinocytes, measure about 20 µm in diameter and have a homogeneous, eosinophilic appearance. Other lesions in which CBs may be present include any interfacial dermatitis in which basal cell damage occurs, such as lupus erythematosus, graft versus host disease (GvHD), and inflammatory keratoses such as actinic lichenoid keratosis, and LP-like keratosis [22,23]. There might be a huge number of CBs in LPs in the form of a cluster [24]. In fact, clusters were found in four cases in the research by Arora [16]. In addition, CBs were reported at 82%, 62.1%, 45%, 37%, and 29% in the studies by Parihar, Dixit, Rampal, Grag and Arora, respectively, while the lowest level was observed in the present research [7, 11,16,18,19]. This could be justified by different sample sizes and variety in LP forms.

In addition, basal cell layer degeneration was detected in all samples of the present study, which was severe in most CLP cases but moderate in the majority of OLP lesions. In many studies, including the current research, basal cell degeneration was observed in 100% of samples [7,11,12,16,25]. However, low amounts were reported in some studies, including the research by Rampal (81.7%) [18]. In a research by Chatterjee et al., which was performed on OLP lesions of subjects below the age of 18, basal cell layer degeneration was observed in all samples, which was moderate and mild in 63.64% and 36.36% of the cases, respectively [26].

According to the results of the present study, the frequency of sawtooth rete ridges was significantly higher in OLP lesions. The mentioned variable was reported at 37%, 53% and 85% in studies by Aminzadeh, Mozafari and Rampal, respectively [17,18,21], which was lower than the present study. This difference might be due to the type of evaluated LP and different sample sizes of studies.

5. CONCLUSION

According to the results of the present study, the histopathological features of hyperkeratosis, acanthosis, spongiosis and epithelial hypertrophy were significantly higher in CLP lesions, compared to OLP lesions. On the other hand, the frequency of saw tooth ridges was significantly higher in OLP lesions, compared to CLP lesions.

In addition, degeneration of the basal cell layer and the presence of CBs were severe in most CLP samples while they were moderate in the majority of OLP samples. In the current research, CLP and OLP lesions did not have similar histopathological features, and different frequencies were observed for some of the features. It is recommended that more comprehensive studies be conducted on these differences and their causes.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s). The ethics code: IR.MAZUMS.REC.1398.519.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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