A retrospective clinicopathologic study of lichen planus and lichenoid lesions in the oral cavity

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ABSTRACT

Lichen planus is a common oral disorder which may represent the manifestation of varies clinical presentation and microscopic findings. In this retrospective study of 86 cases of oral lichen planus (OLP) were compared with 73 cases of oral lichenoid lesions (OLL). Various clinicohistopathological features, were studied. The object of this study was to compare clinical and microscopic findings in order to present evidence that support the position of true lichen planus. Biopsy specimens were obtained from every patient. The biopsy specimens were fixed in 10 percent formalin, embedded in paraffin, sectioned at 4 microns and stained by means of routine hemotoxylin and eosin procedures. The histologic specimens were examined and evaluated without knowledge of clinical findings. The mean age at presentation of patients with OLP was 42.5 years as compared to 47.0 years for OLL. There was no significant difference between the ethnic groups, site of lesions and the distribution of the clinical presentation. Compare to histopathologic findings, there were only 55% clinical and histological agreement in this study, this because of using strict criteria for oral lichen planus there could be an over diagnosis lesions. This study showed that there were no reliable clinical and histopathological features which could differentiate OLL from OLP. The features in the OLL group were non specific. The patient's medical history, oral habits or psychological status appeared to be able to alter the classical clinicopathological findings.

Key words: Lichen planus, lichenoid lesions

INTRODUCTION

The most obvious part of the human body is the skin of mucous membranes which is covered by epithelium. Normal oral epithelium consist of keratinocytes, melanocytes, Langerhans cell and Markel cell. The colour of the oral mucous is affected by the thickness and the structure of the epithelium, by the amount of melanin, and by the vascularity of the underlying connective tissue. On clinical examination, if the colour of normal oral mucous changes to white or red, a disorder of the oral mucous should be suspected. Oral white lesions are often associated with abnormal or increase keratin production. Histopathologically, they are describe as keratoses. The red appreance, however, is a result of atrophy of the epithelium overflying a highly vascular submucous.[1]

For many years the term leukopakia had been used to describe any mucousl lesion with appearance of a white plaque. Today, the classification of white lesions of the oral mucous can be divided according to their etiology, including hereditary, traumatic, infective and idiopathic.[2]

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The term "leukoplakia" has been modified to describe any white lesion or plaque on the oral mucous membran that cannot be characterized as any other definable lesion.[3] Therefore, leukoplakia is essentially a clinical diagnosis by exclusion. Sometimes it is difficult to separate the idiopathic lesion by clinical examination only. Thus, the commonest clinical diagnosis could be: (1) oral lichen planus; (2) leukoplakia; (3) discoid lupus erytematosus or (4) atypical mucositis/stomatitis. These four conditions are very similar to each other.

Oral lichen planus is a relatively common mucocutaneous lesion with a prevalence of about 1 percent in the general population.[4] Lichen planus is diagnosed clinically as a lace-like patch or striae in the oral mucous. They may or may not be a coexistent cutaneous involvement. It is usually present bilaterally on the buccal mucous or continguous areas. The oral lesion of lichen planus tend to be more persistent than those of the skin. In a patient with long standing lichen planus it has been suggested that the risk of oral cancer in the affected site increases.[5] The malignant transformation of lichen planus still remains a debated issue in the literature.[6]

The classical appearance of lichen planus is well recognized. However there are a few types of clinical presentation, i.e. reticular, popular, plaque-like, atrophic, bullous and erosive type. Because of it is variable clinical features and unknown causative factors, the recognition of lichen planus can sometimes be difficult.[7] If the presentation of the lichen planus is not a classical one, a mucousal biopsy will have to be perfomed to obtain a definitive diagnosis. Typically, oral lichen planus show hyperkeratosis with a dense, bandlike lymphocytes infiltrating the superficial lamina propia and there is liquefactive degeneration of basal epithelial cells.[6]

Oral lichenoid lesion is a non specific term to describe any lesion which resemble oral lichen planus clinically and histologically. A term frequently used is lichenoid reaction; this lesion has been attributed to a wide range of drugs (anti-hypertensive, anti-malarias, hypoglicemics and non steroid anti-inflamatory agents), foodstuffs and dental materials. Many studies have tried to prove the causative affected of this lichen planus-like lesion.[8-9] But still, the relationship is unclear. Despite the reported difference between idiopathic oral lichen planus and oral lichenoid reaction, the WHO does not distinguish between the two conditions and several report concurred with this lack of distinguish features.[11,12]

MATERIALS AND METHODS

The data of patients with oral lichen planus and oral lichenoid lesions referred to the Department of Oral Medicine and Oral Pathology in the Faculty of Dentistry, University of Malaya. A total 159 patients have had muscosal biopsies perform on them. Sample of histologically normal tissue were obtained from 7 patients for the control group.

For our purpose the clinical diagnosis for lichen planus consist of any types of the white-red lesions occurring bilaterally on bucal mucous. For lichenoid lesions it was any type of white-red lesions occuring unilaterally on any site.

All the tissue had been processed routine procedures, these specimens had been fixed in 10% buffered formalin and had been embedded with paraffin wax. Four micrometer paraffin section of the specimens had been stained with haematoxylin and eosin. All of the slides were reexamined and evaluated to obtain the definitve diagnosis. The histology criteria used for lichen planus were[13]: (1) Hyperkeratosis or parakeratosis; (2) A dense and wel defined infiltrate of lymphocytes; (3) Predominantly lymphocytic infiltration; (4) Basal cell liquefaction degeneration.

A lichenoid lesion was diagnosed histologically upon exclusion of oral lichen planus. The world lichenoid for purpose is a clinicopathologic term encompassing any two or more of the above criteria. Other histology figures such as type of keratinization, type of epithelium, epithelial connective tissue clefting, type of rete ridges, presence of apoptotic bodies and dysplastic figure were been recorded. The diagnosis of oral lichen planus or oral lichenoid lesion was based on clinical findings with histology agreement. For the purpose of this study, the clinical and histopathological examination to obain the definitive diagnosis: (1) If the clinical and hispathological findings concur, then for purpose of this study, the definitive diagnosis would be lichen planus; (2) If the clinical and hispathological findings are of a lichenoid

lesion, then the definitive diagnosis would be a lichenoid lesion; (3) However, if the clinical findings are of lichen planus but this cannot be confirmed histologically, then the finding diagnosis would be a lichenoid lesions; (4) If the clinical findings are of a lichenoid lesion with no related medical history and the hispathological features are of lichen planus, then the definitive diagnosis would be lichen planus; (5) However, if the clinical features are of a lichenoid lesion but the patients had a medical history and the hispathological features are of lichen planus, then the definitive diagnosis would be a lichenoid lesion.

Statistical analysis

Data from lichen planus was compared with data from lichenoid lesions by using Chi square test. This statistical test was employed to determine whether there was significant difference between lichen planus and lichenoid lesions rather then correlating the variables.

RESULTS

Out of 159 patients, 107 (67%) were females and 52 (33%) were males. The mean age of all the 159 patients in this study was 44.7 ± 13.2 years.The incidence within ethnic goups was highest amongst Chinese (43%) and Indians (39.2%). According to the criteria laid out in the material and method, there were 86 cases (54.1%) of oral lichen planus and 73 cases (45.9%) of oral lichenoid lesions.

The Indians were more prevalent in number among the oral lichen planus patients (41.2%) followed by the Chinese and the Malays at 36.5% and 18.8% respectively. For oral lichenoid lesions, the patients were predominantly Chinese (50.7%). The proportion of Indians (37%) and the Malays (9.6%) was lower. The others race had the lowest prevalance for both conditions (Tab. 2).

Clinical features of lichen planus and lichenoid lesions

From the site of lesions, both types of conditions appear to affect any site of the mouth such as buccal mucous, gingival, tongue, alveolar ridge, gingival and lip. However, neither the palate nor the lip was singly affected. Buccal mucous was the commonest site of involvement for oral lichen planus and oral lichenoid lesion (Tab. 3). Oral lichen planus and oral lichenoid lesions could affect the buccal mucous single or as part of a multisite involvement.

Hispathology of oral lichen planus and lichenoid lesion

From 159 cases of oral lichen planus and oral

Table 1. The definitive diagnosis of lichenoid lesion was based on clinical findings with histology agreement

	Lichen planus		Lichenoid lesion	
	N	%	N	%
Malay	16	18.8	7	9.6
Chinese	31	36.5	37	50.7
India	35	41.2	27	37.0
Others	3	3.5	2	2.7
Total	85	100.0	73	100.0

Table 2. The distribution of lesions according to ethnic groups

	Lichen planus (N = 86)		Lichenoid lesion (N = 73)	
	N	%	n	%
Buccal mucous	72	84.7	59	80.8
Tongue	12	13.9	15	20.5
Gingiva	5	5.8	5	6.8
Alveolar ridge	2	2.3	2	2.7
Palate	0	0.0	1	1.4
Lip	1	1.2	2	2.8

X^2 = 4.3; P=0.2000

Table 3. The distribution of oral lichen planus and lichenoid lesions according to the site of lesions

No	Clinically	Histopathologically	Definitive diagnosis
1	Lichen planus	Lichen planus	Lichen planus
2	Lichenoid lesion	Licheniod lesion	Licheniod lesion
3	Lichen planus	Licheniod lesion	Licheniod lesion
4	Licheniod lesion	Lichen planus	Lichen planus
5	Licheniod lesion	Lichen planus	Licheniod lesion

Table 4. The incidence of keratinizing among the various clinical presentation of oral lichen planus and oral lichenoid lesions

	Lichen planus (%)		Lichenoid lesions (%)	
	N	%	N	%
Reticular type				
Parakeratinized	30	85.7	15	88.2
Orthokeratinized	4	11.4	0	0
Mixed	1	2.9	2	11.8
Atrophic type				
Parakeratinized	17	70.8	17	89.5
Orthokeratinized	3	12.5	0	0
Mixed	4	16.7	2	10.5
Plaque-like type				
Parakeratinized	5	71.4	4	67.7
Orthokeratinized	2	28.6	2	33.3
Mixed	0	0	0	0
Erosive - type				
Parakeratinized	8	72.7	18	100
Orthokeratinized	2	18.2	0	0
Mixed	1	9.1	0	0

Table 5. Epithelium according to clinical presentation of the lesions

	Lichen planus (%)		Lichenoid lesions (%)	
	N	%	N	%
Reticular type				
Acanthotic	21	60.0	8	47.1
Atrophic	13	37.1	9	52.9
Ulcerative	1	2.9	0	0
Atrophic type				
Acanthotic	7	29.2	8	42.1
Atrophic	16	66.7	7	36.8
Ulcerative	1	4.1	4	21.1
Plaque like type				
Acanthotic	2	28.6	3	50.0
Atrophic	4	57.1	3	50.0
Ulcerative	1	14.3	0	0
Erosive type				
Acanthotic	2	18.2	8	44.4
Atrophic	6	54.5	5	27.8
Ulcerative	3	27.3	5	27.8

lichenoid lesions, the covering epithelium were mainly of parakeratinized stratified squamous type. For lichen planus parakeratinization was present in 77.9% of patients, orthokeranitization in 15.1 % while for lichenoid lesion, it was 89.0% and 4.1% respectively. The presence of both parakeratinization and orthokeratinization in the patients were equally in both conditions.

The commonest presentation for oral lichen planus and oral lichenoid lesions was the reticular pattern. The least common was popular and bullae, but still these did not present as a single pattern, they presented together with the reticular type. All types were present in similar amounts in both condition. The exception was the erosive type in which higher numbers and these pattern were seen in lichenoid lesions. There was no significant difference between oral lichen planus and oral lichenoid lesion.

In these findings (Tab.5), appears that for lichen there is a relationship between the clinical and hispathological features (reticular–acanthotic epithelium; atrophic–atrophic epithelium; plaque like–acanthotic epithelium; erosive–ulcerative epithelium). The findings were more variable for oral lichenoid lesion.

Both conditions showed irregular rete ridges with some areas possessing no rete ridges. Saw-thooth appreance were seen in only 11.6% patients with lichen planus and 5.5% patients with lichenoid lesions. Atrophic epithelium was present in 46 patients (53.5%) with lichen planus and 28 patients (38.4%) with lichenoid lesions. Acanthotic epithelium was more frequently found in 36 patients (49.3%) with lichenoid lesion than in 34 patients (39.5%) with lichen planus.

DISCUSSION

In this study, the clinical features of oral lichen planus were shown to be similar to those of other workers.[11,14] There was a female predominance where the male to female ratio was 1:1.7 with a mean age of 45.5 ± 12.03 years. The average age for males was 8 years younger then females. Lacy et al.[11] found that most females oral lichen planus presented at the fifth decade. Most male patients however presented at an average of 10 years earlier than female patients. The mean age of patients in this study was lower than those of others. In a demographic study, Axell and Runquist[4] showed that there was a wide age range

from 15 to 85 years old among patients with oral lichen planus.

The oral lichen planus study in India, Murti et al.[14] showed similar pattern to this study. This may be attributed the racial factors. In this study, Indians (42.2%) had the highest incidence of oral lichen planus, followed by Chinese (36.5%). Genetic factors have been suggested to predispose individuals to a considerable number of autoimmune diseases. Various diseases are associated with different HLA antigens and analysis of these antigens have opened new avenues for the identification of an individual's risk of acquiring certain diseases. Lin and Sun[15] showed that HLA–Te22 and DN1 antigens were only present in orientals. These antigens are closely associated with HLA-DR3 antigen which has been known to be associated with autoimmune disease.[16]

When investigating 44 cases of oral lichen planus in Chinese, Lin and Sun[15] found that Chinese take the place of Caucasians in carrying the HLA–DR3. In this present study, only 5 out of 86 cases of oral lichen planus had a medical history such as asthma and depression. It appears that 94% of patients who did not have any medical problems and genetic factors may also be involved in oral lichen planus. About 9% of cases involved other members of the family in this study. However, it is possible that a gene situated in the short arm of chromosome might be combined with different factors, such as drugs, psychological strain, infection, allergies ect, to produce its localized effect on the mucous and/or skin.

The site and clinical presentation of involvement of oral lichen planus and oral lichenoid lesions were very much the same. They were both found on the buccal mucous (81–85%) and were of the reticular type. However, oral lichenoid lesions tend to be of erosive or atrophic type compared to oral lichen planus found 85% of this cases involved the buccal mucous and presented with the erosive (57%), reticular (36%) and plaque (7%) types. Their findings had similar trends to those of oral lichenoid lesions in this study.

Oral lichen planus occurs relatively often, clinicians are likely to encounter lichen planus in practice. There are several diverse entities sharing common individual histopathological features with oral lichen planus. Non specific stomatitis, allergic phenomena, lichenoid drug reaction, dysplasia and Frank carcinoma can also show hyperkeratosis and discontinuity of basal cell region.[13] The pathologist's failure to observe and there to strict histomorphologic parameters in order to render a diagnosis of oral lichen planus through inclusion of non specific stomatitis.[13]

In this study, it was shown that both oral lichen planus ans oral lichenoid lesions had covering epithelium which were mainly of parakeratinized stratified squamous type. These findings concur with those of McClatchey et al.[17], who found 60% of their cases with mainly parakeratinizied epithelium. However, Van den Haute et al.[18] strongly suggested that focal parakeratosis, focal interruption of the granular layer and cytoid bodies in the cornified layer were never present in lichen planus, instead they were present in more than 50% skin biopsies of lichenoid drug eruption. This may due to the different structure of skin and oral mucous.

Walsh et al.[19] suggested that the adhesive interaction between lymphocytes and keratinocytes were important determinants in the effector phase of oral lichen planus. In this present study, when comparing the keratinization and the infiltration of lymphocytes did not correlate significantly ($p=0.22$). No correlation to keratinization type could be found. This finding was also supported by Maeda et al.[20] who suggested that inflammatory phenomena does not influence the keratin expression in oral lichen planus. Their study of oral lichen planus patients suggested that perhaps that the differentiation pattern of the epithelium in oral lichenplanus lesions may differ from that in orther keratinization disturbances. This may be related to the fact that the clinical manifestation of oral lichen planus is less stable than those of leukoplakia and frictional keratosis. They also concluded that heavy inflammation close to the epithelium in oral lichen planus does not seem to induce changes like those seen in inflamed gingival specimen and the keratin staining pattern in oral lichen planus are not similar to those previously reported in oral epithelial dysplasia. It appeared that the inflammatory reaction in oral lichen planus does not influence keratin expression in a way comparable with those of other inflammatory condition. Karagouni et al.[21] in a study of alteration in peripheral blood mononuclear cell function and serum cytokines in

oral lichen planus showed evidence of impairment in T lymphocyte function.

The only consistent finding in all the various clinical forms of oral lichen planus was the chronic subepithelial inflammation. Immunocytochemical studies on oral lichen planus have shown that lymphocyte numbers and distribution were not altered. Thomas et al.[22] Investigated peripheral blood mononuclear cells and suggested that T cells does not support the concept of a common superantigen in oral lichen planus and reflects the heterogeneity of the disease.

From the observation of this study, 40% of the diabetic patients had a dense and well defined infiltration of lymphocytes in the superficial lamina propria and another 60% involved the deeper submucous. The hypertension and allergic patients also had as inflammatory infiltrate which extended into deeper tissues. One of the oral lichenoid lesions patient who was under depression showed the infiltration of inflammatory cell which involved the deeper submucous.

Hedberg et al.[23] when investigating the relationship of basal degeneration and mono nuclear infiltration revealed a positive correlation between these two parameters. They also stated that there was no linear correlation between parakeratinization and liquefaction degeneration of basal cell. This study found all of the oral lichen planus cases were not related to liquefaction degeneration of basal cells. Because of the hydrophilic degeneration of the stratum germinativum and/or infiltration with lymphocytes the epithelium and connective tissue junction was indistinct in slightly more than half of the specimens. In comparing the clefting in the epithelium, oral lichenoid lesions had a slightly higher incidence than oral lichen planus. McClatchey[17] stated, therefore, that clefting appears to be a major but not essential features of histopathologic diagnosis. However, skin biopsies showed that basal layer damage is the primary event and that the mononuclear infiltration occurs secondarily.

The percentage of the clinicopathological correlation between the epithelium to clinical presentation was 55.0% (42/77) of lichen planus, but only 38.7% in lichenoid lesions. More difficult to presume the histopathologically findings from the clinical presentation. The features of oral lichenoid lesions were also more variable where some of the lesions had inconspicuous liquefaction degeneration and sparse inflammatory infiltrate and some appeared to have extended features of oral lichen planus. However, this could because the strict criteria of well defined and dense infiltration of lymphocytes within the subcorium for lichen planus that had been used for this present study.

McClatchey et al.[17] demonstrated the diverse clinical and microscopic features seen in thir patients and suggested that lichen planus may not be correctly diagnosed unless both the clinician and pathologist are aware of the protean clinical and microscopic manifestations of the disease. Otsman et al.[10] when studying of oral lichen planus, found that only their patients fulfilled the immunohistochemical criteria for lichen planus and no relationship could be found between the clinical and histology diagnosis of oral lichen planus. Because of using strict criteria for oral lichen planus there could be an over diagnosis lesions. There were only 55% clinical and histological agreement in this study. There were clinical and histological agreement 96% of McClatchey et al's study.[17] They cited the presence and density of cellular infiltrate were not important factors when relating it to keratinization. In the absence of hyperkeratosis and a band like infiltrate diagnosis of oral lichen planus cannot be confirmed. On the other hand, lack of the features does not unequivocally rule out lichen planus. A biopsy specimen taken out at another time or from another mucousl site may reveal these confirmatory microscopic characteristic. Therefore, in a small number of cases of clinically suggestive lichen planus the final diagnosis must remain equivocal in the absence a typical manifestation of the disease spectrum or another completely unrelated pathologic process.

Neumann et al.[24] investigated the smoking habits of 611 patients with oral lichen planus and found that the original atrophic and reticular types of lesions were altered into the plaque type of lesions under the habit. In this study, about 8% of lichen planus and about the same number of lichenoid lesions were of the plaque type. None of these cases had a smoking history. When correlating habits with inflammatory cells, there was no significant difference between lichen planus and lichenoid lesions. There was, however, a more

apparent relationship between having a habit and the epithelial thickness. This study showed 6 out of 8 habitual cases (betel chewer, smoker and drinker) of lichen planus had atrophic epithelium. However, for lichenoid lesions, 8 out of 12 habitual cases had normal or acanthotic epithelium. Murti et al.[14] in their observation among tobacco in oral lichen planus found that histologically 75% of 94% biopsies of oral lichen planus showing epithelial atrophy. However, they could not substantiate it with any high degree of certainly that oral lichen planus possessed a significantly higher potentially for malignant transformation.

De Jong et al.[25] found that the number of dysplastic changes persection did not show any significant correlation with the clinical type. They suggested it is then conceivable that histological criteria of epithelial dysplasia planus. The most significant variable in estimating malignant development in oral lichen planus is from the occurrence of cellular atypic or dysplastic change which having no specific clinicopathological features.

Katz et al.[26] believed that erosive lichen planus is a condition that will increase the risk malignant transformation in sites typically associated with the development of squamous cell carcinoma. This present study showed that more of the erosive type of oral lichen planus or oral lichenoid lesions possess cellular atypia or mild dysplasia. Macdonald and Rennie[27] suggested that slight degrees of abnormalities of epithelial atypia may be reactive rather than preneoplastic in nature and this may be true for the cases in this study.

From the results of present study, it appeared that there are no reliable clinicohistopathological features that can clinical as well as histologic features over time as a result of change in the host defensive mechanisms or in the nature of the inciting factors including their ability to act as cytotoxic or allergic stimuli.[10] Others have tested immunologic parameters in attempt to discriminate between different oral lichenoid lesions anf oral lichen planus but none of the examined parameters were of value.[28,29]

CONCLUSIONS

Oral lichen planus showed relationship between clinical and histopathological features. Oral lichenoid lesions clinical and histopathological features were more inconsistencies. For oral lichenoid lesions, the inflammatory cell infiltrate extended into deeper tissue in patients with a systemic disease than those without. This was not seen in oral lichen planus. These findings suggest that any medical history or other condition (duration of lesion, habit) could vary clinicopathological features for oral lichenoid lesions and perhaps also for oral lichen planus.

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