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A clinical study of 674 patients with oral lichen planus in China

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BACKGROUND: Oral lichen planus (OLP) is a chronic inflammatory disease with different clinical presentations that can be classified as reticular, atrophic or erosive. Although OLP is a relatively common disorder, the reports comprising large numbers of OLP patients with specific character are lacking in the literature. The purpose of this paper was to describe the clinical characteristics of OLP in 674 Chinese patients.

METHODS: A total of 674 charts of patients with histologically confirmed OLP were collected from Stomatological Hospital of Wuhan University between 1963 and 2003.

RESULTS: Of the 674 patients, 65.9% were women and 34.1% were men. The most common clinical presentation was the reticular type (51.3%), and symptomatic OLP was noted in 67.5% of the patients, mainly in those with the erosive form. The erosive presentations showed significantly longer duration, more sites affected and a much greater old patients predominance than reticular or atrophic ones. About 90.9% of the patients had multiple oral sites of involvement and isolated lower lip lichen planus were observed in 60 cases (8.9%) and isolated gingiva lichen in only one case (0.2%). Skin involvement of lichen planus was found in 11.4% of patients. No statistically significant differences could be identified between OLP and diabetes, cardiovascular disease, smoking or alcohol use. Precipitating factors that resulted in an exacerbation of the disease were frequently noted and included foods, stress, dental cusp and poor oral hygiene. The transformation of OLP into malignancy was observed in four patients at sites previously diagnosed by clinical examination as erosive or atrophic lichen planus.

CONCLUSIONS: Patients with OLP in China usually present with distinctive clinical morphology and characteristic distribution and few may display lesions with a confusing array of forms mimicking other diseases. A long time follow up is of utmost importance to detect its malignant transformation.

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Introduction

Lichen planus is a chronic inflammatory disease of the skin and mucous membranes that frequently involves the oral mucosa. The exact aetiopathogenesis has not been disclosed, but the immunological system is believed to play a leading role in it. Oral lichen planus (OLP) characteristics have been well described in several series comprising large numbers of patients all over the world, such as in Hungary (1), America (2), Australia (3), Spain (4) and Israel (5). A general similarity, including a mild predilection for females and a mean age at onset in the fourth to fifth decade, buccal mucosa being the most common site, in the nature of this disease in different populations have been confirmed. To the best of our knowledge a similar study has not yet been conducted in a Chinese population. OLP eruptions always have distinct clinical morphological features and characteristic distribution, but they may also present in an array of confusing patterns and forms simulating other diseases. Andreasen's (6) classical classification consisted of six forms and it was simplified by other authors (7) who consider only three types of lesions: reticular, including white lines, plaques and papules; atrophic or erythematous; and erosive, including ulcerations and bullae. Patients with OLP frequently have concomitant lesion in one or more extraoral sites, which was emphasized in a study (8) demonstrating vulvar and vaginal involvement in approximately 25% of women with OLP and cutaneous lesions in approximately 15%. Thus, having patients with OLP evaluated by a multidisciplinary group of health care providers is of great importance due to the occasional concomitant involvement in other

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body sites. The possible malignant transformation of OLP is the subject of an ongoing and controversial discussion in the literature. Many cases of OLP with malignant degeneration have been reported by authors around the world. Up to date there were few reports about these cases in a group of Chinese.

The purpose of this study was to assess the natural history of OLP in a group of Chinese, describe similarities and differences in the clinical features of these patients relative to those in previously reported series and report four cases of malignant transformation.

Material and methods

First a set of strict diagnostic criteria proposed by Van der Meij et al. (9) in 2003 based on the 1978 clinical and histopathological definition of OLP by the World Health Organization was utilized. These criteria are summarized with two parts.

Clinical criteria
Presence of bilateral, mostly symmetrical lesions. Presence of lace-like network of slightly raised grey-white lines (reticular pattern). Erosive, atrophic, bullous and plaque type lesions (accepted as a subtype only in the presence of reticular lesions elsewhere in the oral mucosa).

Histopathological criteria
Presence of well-defined band-like zone of cellular infiltration confined to the superficial part of the connective tissue, consisting mainly of lymphocytes. Signs of 'liquefaction degeneration' in the basal cell layer.

Absence of epithelial dysplasia
A diagnosis of OLP requires the fulfilment of both clinical and histopathological criteria.

A total of 674 charts of patients with OLP in Stomatological Hospital of Wuhan University (Wuhan, China) from January 1963 through January 2003 were retrospectively analysed. All data had been diagnosed by pathologists and medical professors. Patients with oral lichenoid lesions caused by an identifiable cause such as a hypersensitivity reaction to dental restorative materials or drugs and charts that did not include histological confirmation of OLP were excluded from this study.

Information regarding age at first onset of oral signs or symptoms, approximate duration of disease at presentation, gender, family history of lichen planus (first-degree relatives), sites of oral involvement, symptoms, predominant clinical forms (reticular, atrophic and erosive), skin involvement, general health condition, habits regarding tobacco and alcohol consumption and histologically proven malignant transformation at a previously diagnosed OLP site was reviewed and analysed. In patients with more than one clinical type of lesions, such as reticular and erosive, the most severe form of the disease (i.e. erosive) was used to classify the lesions. Exacerbating factors of OLP identified by either patients or the examiner were also noted.

Statistical analysis was carried out with the chi-squared test for significance. The results were considered statistically significant if the P-value was ≤ 0.05.

Results

Table 1 summarizes the profile of our study group. Of the 674 patients, 444 (65.9%) were women and 230 (34.1%) were men. The ratio of men and women was 1:1.91. The mean age at presentation was 49 years for women and 52 years for men, with an overall age range of 10–78 years. The age distribution of 674 patients at diagnosis are shown in Fig 1. A total of 78 patients matched in age with lesions other than vesiculobulous lesions served as a control group for the prevalence of diabetes and cardiovascular disease. No evident association of diabetes ($P > 0.05$) or cardiovascular disease ($P > 0.05$) was found. More than one-tenth (11.4%) of the patients had skin involvement. About 25.8% of the study group smoked and 24.0% had taken alcohol.

Table 1 Profile of patients with oral lichen planus (OLP)

Profile	*Female n = 444 (65.9%)*	*Male n = 230 (34.1%)*	*Total n = 674 (100%)*	*Control group 78 (100%)*
Age at onset (years)				
Mean	49	52	50.4	53
Range	10–78	11–71	10–78	20–77
Diabetes	37 (8.3)	41 (17.8)	78 (11.6)[a]	10 (13)
Cardiovascular diseases	49 (11.0)	36 (15.7)	85 (12.6)[b]	11 (14)
Skin involvement	46 (10.4)	31 (13.5)	77 (11.4)	
Smoking	76 (17.1)	98 (42.6)	174 (25.8)	
Alcohol	57 (12.8)	105 (45.7)	162 (24.0)	

[a]Chi-squared = 0.11, d.f. = 1, $P > 0.05$ (NS) when compared with control group.
[b]Chi-squared = 0.39, d.f. = 1, $P > 0.05$ (NS) when compared with control group.

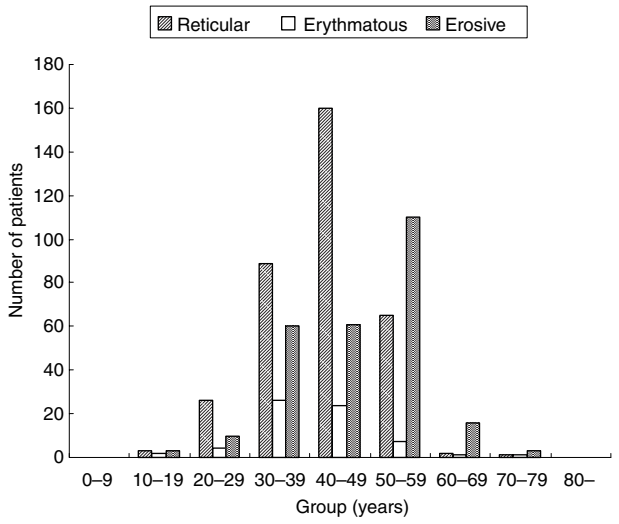

Figure 1 Age distribution of 674 patients with oral lichen planus (OLP).

Table 2 Differential features of reticular, atrophic and erosive oral lichen planus (OLP)

Variable	*Reticular 346 (51.3%)*	*Atrophic 65 (9.6%)*	*Erosive 263 (39.1%)*
Sex			
Female	244 (70.5)	35 (53.8)	165 (62.7)
Male	102 (29.5)	30 (46.2)	98 (37.3)
Age (years)			
< 50	278 (80.3)	56 (86.1)	134 (50.9)
≥50	68 (19.7)	9 (13.9)	129 (49.1)
Duration of disease (months)			
< 6	73 (21.1)	25 (38.5)	21 (8.0)
> 6	273 (78.9)	40 (61.5)	242 (92.0)
Symptomatic			
Yes	62 (18)	35 (54)	358 (98.6)
No	284 (82)	30 (46)	5 (1.4)
Number of sites			
≤2	209 (60.4)	38 (58.5)	76 (28.9)
≥3	137 (39.6)	27 (41.5)	187 (71.1)

Data given as *n* (%).

Table 3 Prevalence of site involvement in each clinical form of oral lichen planus (OLP)

Site	*Total 674 (%)*	*Reticular 346 (51.3%)*	*Atrophic 65 (9.6%)*	*Erosive 263 (39.1%)*
Buccal	503 (74.6)	301 (87.0)	36 (55.4)	166 (63.1)
Dorsal tongue	218 (32.3)	146 (42.2)	30 (46.2)	42 (16.0)
Lateral and ventral tongue	200 (29.7)	92 (26.6)	31 (47.7)	77 (29.3)
Upper lip	13 (1.91)	3 (0.9)	2 (3.1)	8 (3.0)
Lower lip	218 (32.3)	104 (30.1)	48 (73.8)	66 (25.1)
Labial	80 (11.9)	61 (17.6)	10 (15.4)	9 (3.4)
Gingiva	205 (30.4)	135 (39.0)	47 (72.3)	33 (12.5)
Hard palate	3 (0.4)	0 (0.0)	1 (1.5)	2 (0.8)
Soft palate	14 (2.2)	7 (2.0)	2 (3.1)	5 (1.9)
Floor of mouth	13 (1.91)	2 (0.6)	3 (4.6)	8 (3.0)

Data given as *n* (%).

Differential features of reticular, atrophic and erosive OLP were summarized in Table 2. The reticular form of the disease was the predominant type in 51.3% of the patients at initial presentation. In the 9.6% of patients with atrophic lesions as the predominant type, reticular lesions were almost always detected concomitantly. The erosive form was the predominant type in 39.1% of 674 cases. When the three groups of patients with reticular, atrophic and erosive lesions were compared with each other, we found that there were highly significant differences in terms of duration of disease ($P < 0.01$) and symptom ($P < 0.005$). Erosive lesions showed a significantly longer duration of disease ($P < 0.05$) and were easier to have symptoms. Symptoms, in addition to pain, the single most frequent complaint, including burning, swelling, irritation and bleeding were reported. Isolated reticular lesions were generally asymptomatic. Patients with erosive lesions seemed to be older and have more number of sites than patients with reticular or atrophic lesions. In terms of gender, females were proportionately more common in reticular form than in other two forms.

Although most patients had multiple oral sites of involvement, the disease was confined to the lower lips in 60 patients and to gingiva in one patient. Among all cases, the buccal mucosa was the single most common site of involvement in each form followed by the tongue, the lower lip, gingiva and labial mucosa (Table 3). Lesions on the palate, floor of the mouth and upper lip were uncommon. Statistical analysis performed for each of the three most prevalent sites (buccal, tounge and lip) showed no significant association between the site and the clinical form of the disease ($P > 0.05$).

The exacerbations of the disease were common. Precipitating factors that resulted in an exacerbation of the disease including stress, foods, dental cusp, systemic illness, poor oral hygiene, sunshine and the flu.

Four patients (Table 4) had histologically proven malignant transformation at a site previously diagnosed clinically and histologically as OLP. All of them displayed erosive or atrophic form clinically. Figures 2 and 3 showed the histological changes of one case and similar histological changes were observed in other three cases.

Discussion

So far, there are no universally accepted specific diagnostic criteria for OLP. Some studies (10) were solely based on a clinical diagnosis while other conditions such as leukoplakia, lupus erythematous and even squamous cell carcinoma can present a similar clinical appearance. Furthermore, histopathological assessment of OLP is a rather subjective, which was demonstrated in a study (11). Many studies (12) showed that some oral lesions diagnosed clinically or histologically as lichen planus in previous reports might actually have been lichenoid dysplasias, i.e. premalignant dysplasias with lichenoid appearances. In our study, we utilized the latest criteria proposed by Van der Meij et al. (9) in 2003 based on the 1978 clinical and histopathological definition of OLP by the World Health Organization. The criteria include both histopathological and clinical

Table 4 Characteristics of patients with oral lichen planus (OLP) who developed carcinoma

Case (n)	*Age (years) at onset of OLP*	*Sex*	*Clinical form*	*Location*	*Time from first visit of OLP to transformation (years)*	*Tobacco or alcohol use*	*Systemeric disease*
1	35	Male	Atrophic	Buccal	21	Both	None
2	57	Male	Erosive	Buccal	9	Both	Oesophagus carcinoma
3	50	Male	Erosive	Buccal	3	Both	None
4	65	Female	Erosive	Dorsal tounge	3	None	Digestive disease

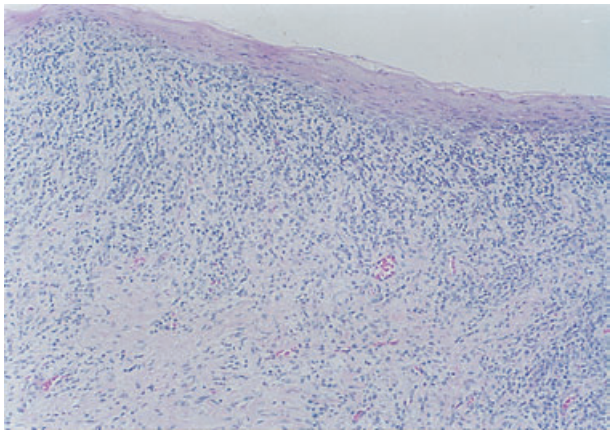

Figure 2 Oral lichen planus (OLP) histological feature of case 1 (haematoxylin-eosin stain, original magnification ×100).

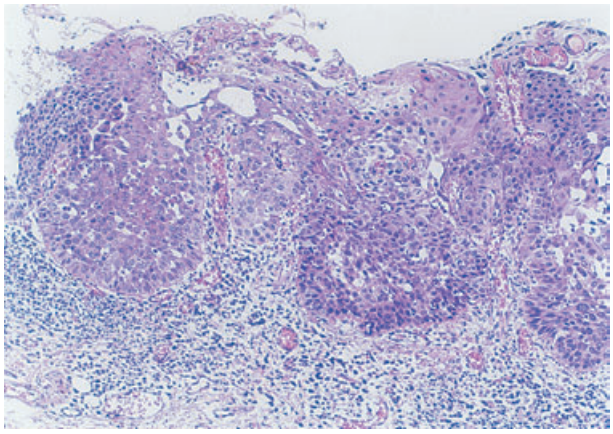

Figure 3 Histological feature of malignant transformation of case 1 (haematoxylin-eosin stain, original magnification ×100).

features. Patients with oral lichenoid lesions caused by an identifiable cause such as a hypersensitivity reaction to dental restorative materials or drugs and patients with epithelial dysplasia were excluded from this study.

The clinical features of patients in our survey share many similarities with those reported previously. For example, as noted by others and confirmed in this study, there is a predominance of female patients and the largest number of cases occur between the ages of 40 and 59 years and OLP developed most commonly on the buccal mucosa, and was most symptomatic in its erosive form. OLP in children is uncommon and in our study it was observed in four patients, age ranging from 10 to 13, and two were with reticular lesion and two were with erosive lesion. The longest duration was 6 years and one child had cutaneous lesions. In 1999, Sharma and Maheshwari (13) reported 50 cases of childhood cutaneous lichen planus, with 15 exhibiting concomitant oral mucosal involvement. Although childhood OLP is uncommon, early recognition is very important to make appropriate treatment and alleviate the sorrow of little children.

A number of reports (14, 15) have suggested that patients with lichen planus have associated diabetes more often than the general population. Grinspan et al. (16) suggested that there was a link between OLP and diabetes too. However, our study and others (5) did not support their observation. Although some of our patients had diabetes, when compared with the general population the prevalence of diabetes in our group was within the limits.

Reticular lesion, the most clinical form of OLP, resulted in few symptoms. Although most patients with the reticular form had no symptoms, 71% of our study group were given the diagnosis of this form of the disease. The finding shows that there is a high awareness of the issue of OLP among Chinese dentists and doctor. Moreover, reticular lesions were histologically diagnosed as OLP more commonly than atrophic or erosive lesions when patients underwent several biopsies of different forms of OLP lesions. In 1981, Zegarelli (17) proposed choosing a reticular lesion for biopsy when confirming the diagnosis. In OLP, atrophic and reticular lesions always surround or developed within all erosive lesions which is an important feature in clinically distinguishing OLP from other vesiculoerosive diseases such as pemphigoid and pemphigus. Similarly, only in OLP and oral discoid lupus erythematosus, reticular lesions and atrophic lesions coexist. We had not observed isolated atrophic lesions as Eisen (18) did while Holmstrup et al. (19) had reported some and suggested these lesions should be regarded as pre-cancerous.

On comparing our study groups, statistically significant differences were observed in some instances proved to be important. Greater differences were found on comparing sex distribution, i.e. reticular lesions presented a much greater female predominance than the other two lesions. An association of atrophic clinical presentations with age older than 60 years has been suggested (20). In the present study, patients with erosive lesions showed a higher mean age than those with reticular or atrophic lesions. The mean duration of OLP is usually longer than a year. Our results suggested that erosive clinical lesions has a longer period of duration and a higher number of sites affected, which is similar to the results reported by Seoane et al. (21).

In our survey, among all cases, the buccal mucosa was the single most common site of involvement followed by the tongue, the lower lip and gingiva (Table 4). Lesions on the palate, floor of the mouth and upper lip were uncommon. Eisen (18) and others had reported the most common site was the buccal mucosa, followed by the tongue, the gingiva and the lower lip. The discrepancy may be attributed to races and geography of the patients and the limitation of the samples. In our study, lichen planus confined to a single oral site is infrequent occurrence. In 1996, Allan and Buxton (22) reported isolated lip lesions firstly and we found 60 cases of isolated lip lesions, among which 37 cases were clinically diagnosed as oral discoid lupus erythematous and 30 cases with erosive lesion. The clinical features of isolated lip lesions of OLP are similar to those of oral discoid

lupus erythematous and we could distinguish them by histology and immunofluorescence. Our reports showed only 0.2% of patients with OLP, while Scully (23) noted approximately 10% and Eisen (18) noted 8.6%, presented isolated gingiva lesions. When lichen planus is confined to the gingiva, especially in the form of desquamative gingivitis, we should tell them from the vesiculoerosive diseases.

In 1910, Hallopeau (24) reported a case of OLP with malignant degeneration. But then on, many sporadic cases of transformation have been reported in the literature (25, 26). Nevertheless, controversy still exists today as to whether OLP is considered a pre-malignant condition. Previous retrospective studies showed a frequency ranging from 0.04 to 5%. In China, Chen and Chen (27) found seven cases of OLP with malignant degeneration in 595 patients while Zhou et al. (28) reported nine cases. Our study showed that there were four cases of malignant degeneration, which had histological evidence of both OLP and malignant transformation in 674 patients. Although most of 674 patients have been treated and observed in our hospital, we cannot role out this possibility that very few patients have run off. So it is impossible for us to reconstruct the annual malignant transformation rate in the entire group of patients. In the reported series, none of the carcinomas developed from reticular lesions and it has been suggested that atrophic and erosive lesion of OLP is potentially more dangerous. In our study three malignant transformations arose in a pre-existing erosive lesion, and one in a atrophic lesion, which supported the speculation. One of the four patients with OLP who had malignant transformation was with 21 years of duration of disease. The fact of the malignant transformation with 21-year duration necessitates a long follow up to detect OLP in China, considering there may be an extended exposure to carcinogenic causative factors with long duration. All of three male patients had the habits of smoking and alcohol consuming and the female patient had a history of digestive disease. The smoking, alcohol consuming and the systemic disease may be risk factors, which promoted the malignant transformation of OLP, but some (28, 29) reported patients with malignant degeneration had no history of any known risk factors (alcohol or tobacco). We also observed that one patient had oesophagus carcinoma before the lesion of OLP transformed malignant, which has not been reported earlier. Whether OLP lesions with cancer in other sites may tend to get malignant is unknown and requires further investigation.

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