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Original Article

Clinical, histological and direct immunofluorescence features in oral mucosal patches striae diseases with malignant potential

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KEYWORDS
Direct immunofluorescence;
Oral mucosal patches striae diseases;
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Oral potentially malignant disorders

Abstract *Background/purpose:* Oral mucosal patches striae diseases (OMPSD) represent an important category of oral mucosal disease, most of which may have malignant potential (OMPSD-MP). The differential diagnosis is challenging due to overlap of their clinical and pathological features.
Materials and methods: 116 OMPSD-MP patients were included in this cross-sectional study from November 2019 to February 2021, including oral lichen planus (OLP), oral lichenoid lesions (OLL), discoid lupus erythematosus (DLE), oral submucous fibrosis (OSF) and oral leukoplakia (OLK). The general information, clinical manifestation, histopathological and direct immunofluorescence (DIF) features were statistically analyzed and compared.
Results: OLP was the major type of OMPSD-MP (64.7%), followed by OLL (25.0%), OLK (6.0%), DLE (2.6%) and OSF (1.7%), which were pooled as non-OLP group for further assessment. They shared many clinical and histological features in common. The rate of clinical-pathological

Abbreviations: DIF, Direct immunofluorescence; OMPSD, Oral mucosal patches striae diseases; OLP, Oral lichen planus; OPMD, Oral potentially malignant disorders.

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diagnosis concordance was 73.5% for OLP, and 76.7% for total OMPSD-MP. DIF positive rate was significantly higher in OLP group than non-OLP group (76.0% *vs*. 41.5%, $P < 0.001$), in which the deposition of fibrinogen (Fib) and IgM were most frequently found.
Conclusion: A significant overlap in clinical and histopathological features of OMPSD-MP was found, while DIF could be useful in differential diagnosis. Fib and IgM might be important immunopathological factors in OLP, which need further exploration.

Introduction

Oral mucosal patches striae diseases (OMPSD) are constituted an important category of oral mucosal disease, characterized by white patches and striate lesions of the oral cavity. Oral lichen planus (OLP), oral lichenoid lesions (OLL), discoid lupus erythematosus (DLE), oral submucous fibrosis (OSF) and oral leukoplakia (OLK) are composed the major types of OMPSD. It is noteworthy that all of the disorders mentioned above are defined as oral potentially malignant disorders (OPMD) due to their malignant potential. The malignant transformation rate was 0.4–2.3% for OLP, 1.9–3.8% for OLL, 2.0% for DLE, 7.0–14.0% for OSF and 7.5% for OLK, respectively.[1–5] Since the therapy strategy varies from each disorder and inappropriate treatment approach may lead to profound adverse effect, the accurate diagnosis is of great importance for OMPSD with malignant potential (OMPSD-MP).

The diagnosis of OMPSD-MP is usually made based on clinical and histological examination. However, the significant clinical manifestation and pathological features overlap among the diseases complicates a definitive diagnosis.[6,7] Clinically, the untypical smeared-out boundary white plaque lesions are commonly and un-specifically found in several types of OMPSD-MP. Histologically, lymphocytes infiltration in the shallow layer of connective tissue, one of the characteristics of OLP, can also be found in OLL and initial OSF.[4] Moreover, the coherence of clinical and pathologic diagnosis of some OMPSD-MP failed to perform well. For OLP, which is one of the most common OMPSD-MP, the reported clinic-pathological consistency only ranges from 38% to 54%.[8] Thus, some auxiliary tests are required.

Direct immunofluorescence (DIF) served as a diagnostic tool that has been widely used in immunological mucocutaneous diseases and used as an adjunctive diagnostic tool in differentiating immunological bullous diseases and OLP.[9] However, the studies were limited regarding to characteristics of immunofluorescent deposition of other OMPSD-MP,[10,11] as well as the role of these immune factors with the diseases. This study aims to summarize and compare the clinical, histological and DIF features of OMPSD-MP.

Materials and methods

Ethical approval

This study was approved by the Peking University Institutional Review Board, China [PKUSSIRB-201951177a]. All methods were performed in accordance with the relevant guidelines and regulations. Each adult participant singed the informed consent form before sample gathering.

Participants

116 patients with clinically suspected oral lesions of OMPSD-MP who referred to the Department of Oral Medicine, Peking University School and Hospital of Stomatology, China from November 2019 to February 2021 was recruited to the present study.

Inclusion and exclusion criteria

Inclusion criteria

This study included patients who were between 18 and 75 years of age, patients who met the following classification term for OMPSD-MP such as OLP, OLL, OLK, DLE and OSF in clinic.

The clinical diagnosis for OLP was made in patients presenting with classic bilateral, reticular or lace-like lesions; for OLL was unilateral or bilateral, reticular or lace-like lesions irritated by dental restoration; for OLK was white patch or plaque lesions, in homogeneous, nodular, verrucous pattern; for DLE was typical discoid plaque surrounded by whitish striae; for OSF was blanched and opaque lesions with appearance of fibrotic bands.[12,13]

Exclusion criteria

The study excluded patients with systemic immune diseases or tumor; patients who had received immunotherapy or systemic medication within 3 months; patients with other established oral mucosa diseases.

Clinical information

General information including age, sex, duration of disease was obtained from each subject. The clinical manifestation including morphology of lesions and site of involvement were recorded.

Histological examination

All 116 patients underwent biopsy in the Department of Oral Medicine, Peking University School and Hospital of Stomatology. Tissues for H&E testing were fixed in 10%

neutral formalin and sent to the Department of Oral Pathology, Peking University School and Hospital of Stomatology. The histological features were recorded as follows: mucosa (hyperkeratosis, dysplasia, hypergranulosis, spongiosis, colloid body, etc.), mucosal—submucosal junction (basal liquefaction degeneration, lichenoid infiltration and basement membrane thickening, pigmentary incontinence, etc.) and submucosa (fibrosis, telangiectasia and perivascular infiltrate). Additionally, the degree of lichenoid infiltration along the basement member and superficial connective tissue is determined as: none (no inflammation), untypical/slight (untypical band-like lymphocytic inflammatory with other cells), typical (band-like lymphocytic inflammatory).[14]

Direct immunofluorescence (DIF)

Tissues for DIF test were stored in normal saline. The specimen were frozen and cut to 4 μm-thick sections and stained for the following fluorescein isothiocyanate antibodies: goat polyclonal anti-human IgM mu chain (ab97204, Abcam, Cambridge, UK), rabbit polyclonal anti-human IgA alpha chain (ab97219, Abcam), goat polyclonal anti-human IgG H&L (ab6854, Abcam), rabbit polyclonal anti-human Fibrinogen (ab4217, Abcam), rabbit polyclonal anti-human C3c (ab4212, Abcam). The DIF examination was carried out by computer aided Nikon eclipse 80i microscope.

Diagnosis

The diagnosis was made by clinical manifestation and histopathological examination by experienced clinicians and pathologist, respectively. The criteria of clinical diagnosis was described above. The criteria of histological diagnosis for OLP was the presence of basal cell degeneration and band-like lymphocyte infiltration in the juxtaepithelial region; for OLL was the less obvious liquefaction degeneration and/or cellular infiltration in the superficial part of the connective tissue; for OLK was variable characteristics of dysplasia in the oral epithelium, such as nuclear hyperchromatism, presence of several layers cells with basaloid appearance and irregular epithelial stratification; for DLE was hyperkeratosis with keratotic plugs, atrophy of the rete ridges, liquefactive degeneration of basal cell layer and perivascular infiltrate; for OSF was severe flattened epithelium with loss of rete ridges, connective tissue fibrosis, reduced cellular elements and blood vessels.[12,13,15]

When the diagnosis is vague, both clinicians and pathologist would be consulted and give the final diagnosis.

Statistic data analysis

Data were analyzed using the SPSS version 26.0 statistical package (SPSS® Inc., Chicago, IL, USA). Categorical data was analyzed by Chi-square test or Fisher exact test in different groups. Continuous data was presented as mean ± standard deviation (SD), and independent-samples t-test or nonparametric test were used to data analysis in different groups. Statistical significance was established as $P < 0.05$.

Results

Patient characteristics

All of the 116 patients were included in the present study. They were clinically diagnosed as OLP (102 patients, 87.9%), OLL (3 patient, 2.6%), DLE (3 patients, 2.6%), OSF (2 patients, 1.7%) and OLK (6 patients, 5.2%). When combined with histological examination, these patients were finally diagnosed as OLP (75 patients, 64.7%), OLL (29 patients, 25.0%), DLE (3 patients, 2.6%), OSF (2 patients, 1.7%) and OLK (7 patients, 6.0%). The rate of clinical-pathological diagnosis concordance was 73.5% for OLP, and 76.7% for OMPSD-MP.

Since OLP patients accounted for over half of the total participants, the patients with OLL, DLE, OSF and OLK were pooled as non-OLP group for further assessment.

A female predominance in OLP group (female: male ration = 1.68:1) and slight male predominance in non-OLP group (female: male ratio = 0.86:1) was found with no statistically significance ($P = 0.090$). The mean age was similar between OLP group (44.73 ± 13.04Y) and non-OLP group (47.95 ± 14.57 Y) ($P = 0.225$). The duration of disease between OLP (9.19 ± 18.31M) and non-OLP group (14.99 ± 18.47 M) showed no significantly difference ($P = 0.158$).

Clinical manifestations

Reticular and plaque-like type white lesions were the main clinical feature of the patients (Fig. 1). In addition, white stripes were found more frequently in OLP patients than non-OLP patients with statistical significance (100.0% vs. 82.9%, $P = 0.001$) (Table 1).

Lesions of OMPSD-MP were almost found in all oral mucosal surfaces, buccal mucosa was the most common site of involved, followed by tongue, lip, gingiva and palate. Moreover, significantly higher percentage of OLP lesions were located in buccal mucosa than in non-OLP group (96.0% vs. 82.9%, $P = 0.001$) (Table 1).

Histopathological features

A total of 116 biopsy specimens were obtained and underwent histopathological examination (Fig. 2). OMPSD-MP shared common histopathological features but some distinctive characteristics were observed (Table 2). In detail, OLP group showed higher percentage of mucosal spongiosis (70.7% vs. 46.3%, $P = 0.010$), colloid bodies (66.7% vs. 17.1%, $P < 0.001$), basal liquefaction degeneration (100.0% vs. 75.6%, $P < 0.001$), lichenoid infiltration (100.0% vs. 78.1%, $P < 0.001$) than pooled non-OLP group, whereas non-OLP group showed higher percentage of epithelium dysplasia (0.0% vs.9.7%, $P = 0.026$), telangiectasia (68.3% vs. 40.0%, $P = 0.004$) and perivascular infiltrate (75.6% vs. 37.3%, $P < 0.001$).

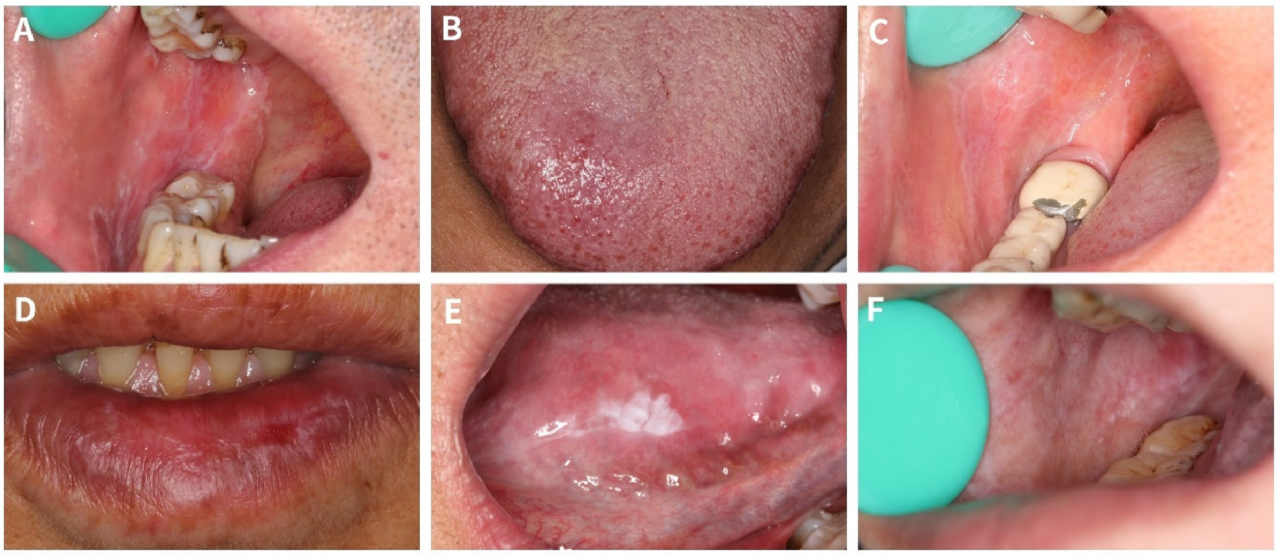

Figure 1 Clinical manifestations of oral mucosal patches striae diseases with malignant potential. Reticular patch on the right buccal mucosa (A) and white stripes on the dorsal tongue (B) in OLP patient. White stripes on the right buccal mucosa irritated by dental restoration (C) in OLL patient. White stripe on the lip with blurred mucosa-skin boundaries (D) in DLE patient. Homogeneous white patch on the right ventral tongue (E) in OLK patient. Blanched and opaque lesions on the right buccal mucosa (F) in OSF patient. OLP, oral lichen planus; OLL, oral lichenoid lesions; DLE, discoid lupus erythematosus; OSF, oral submucous fibrosis; OLK, oral leukoplakia

Direct immunofluorescence features

All of 116 biopsy specimens were subjected to DIF examination. The positive yields were found in OLP patients (57/75), OLL patients (14/29), DLE (2/3) and OLK (1/7) patients, while OSF patients showed completely negative findings. In addition, OLP group had significantly higher DIF positive rate than non-OLP group (76.0% vs. 41.5%, $P < 0.001$). Among the testing index, fibrinogen (Fib) was the commonest immunoreactant deposit in all OMPSD-MP cases. It was typically deposited at the basement membrane zone (BMZ) in a linear pattern. IgM was the second commonest immunoreactant deposit, which was typically deposited in colloid body in a shaggy pattern. The scarred deposition of IgG, IgA and C3 in

Table 1 Clinical features of oral mucosal patches striae diseases with malignant potential.

Clinical features	OLP group n = 75	Non-OLP group (n/total N)					*P*-value between OLP and pooled non-OLP group
		OLL n = 29	DLE n = 3	OSF n = 2	OLK n = 7	POOLED n = 41	
Morphology of lesions, n (%)							
white stripes	75 (100.0)	29 (100.0)	3 (100.0)	0 (0.0)	2 (28.6)	34 (82.9)	0.001*
white plaques	28 (37.3)	11 (37.9)	1 (33.3)	2 (100.0)	7 (100.0)	21 (51.2)	0.148
white papules	7 (9.3)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (2.4)	0.309
Vesicles	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Distribution, n (%)							
Buccal	72 (96.0)	28 (96.5)	1 (33.3)	2 (100.0)	3 (42.8)	34 (82.9)	0.040*
Dorsal tongue or lateral tongue	38 (50.7)	12 (41.4)	1 (33.3)	1(50.0)	3 (42.8)	17 (41.5)	0.343
Ventral tongue or mouth floor	27 (36.0)	11 (37.9)	0 (0.0)	0 (0.0)	2 (28.6)	13 (31.7)	0.642
Lip vermillion	18 (24.0)	5 (17.2)	3 (100.0)	0 (0.0)	1 (14.3)	9 (21.9)	0.803
Lip mucosa	3 (4.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1.000
Gingiva	10 (13.3)	3 (10.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (7.3)	0.500
Hard palate	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0.353
Soft palate	1 (1.3)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	1.000

*$P < 0.05$ indicates statistical significance; OLP, Oral lichen planus; OLL, oral lichenoid lesions; DLE, discoid lupus erythematosus; OSF, oral submucous fibrosis; OLK, oral leukoplakia.

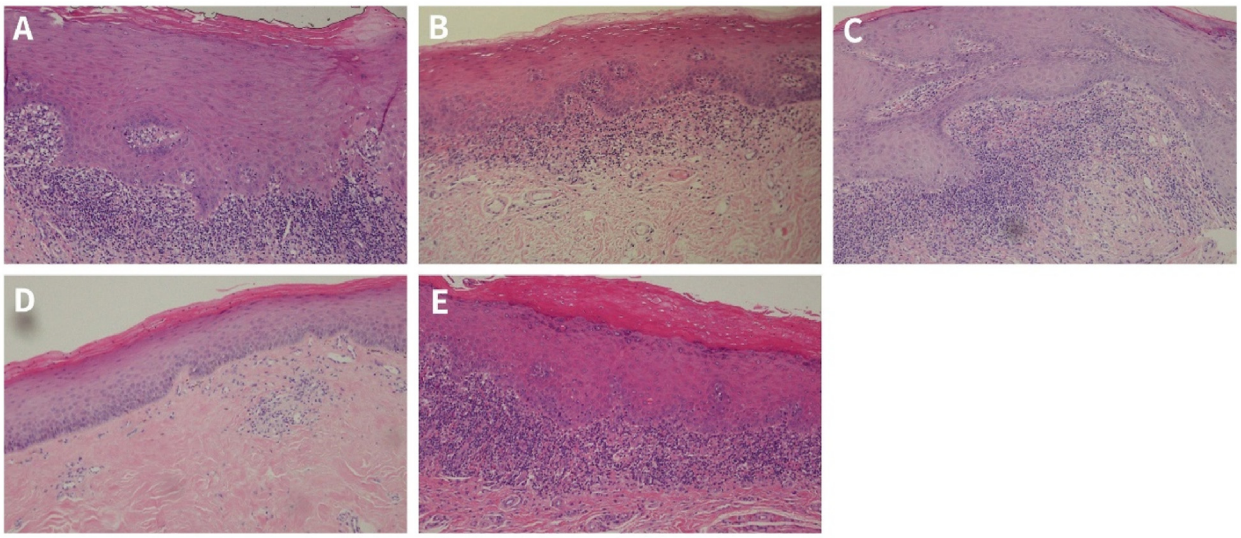

Figure 2 Histopathological manifestations of oral mucosal patches striae diseases with malignant potential. (A) Hyperparakeratosis, basal liquefaction degeneration and typical lichenoid infiltrate in OLP. (B) Hyperparakeratosis, basal liquefaction degeneration and untypical lichenoid infiltrate in OLL. (C) Mucosal atrophy, telangiectasia and perivascular infiltrate in DLE. (D) Flattened epithelium with loss of rete ridges and connective tissue fibrosis in OSF. (E) Simple mucosal dysplasia, typical lichenoid infiltrate and perivascular infiltrate in OLK. Hematoxylin-eosin stain; A, B, C, D and E, ×40. OLP, oral lichen planus; OLL, oral lichenoid lesions; DLE, discoid lupus erythematosus; OSF, oral submucous fibrosis; OLK, oral leukoplakia

Table 2 Histopathological features of oral mucosal patches striae diseases with malignant potential.

Histopathological features, n (%)	OLP group n = 75	Non-OLP group (n/total N)					*P*-value between OLP and pooled non-OLP group
		OLL n = 29	DLE n = 3	OSF n = 2	OLK n = 7	POOLED n = 41	
Hyperkeratosis							0.510
Normal	*0 (0.0)*	*1 (3.4)*	*0 (0.0)*	*0 (0.0)*	*0 (0.0)*	*1 (2.4)*	
Hyperorthokeratosis	*35 (46.7)*	*11 (37.9)*	*3 (100.0)*	*1 (50.0)*	*6 (85.7)*	*21 (51.2)*	
Hyperparakeratosis	*35 (46.7)*	*14 (48.3)*	*0 (0.0)*	*1 (50.0)*	*1 (14.3)*	*16 (39.0)*	
Hyperorthokeratosis & Hyperparakeratosis	*5 (6.7)*	*3 (10.3)*	*0 (0.0)*	*0 (0.0)*	*0 (0.0)*	*3 (7.3)*	
Epithelium dysplasia	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	3 (42.8)	4 (9.7)	0.026*
Hypergranulosis	41 (54.7)	16 (55.2)	3 (100.0)	1 (50.0)	6 (85.7)	26 (63.4)	0.362
Spinous layer							0.869
Normal	*7 (9.3)*	*5 (17.2)*	*0 (0.0)*	*0 (0.0)*	*0 (0.0)*	*5 (12.2)*	
Atrophy	*11 (14.7)*	*8 (27.6)*	*3 (100.0)*	*2 (100.0)*	*0 (0.0)*	*13 (31.7)*	
Acanthosis	*53 (70.7)*	*15 (51.7)*	*0 (0.0)*	*0 (0.0)*	*7 (100.0)*	*22 (53.7)*	
Atrophy & Acanthosis	*4 (5.3)*	*1 (3.4)*	*0 (0.0)*	*0 (0.0)*	*0 (0.0)*	*1 (2.4)*	
Mucosal spongiosis	53 (70.7)	17 (58.6)	0 (0.0)	1 (50)	1 (14.3)	19 (46.3)	0.010*
Colloid bodies	50 (66.7)	5 (17.2)	2 (66.7)	0 (0.0)	0 (0.0)	7 (17.1)	<0.001*
Basal liquefaction degeneration	75 (100.0)	23 (79.3)	3 (100.0)	1 (50.0)	4 (57.1)	31 (75.6)	<0.001*
Lichenoid infiltration							<0.001*
None	*0 (0.0)*	*3 (10.3)*	*0 (0.0)*	*2 (100.0)*	*4 (57.1)*	*9 (21.9)*	
Untypical/Slight	*11 (14.7)*	*22 (75.9)*	1 (33.3)	*0 (0.0)*	*2 (28.6)*	*25 (61.0)*	
Typical	*64 (85.3)*	*4 (13.8)*	2 (66.7)	*0 (0.0)*	*1 (14.3)*	*7 (17.1)*	
Basement-membrane thickening	48 (64.0)	21 (72.4)	2 (66.7)	0 (0.0)	4 (57.1)	27 (65.9)	0.842
Pigmentary incontinence	27 (36.0)	12 (41.4)	1 (33.3)	2 (100.0)	2 (28.6)	17 (41.5)	0.562
Fibrosis	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	2 (4.9)	0.123
Telangiectasia	30 (40.0)	19 (65.5)	3 (100.0)	0 (0.0)	6 (85.7)	28 (68.3)	0.004*
Perivascular infiltrate	28 (37.3)	19 (65.5)	3 (100.0)	2 (100.0)	7 (100.0)	31 (75.6)	<0.001*

*$P < 0.05$ indicates statistical significance; OLP, Oral lichen planus; OLL, oral lichenoid lesions; DLE, discoid lupus erythematosus; OSF, oral submucous fibrosis; OLK, oral leukoplakia.

colloid body was observed as well (Fig. 3). In addition, the positive rate of Fib and IgM was significantly higher in OLP group than in non-OLP group (72.0% vs. 39.0%, $P = 0.001$ and 36.0% vs.7.3%, $P = 0.001$, respectively) (Table 3).

Discussion

Despite some distinctive clinical features, such as apparent white strips lesion and buccal mucosa involvement in OLP cases described in our study, the rate of clinical-pathological diagnosis concordance was 73.5% for OLP, and 76.7% for OMPSD-MP. It is recommended that diagnosis of OMPSD-MP should not be made based on clinical grounds solely. A mucosa biopsy is required for each patient.

It is of note, even in histology, that OMPSD-MP shares some patterns of changes in common. According to our data, none feature was unique for each type of disease except for fibrosis in OSF. Nonetheless, there were some conspicuous

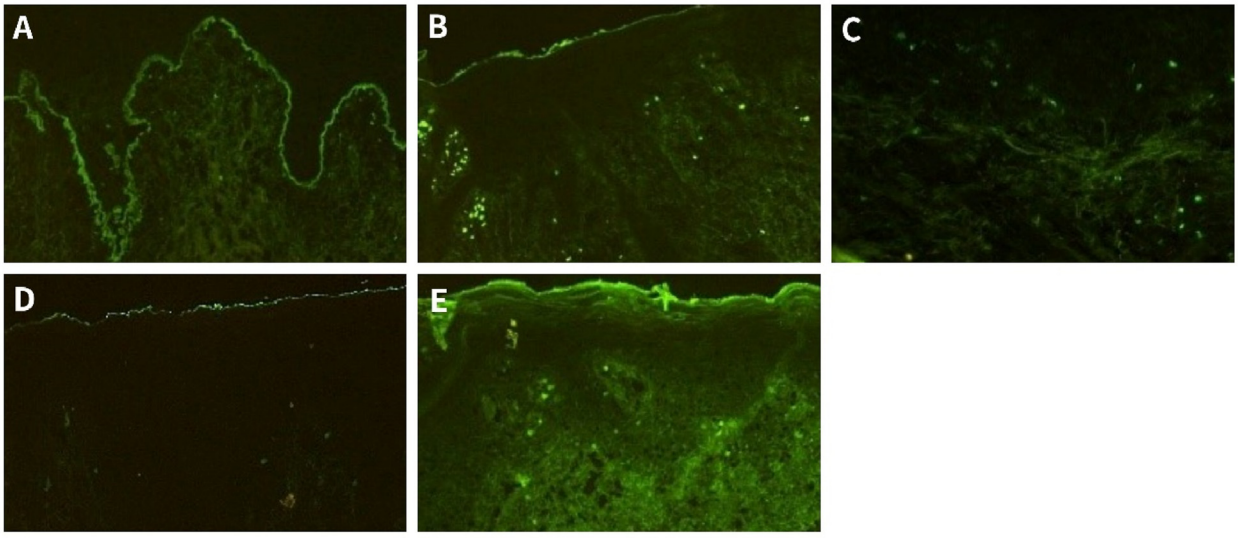

Figure 3 Characteristics of direct immunofluorescence in oral mucosal patches striae diseases with malignant potential. Liner-like Fib immune deposits in basement membrane zone (A), lobular immune deposits in the colloid body of IgM (B), C3 (D), IgG (E) in OLP patient. Ig A deposits in the colloid body in OLL patient(C). OLP, oral lichen planus; OLL, oral lichenoid lesions

Table 3 Characteristics of DIF in oral mucosal patches striae diseases with malignant potential.

DIF results n(%)	OLP group n = 75	Non-OLP group n/total N					*P*-value between OLP and pooled non-OLP group
		OLL n = 29	DLE n = 3	OSF n = 2	OLK n = 7	POOLED n = 41	
Positive DIF	57 (76.0)	14 (48.3)	2 (66.7)	0 (0)	1 (14.3)	17 (41.5)	<0.001*
Immunoreactant							
Fib	54 (72.0)	14 (48.3)	1 (33.3)	0 (0.0)	1 (14.3)	16 (39.0)	0.001*
IgM	27 (36.0)	2 (6.9)	1 (33.3)	0 (0.0)	0 (0.0)	3 (7.3)	0.001*
IgG	5 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.091
IgA	6 (8.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	0.526
C3	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0.941
Pattern of deposits							
Only Fib	28 (37.3)	11 (37.9)	0 (0.0)	0 (0.0)	1 (14.3)	12 (29.3)	
Fib + IgM	15 (20.0)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	
Fib + IgA	0 (0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	
Fib + C3	1 (1.3)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Fib + IgG	1 (1.3)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Fib + IgM + IgA	6 (8.0)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Fib + IgM + IgG	2 (2.7)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Fib + IgA + C3	0 (0)	0 (0)	1 (33.3)	0 (0.0)	0 (0.0)	1 (2.4)	
Fib + IgM + IgG + C3	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Only IgM	2 (2.7)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	1 (2.4)	
IgM + IgG	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

*$P < 0.05$ indicates statistical significance; DIF, direct immunofluorescence; OLP, Oral lichen planus; OLL, oral lichenoid lesions; DLE, discoid lupus erythematosus; OSF, oral submucous fibrosis; OLK, oral leukoplakia; Fib, Fibrinogen.

histological features to identify them. In accordance with previous studies,[15] basal liquefaction degeneration and typical lichenoid infiltration at superficial connective tissue were the main characteristics of OLP, as well as mucosal spongiosis and colloid bodies. On the contrary, epithelium dysplasia, telangiectasia and perivascular infiltrate were more frequently recognized in other OMPSD-MP.

DIF has been served as adjunctive diagnostic tool in OLP for decades, with the positive rate ranges from 37% to 97%.[16] In our study, DIF positive rate was 76.0% in OLP group (57 of 75), which was significantly higher than other OMPSD-MP (41.5%, 17 of 41) ($P < 0.001$). Similar to previous studies, the most immunoreactant deposition was Fib and IgM, suggesting that they might play an important role in local immunopathology of OMPSD-MP, especially for OLP.

Fib is a plasma protein important to tissue damage and healing.[17,18] The mechanism of Fib deposition in the tissues is largely unknown. It is generally accepted that fib and its superfamily member play pivotal roles in immune response and carcinogenesis. Accumulated fib is capable to activate inflammatory cells and induce immune response, participating in the development many inflammatory diseases such as periodontitis and colitis.[19,20] In addition, fibrinogen-like protein-1 (FGL1), a member of fibrinogen superfamily, might be a key factor in various types of carcinoma. It has been reported that the expression of FGL1 upregulated in cervical, prostate, colorectal and lung carcinoma, but downregulated in head/neck cancer and liver carcinoma.[21] Further, FGL1 levels increases in acute liver inflammation to promote the proliferation of normal hepatocytes, whereas deceases in hepatocellular carcinoma contributing to the growth and proliferation of hepatocellular carcinoma cells.[22]

T-cell lymphocytes mediated inflammatory response is of crucial importance in OLP, which may lead to destruction of basal keratinocytes.[23] Meanwhile, there is a counterbalancing of increased cellular proliferation that repairs the damaged epithelium to maintain its integrity.[24] Shirol et al. considered Fib deposition as a consequent event to tissue damage and could further promote inflammation,[17] whereas Montague et al. considered it as a repair phenomenon.[14] Herein, we speculate that Fib might have complicated functions. It is assumed that Fib initially deposits at damaged BMZ as a consequence of tissue repairment and prevention the occurrence of severe lesions or malignancy. Along with the increasing accumulation of Fib, however, it may promote the migration of inflammatory cells and release of cytokine, lead to the abnormal immune response in local mucosa and contribute to the development of OLP. The hypothesis needs further exploration.

Another salient feature noted in our study is that various immunoglobulins, especially IgM, deposit at colloid bodies in OLP cases. The pathogenesis of antibodies production in tissues is unclear. Colloid body is generally believed to be origin from apoptosis of basal keratinocytes or destruction of thickened basement membrane.[25,26] Colloid body may have antigenicity, for its ability to combine with many immunoreactants such as IgM, IgA and IgG.[27] It is assumed that colloid body with autoantigen property might be presented to Th cells by antigen presenting cell, which further activate B cells to produce antibodies in oral lesions. The hypothesis also needs further exploration.

In conclusion, we have demonstrated the characteristics and differences of clinical, histopathological and DIF features and confirmed some significant overlap features among OMPSD-MP in the present study. DIF may be useful in differentiating OLP from other OMPSD-MP. Moreover, the most common immunoreactants in OLP were Fib and IgM that might be served as potential indicators. The role of Fib and IgM in the immunopathogenesis of OLP needs further exploration.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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