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Original Article

Oral mucous membrane pemphigoid in a group of Thai patients—A 15-year retrospective study

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KEYWORDS

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Abstract *Background/purpose:* Mucous membrane pemphigoid (MMP) is a rare autoimmune disease affecting mucous membrane of the body. Oral involvement is common causing chronic and painful lesions. This study aimed to characterize oral MMP in a group of Thai patients and to analyze treatment regimens.

Materials and methods: The files of patients attending Oral Medicine Clinic were retrospectively studied. Patients fulfilled diagnostic criteria of MMP were included. Chief complaints, medical and dental history, oral manifestations and investigations of individual patients were summarized. Treatment regimens and efficacy were also analyzed.

Results: There were fourteen patients (age range 33–70 years) with a diagnosis of MMP. The prevalence of oral MMP was 0.51%. The lesions presented as vesicles, blood blisters, erosions, ulcers, erythema, either one type or in combination. Common complaints were chronic painful and bleeding gums. Gingival lesions were found in 13 of 14 patients (92.86%). The most common direct immunofluorescence findings were linear C3 at basement membrane zone (92.31%) followed by linear IgG deposition (84.62%). Most lesions were successfully managed with topical and/or systemic corticosteroids. The average time to control disease was 1.97 months (IQR, 0.69–12.73 months).

Conclusion: Gingival lesions are very common in MMP. Mainstay of treatment is combination of systemic and topical corticosteroids. Multidisciplinary care including oral hygiene maintenance is necessary.

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Introduction

Mucous membrane pemphigoid (MMP) is a rare chronic autoimmune disease causing subepithelial vesiculobullous lesions that mostly affects the mucous membrane.¹ The disease is characterized by deposition of IgG, IgA and/or C3 along the epithelial basement membrane zone in a linear pattern.^{1,2} Oral involvement is found in about 85% of patients with MMP.^{3–5} Skin lesions have been reported in about one-fourth of the patients.^{2,6} Ocular, nasopharyngeal, anogenital and esophageal mucosa may also be involved.^{7–9} Oral lesions present as erythema, vesicles or bullae and ulcers mostly affected attached gingivae causing “desquamative gingivitis” (DG).¹ Other sites of oral involvement include palate, labial mucosa, tongue and buccal mucosa.

Oral lesions may be the first sign of MMP. They are chronic and painful, leading to limitations in daily activities. Therefore, quality of life is affected.¹⁰ Patients with oral lesions usually seek treatment from dentists. In addition, early lesions may be readily recognized during oral examination or dental treatment. Therefore, the role of dentists in diagnosis of oral MMP is of importance and value. Diagnosis of MMP is based on clinical and immunological features.¹ Treatment of oral MMP depends on severity of the disease ranging from only topical medication to combination of topical and systemic therapy.

According to the literature, cases of oral MMP including management have seldomly been reported. The objective of this study was to characterize oral MMP in a group of Thai patients and to analyze treatment regimens for controlling oral lesions.

Materials and methods

Dental records of patients attending Oral Medicine Clinic, Faculty of Dentistry, Mahidol University, Bangkok Thailand, during 2001–2015 were retrospectively reviewed against the study inclusion and exclusion criteria. The inclusion criteria were patients diagnosed as MMP as per the first international consensus on MMP which are based on both clinical features and direct immunofluorescence (DIF).¹ Exclusion criteria were patients without DIF characteristics of MMP. The patients’ chief complaints, medical and dental history, clinical features, histopathological and DIF reports were obtained. Data regarding treatment regimens and efficacy as well as disease progression and remission were also collected. The study was approved by the Committee on Human Rights Related to Human Experimentation, Mahidol University (MU-IRB 2008/262.2512). Fig. 1 demonstrates the flowchart of patient selection process.

Statistical analysis

All statistical analyses were performed using STATA version 15.1 (StataCorp LP, Texas, USA). Baseline demographics were described using frequencies and percentages for categorical data and median and interquartile range (IQR) were used for non-normally distributed continuous variables. Wilcoxon rank-sum test was used to compare the

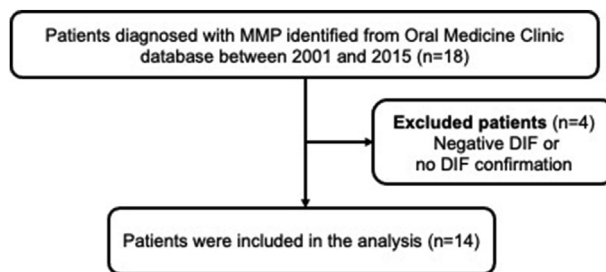


Figure 1 Flowchart of the patient selection process.

time to control disease activity. A p-value < 0.05 was considered as statistically significant.

Results

A total of 14 patients with a definite diagnosis of MMP out of the total 2,720 new oral medicine patients during 2001–2015 were identified. The prevalence of oral MMP was 0.51% among these oral medicine patients. Demographic data of the MMP patients were shown in Table 1. They were 6 males and 8 females with the median age at diagnosis of 49.57 years (range 33–70 years). Their complaints were burning sensation, gum blisters, sore gums, oral ulcers, or bleeding due to tooth brushing. The self-reported duration of their lesions at the first visit ranged from 8 days to 15 years. Seven patients denied medical problems whereas five of them had medical conditions including hypertension, diabetes mellitus, thalassemia, heart disease, asthma, premenopausal syndrome and dyslipidemia (Table 1).

Location and type of oral lesions in individual patients are shown in Table 1. The lesions presented as vesicles, blood blisters, erosions, ulcers, erythema, either one type or in combination. Of note, white striation was also found in five patients. Table 2 summarizes the frequency of lesions by anatomical distribution. Gingiva was the most common affected site (Fig. 2) followed by palate (21.42%), buccal mucosa (14.28%) and vermilion border (7.14%). Thirteen out of 14 (92.86%) were MMP patients with gingival lesions; 10 (10/13, 76.92%) had only gingival involvement and 3 (3/13, 23.08%) had lesions involved gingivae and other locations including buccal mucosa, buccal vestibule, palate and vermilion border.

Regarding histopathological and DIF examination, details on histopathological and DIF reports were available for only 13 patients. The other patient was referred to our clinic with histopathological and DIF results reported as consistent with MMP without further information provided. Of these 13 patients, the gingival biopsies were taken from 12 patients with oral MMP. One biopsy (patient No.8) was performed at the right buccal mucosa where Nikolsky’s sign was observed during the oral examination. The biopsy site, histopathological diagnosis and immunofluorescence findings are shown in Table 3. The most common DIF finding was linear C3 at basement membrane zone (BMZ) demonstrated in 12 of 13 patients (92.31%) followed by linear IgG deposition (84.62%). Other positive autoantibodies at BMZ were linear IgA (7.69%) and fibrinogen (23.08%). In addition, IgM and/or IgA at colloid

Table 1 Demographic data, chief complaints, underlying medical conditions and characteristics of oral mucous membrane pemphigoid lesions (n = 14).

Patient No.	Age (years)	Gender	Chief complaint	Duration of lesions (months)	Medical problems	Location of lesions	Lesion morphology	Type of lesions
1	70	Female	Gum blister & sore gums	4/15	None	Buccal gingiva region 15-17	Localized DG	Erythema, ulcers
2	43	Male	Burning sensation due to spicy food	4	HT, DM	Labial gingiva region 42-44 Generalized gingiva Q1,2,3,4 Hard palate	Generalized DG, erosion at palate	Erythema with white striae Erythema Erosions
3	33	Female	Gum blister & sore gums	12	None	Generalized gingiva Q1,2,3,4	Generalized DG,	Erythema, fine white striae
4	57	Female	Burning sensation in the mouth	36	Thalassemia	Buccal gingiva region Q1 and 2	Generalized DG	Erythema
5	68	Male	Oral ulcer	90	Heart disease, HT, DM	Generalized gingiva Q1,2,3,4 Buccal mucosa Hard palate Lower vermilion border	Generalized DG, erythema, ulcers at BM	Erythema, Erythema, ulcers, white striae Ulcers
6	39	Male	Gum blister	2	None	Generalized gingiva Q1,2,3,4	Generalized DG	Ulcers Blood vesicles
7	35	Female	Gum ulcers	180	None	Generalized gingiva Q1,2,3,4	Generalized DG	Vesicles, ulcers, erythema
8	50	Male	Blister at palate	2	Asthma	Soft palate, glossopalatal arch (Buccal mucosa)	Nikolsky sign	Vesicles (Nikolsky sign)
9	46	Male	Bleeding due to tooth brushing	3	None	Generalized gingiva Q1,2,3,4	Generalized DG	Ulcers with pseudomembrane
10	52	Female	Sore gums	N/A	Premeno-pause syndrome, Dyslipidemia	Labial gingiva region 22-23 Generalized attached gingiva	Generalized DG	Erosions, white striae
11	43	Male	Oral ulcer & blister	12	None	Generalized gingiva Q1,2,3,4	Generalized DG	Erythema, erosion
12	57	Female	Oral ulcer	36	None	Buccal gingiva region 46-47 Palatal gingiva region 26	Generalized DG	Erythema, ulcer Erosion, ulcer
13	34	Female	Gum ulcers with burning sensation	4	Gastric ulcer	Generalized gingiva Q1,2,3,4	Generalized DG with ulcers	Erythema, ulcers

(continued on next page)

Table 1 (continued)

Patient No.	Age (years)	Gender	Chief complaint	Duration of lesions (months)	Medical problems	Location of lesions	Lesion morphology	Type of lesions
14	67	Female	Burning sensation in the mouth	3/4	HT	Generalized gingiva and vestibule of Q1,2,3,4	Generalized DG with ulcers	Erythema, ulcers, white striae

Abbreviations: DG, desquamative gingivitis; DM, diabetes mellitus; HT, hypertension; MMP, mucous membrane pemphigoid; N/A, not available; Q, quadrant.

bodies (CB) were also observed in five cases (38.46%). Indirect immunofluorescence (IIF) was available as requested for diagnosis in only four patients. Of these four patients, one had weak positive of linear IgG at BMZ (titer 1:10) while negative results were found in the other three cases.

Focusing on the management of oral lesions, three patients (patient No.1, 3 and 12) were managed with only topical medications (Triamcinolone acetonide in orabase (TAO) 0.1%, Fluocinolone acetonide in orabase (FAO) 0.1% and dexamethasone mouthwash (MW)) and the remaining 11 patients (11/14, 78.57%) were treated with a variety of topical corticosteroids in combination with short courses of systemic corticosteroids (Fig. 3). Oral prednisolone (0.5–1 mg/kg) was added (Fig. 4a and b) in the severe cases. The MMP lesions were considered under control once ulcers were healed, and no new lesions developed. Mild erythema with no or mild symptoms were also considered under control. Then, the medications were adjusted accordingly. Systemic therapy was cut down or discontinued and the frequency of topical medications was decreased from 3 to 4 times/day to 1–2 times/day depending on the disease severity. Two patients wore custom-made trays for holding the topical medications twice daily. The median time to control disease was 1.97 months (IQR, 0.69–12.73 months) (Table 3). Interestingly, the median time to control disease activity was 1.51 months (IQR, 0.89–2.89 months) in patients who followed the recommended treatment regimens or good compliance (n = 10) whilst 1.97 months (IQR, 1.38–12.73) for those who had poor compliance (n = 3). However, there was no statistically significant difference in the median time to control MMP lesions between patients with good and bad compliance (p = 0.39).

During the course of treatment, 6 out of 14 patients (42.86%) developed pseudomembranous candidiasis. Antifungals including 2% miconazole gel or 1:100,000 nystatin oral suspension were then prescribed 3–4 times daily with good response. Application of chlorhexidine solution at cervical parts of teeth could help plaque control for patients with painful gingival lesions as tooth brushing was compromised. The lists of regimens prescribed for the treatment of these MMP patients are described in Table 3.

During the follow-up period, two patients had a relapse presenting blood blisters and vesicles in the oral cavity. Patient No. 8 subsequently developed skin lesions at the first visit (at back of left ear and right palm) and two weeks later (at front of left ear). He was referred to see a dermatologist. The investigations for this patient showed negative IIF. With prominent oral lesions during course of the disease, the final diagnosis of his lesions was MMP. All patients were referred to see ophthalmologists. Eleven out of 14 patients had their eyes examined regularly. None of them had eye lesions related to MMP. Although three patients did not had ophthalmologists check their eyes, they denied any eye problems during our follow-up period.

Discussion

Regarding to this 15-year retrospective study, the prevalence of oral MMP in oral medicine patients was 0.51%. This low prevalence was comparable to a 19-year-study in a

Table 2 Anatomical distribution of lesions in the oral mucous membrane pemphigoid patients (n = 14).

Sites of lesions	No. of lesions (%)
Gingiva	
Localized	1 (7.14)
Generalized	12 (85.71)
Palate	
Hard palate	2 (14.28)
Soft palate	1 (7.14)
Buccal mucosa	
Bilateral buccal mucosa	2 (14.28)
Unilateral buccal mucosa	1 (7.14)
Labial mucosa	0 (0.0)
Tongue	0 (0.0)
Vermilion border	1 (7.14)
Floor of mouth	0 (0.0)

**Figure 2** A female patient with oral mucous membrane pemphigoid causing desquamative gingivitis at upper and lower labial and buccal gingiva.

group of Thai patients with vesiculobullous lesions by Kulthanan K et al.¹¹ Therefore, a lower prevalence of oral MMP in general Thai population would be expected. The global reported incidence of MMP ranges from 2 cases/million/year¹² to 1.5–9.5 case/100,000/year.¹³

In this study, a female predilection was observed for MMP, which is consistent with other studies.^{13,14} Age range in our MMP patients were in accordance with previous reports.^{13,14}

With regards to immunofluorescence and histopathological studies, DIF is an essential tool for a final diagnosis of chronic vesiculobullous diseases including pemphigus vulgaris, MMP, and oral lichen planus (OLP).¹⁵ The common DIF pattern of MMP is linear IgG and/or C3 at BMZ.^{1,14} Similarly, linear C3 at BMZ was the most common DIF pattern (92.31%) followed by linear IgG at BMZ (84.62%) in this group of Thai patients. Combination of immunoreactants, IgG and C3 at BMZ in linear pattern was observed with the prevalence of 76.92%. The presence of both IgG and IgA, found in one case in this study, did not correlated to severe oral lesions as indicated previously.¹⁵ Of note, the histopathological examinations of four patients (patient No. 5, 8, 9 and 10) in the present study were not reported as MMP. These could be explained by the fact that artifacts in histopathologic specimens could occur during tissue

handling or preparation, leading to incorrect diagnosis.¹⁶ In addition, inconclusive biopsies of MMP is a diagnostic dilemma causing delayed diagnosis.⁵ As a variety of clinical features of MMP might overlap with oral presentations of other mucosal vesiculobullous diseases (i.e., pemphigus vulgaris or OLP),¹⁷ both clinical presentations and DIF on oral mucosa were deployed as suggested by the oral pathologist who evaluated the biopsy specimens in the present study to obtain a final diagnosis of MMP which is in line with the first international consensus on MMP;¹ the clinical and DIF must be exhibited prior to a diagnosis of MMP is confirmed.

Blisters and ulcers on the gingiva were common clinical features in our patients, causing complaint of chronic bleeding or sore gums. The present study found that over 90% of the patients in this study suffered from gingival lesions either in combination with other areas (23.08%) or gingival involvement alone (76.92%). This finding was in agreement with other previous reports.^{13,14} Tongue is not commonly affected by oral MMP.^{18,19} The MMP lesions affecting the tongue was neither observed in our MMP patients nor in a retrospective study on oral MMP by Sultan et al.¹⁹

Our results showed that DG is a common clinical presentation in Thai patients with MMP. Patients with oral MMP cannot brush their teeth properly due to painful and bleeding gingiva leading to plaque accumulation. This in turn could aggravate an immune response.²⁰ Therefore, plaque control and periodontal treatment are essential for oral MMP patients. Regular scaling and root planing help control the disease and maintain good oral hygiene.

Regarding to our data, the correct diagnosis for many patients was quite delayed from the first occurrence of the oral signs and symptoms. The patients had suffered from the lesions for 2–180 months except only 8 days in one patient. Delay in diagnosis of MMP has also been concerned in a study in the US.¹⁰ Therefore, dentists should be able to recognize DG involving entire attached gingiva without significant plaque deposit and pocket formation²¹ as well as gingival lesions not responded to oral prophylaxis and plaque control. These lesions should be therefore investigated further to obtain a definitive diagnosis. As MMP-induced DG does not respond well to systemic medications,²² topical corticosteroids are the mainstay of treatment. All of our patients had benefit from topical corticosteroid either with or without topical antifungals depending on history of secondary oral candidiasis. Severe DG with refractory response might require a custom-made tray to enhance contact time of the medication. Ultimately, patient compliance is one of the most important factors contributing to successful management of MMP. In the present study, the median time to control disease observed in patients with good compliance was slightly shorter than in those who did not adhere to the treatment regimens; although the difference between these two groups did not reach statistical significance. This could be due to the fact that MMP is considered as a rare condition and hence there was limited sample size. It would be interesting to investigate the association between patient compliance, time to control disease activity as well as outcomes of different treatment regimens for MMP in a large cohort of patients with oral MMP.

Table 3 Histopathological and direct immunofluorescence findings of the MMP patients.

Patient No.	Biopsy site	Histopatho-logical diagnosis	Immunofluorescence		Treatment	Custom-made tray	Time to control lesions	Secondary candidiasis	Patient compliance
			DIF	IIF					
1	Gingiva	MMP	IgG-L BMZ,C3-L BMZ	N/A	Triamcinolone in orabase 0.1% Fluocinolone acetonoide in orabase 0.1% Chlorhexidine mouthwash 0.12%	No	0.89	Yes	Good
2	Gingiva	MMP	IgG-L BMZ,C3-L BMZ, IgA-CB, IgM-CB	N/A	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	No	2.01	No	Good
3	Gingiva	MMP	C3-L BMZ	IgG-L BMZ	Triamcinolone in orabase 0.1% Fluocinolone acetonoide in orabase 0.1%	No	0.69	No	Good
4	Gingiva	MMP	IgG-L BMZ, IgA-L BMZ, IgA-CB, IgM CB	N/A	Fluocinolone acetonoide in orabase 0.1% Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	Yes	1.97	No	Poor
5 ^a	Unknown (previous report)	Lichenoid mucositis	Consistent with MMP ^a	N/A	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	No	1.38	No	Poor
6	Gingiva	MMP	C3-L BMZ, IgM-CB, Fibrinogen BMZ	N/A	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	No	12.73	No	Poor
7	Gingiva	Consistent with MMP	IgG-L BMZ,C3-L BMZ	N/A	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	No	0.86	Yes	Good
8	Buccal mucosa	Unremarkable	IgG-L BMZ,C3-L BMZ	Neg	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5–1 mg/kg) Chlorhexidine mouthwash 0.12%	No	N/A	No	N/A
9	Gingiva	PV	IgG-L BMZ,C3-L BMZ, Fibrinogen BMZ	Neg	Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	Yes	0.95	Yes	Good
10	Gingiva	Chronic nonspecific inflammation	IgG-L BMZ,C3-L BMZ	N/A	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	No	7.63	Yes	Good
11	Gingiva	MMP	IgG-L BMZ,C3-L BMZ, IgM-CB, Fibrinogen BMZ	N/A	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg)	No	2.89	No	Good
12	Gingiva	MMP	IgG-L BMZ,C3-L BMZ, IgA-CB, IgM-CB	Neg	Fluocinolone acetonoide in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash	No	2.07	No	Good

13	Gingiva	MMP	IgG-L BMZ, C3-L BMZ	N/A	Fluocinolone acetone in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg)	No	1.02	No	Good
14	Gingiva	MMP	IgG-L BMZ, C3-L BMZ	N/A	Fluocinolone acetone in orabase 0.1% Dexamethasone 0.5 mg/5 ml mouthwash Prednisolone (0.5 mg/kg) Chlorhexidine mouthwash 0.12%	No	5.20	Yes	Good

Abbreviations: BM, buccal mucosa; DG, desquamative gingivitis; DIF, direct immunofluorescence; Fibrinogen BMZ, Fibrinogen at basement membrane zone; IIF, indirect immunofluorescence; IgG-L BMZ, linear IgG at basement membrane zone; C3-L BMZ, linear C3 at basement membrane zone; IgA-L BMZ, linear IgA at basement membrane zone; IgA-CB, IgA at colloid bodies; IgM-CB, IgM at colloid bodies; MMP, mucous membrane pemphigoid; N/A, not available; Neg, negative; PV, pemphigus vulgaris.
^a DIF results from previous report being consistent with MMP.

OLP-like lesions have been noticed in MMP patients.^{23,24} Five of our MMP patients developed white lesions similar to OLP lesions in addition to erythematous and/or ulcerative gingiva. One of these patients also had histopathological diagnosis as “lichenoid mucositis” which was reported in a group of MMP patients with oral lesions resemble those of OLP by Benzaquen et al.²³ It has been postulated that OLP-like lesions occurred in these MMP patients may result from dual response of humoral and cellular immune response against components of hemidesmosome.²³ These mechanisms seem to happen in a subset of MMP leading to clinical and immunological features similar to the two diseases, OLP and MMP. Nonetheless, this condition should be differentiated from lichen planus pemphigoides (LPP).

LPP is a rare disease presenting as lichenoid plaques and tense blisters on skin. It is characterized by autoantibodies against type XVII collagen showing IgG and C3 at BMZ in DIF pattern.²⁵ The criteria for oral LPP have been described as follows: typical OLP lesions, histopathological findings similar to both LP and MMP, and DIF patterns of MMP.²⁶ Detection of specific autoantibodies would lead to a definitive diagnosis.

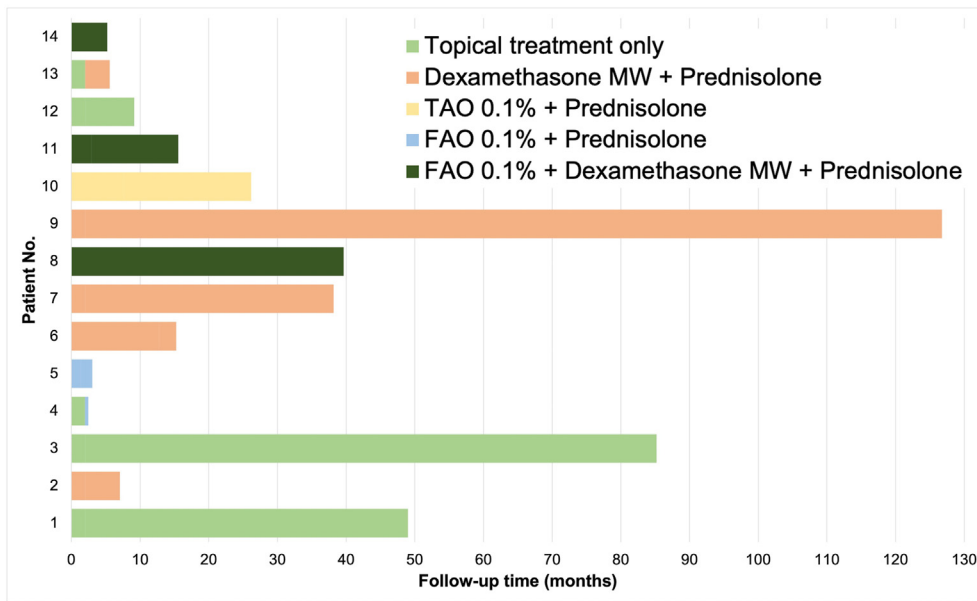
It should be noted that fibrinogen at BMZ, a characteristic DIF pattern of OLP, was demonstrated together with linear IgG and/or C3 in our three cases. As these three patients had no any oral white lesions, this finding may be related to both humoral and cellular immune response.²¹

Skin lesions are rare in oral MMP patients. They usually affect face, scalp, neck, trunk and extremities.²⁷ One of our MMP patients had vesicles near the ear and on the palm at the first visit as well as during follow-up period.

Regular eye examination is essential in patients with oral MMP. Ocular involvement is found in about 40% of MMP patients and may later develop symblepharon, ankyloblepharon and cicatricial bridles leading to blindness.¹³ None of our MMP patients had eye problems during follow up period. This implied that oral MMP may be a subtype of MMP.

Treatment could be started once the final diagnosis was achieved. The treatment regimens varied on severity of the disease. It is noted that the location, type, and severity of lesions determined proper regimens. Antifungals might be required in cases with secondary candidiasis. Patients’ compliance to the medication could also affect the efficacy of the treatment. Adjunctive medications such as chlorhexidine mouthwash and xerostomia mouthwash might be useful. Topical application of chlorhexidine mouthwash is of benefit to patients with painful gingival lesions and plaque deposit. Xerostomia mouthwash is suitable for patients with dry mouth. Severe DG with refractory to the treatment might require a custom-made tray to enhance adherence and contact time of topical medication.

Nevertheless, this study should be considered in light of its limitations. Firstly, due to the low incidence of MMP, the MMP sample in the present study was quite limited. Moreover, the identification of specific autoantibodies by immunoassay techniques could not be conducted. In addition, a few patients lost to follow-up.



Abbreviations: FAO, Flucinolone acetoneide in orabase; MW, Mouthwash; TAO, Triamcinolone acetoneide in orabase.

Figure 3 Demonstrates medications used over the course of MMP treatment in each patient.

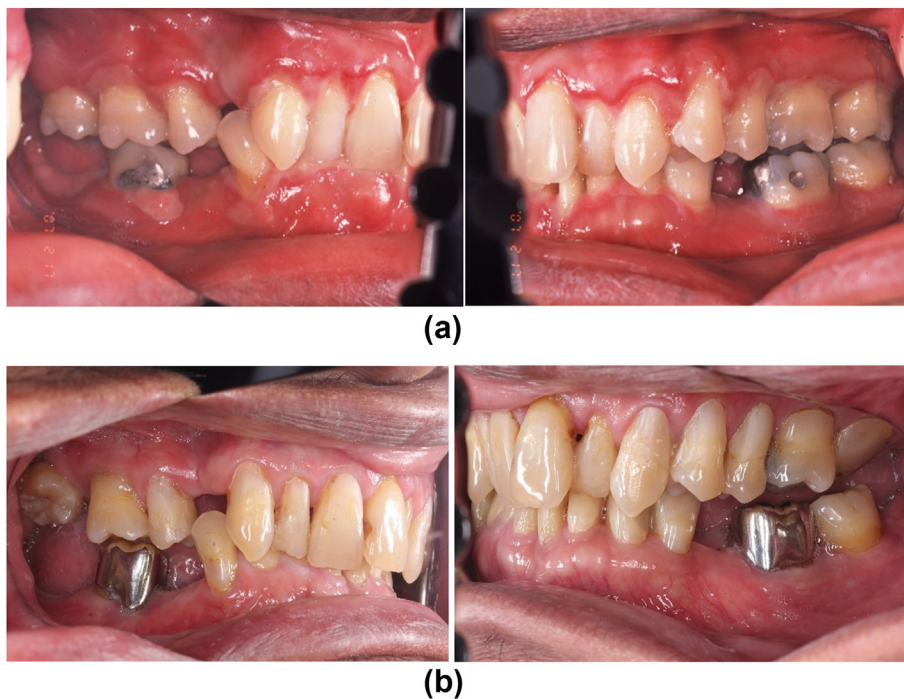


Figure 4 A male patient with oral mucous membrane pemphigoid. (a) Ulceration of gingiva in generalized at the first visit. (b) Resolution of the lesions after initial treatment with topical and systemic corticosteroids and later controlled with only topical medication. The oral status after 11 year-follow-up.

In conclusion, oral mucosal involvement is very common in MMP. The most commonly affected location is gingivae presenting as desquamative gingivitis. The role of dentists in early recognition of oral MMP is of importance for an early diagnosis, treatment and prevention of a full-blown condition.²⁸

Oral hygiene maintenance by plaque control and regular scaling and root planning is also needed for successful treatment of oral MMP. Furthermore, it is crucial for oral MMP patients to have multidisciplinary care including an ophthalmologist, a dentist, and a dermatologist as necessary.

Declaration of competing interest

The authors declare no conflict of interest related to this study.

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References

- Chan LS, Ahmed AR, Anhalt GJ, et al. The first international consensus on mucous membrane pemphigoid: definition, diagnostic criteria, pathogenic factors, medical treatment, and prognostic indicators. *Arch Dermatol* 2002;138:370–9.
- Schmidt E, Zillikens D. Pemphigoid diseases. *Lancet* 2013;381:320–32.
- Chan LS. Mucous membrane pemphigoid. *Clin Dermatol* 2001;19:703–11.
- Thorne JE, Anhalt GJ, Jabs DA. Mucous membrane pemphigoid and pseudopemphigoid. *Ophthalmology* 2004;111:45–52.
- Xu HH, Werth VP, Parisi E, Sollecito TP. Mucous membrane pemphigoid. *Dent Clin* 2013;57:611–30.
- Ahmed AR, Hombal SM. Cicatricial pemphigoid. *Int J Dermatol* 1986;25:90–6.
- Chan LS, Yancey KB, Hammerberg C, et al. Immune-mediated subepithelial blistering diseases of mucous membranes. Pure ocular cicatricial pemphigoid is a unique clinical and immunopathological entity distinct from bullous pemphigoid and other subsets identified by antigenic specificity of autoantibodies. *Arch Dermatol* 1993;129:448–55.
- Hanson RD, Olsen KD, Rogers 3rd RS. Upper aerodigestive tract manifestations of cicatricial pemphigoid. *Ann Otol Rhinol Laryngol* 1988;97:493–9.
- Hardy KM, Perry HO, Pingree GC, Kirby Jr TJ. Benign mucous membrane pemphigoid. *Arch Dermatol* 1971;104:467–75.
- Lee J, Seiffert-Sinha K, Attwood K, Sinha AA. A retrospective study of patient-reported data of bullous pemphigoid and mucous membrane pemphigoid from a US-based registry. *Front Immunol* 2019;10:2219.
- Kulthanan K, Chularojanamontri L, Tuchinda P, Sirikudta W, Pinkaew S. Prevalence and clinical features of Thai patients with bullous pemphigoid. *Asian Pac J Allergy Immunol* 2011;29:66–72.
- Carey B, Setterfield J. Mucous membrane pemphigoid and oral blistering diseases. *Clin Exp Dermatol* 2019;44:732–9.
- Schifter M, Yeoh SC, Coleman H, Georgiou A. Oral mucosal diseases: the inflammatory dermatoses. *Aust Dent J* 2010;55(Suppl 1):23–38.
- Ata-Ali FA-AJ. Pemphigus vulgaris and mucous membrane pemphigoid: update on etiopathogenesis, oral manifestations and management. *J Clin Exp Dent* 2011;3:e246–50.
- Sun S, Zhong B, Li W, et al. Immunological methods for the diagnosis of oral mucosal diseases. *Br J Dermatol* 2019;181:23–36.
- Kargahi N, Keshani F, Khosravian M. Analysis of artifacts in oral and maxillofacial histopathologic sections and related reasons. *Dent Res J* 2019;16:384–8.
- Rashid H, Lamberts A, Diercks GFH, et al. Oral Lesions in Autoimmune Bullous Diseases: an overview of clinical characteristics and diagnostic algorithm. *Am J Clin Dermatol* 2019;20:847–61.
- Laskaris G, Sklavounou A, Stratigos J. Bullous pemphigoid, cicatricial pemphigoid, and pemphigus vulgaris. A comparative clinical survey of 278 cases. *Oral Surg Oral Med Oral Pathol* 1982;54:656–62.
- Sultan AS, Villa A, Saavedra AP, Treister NS, Woo SB. Oral mucous membrane pemphigoid and pemphigus vulgaris—a retrospective two-center cohort study. *Oral Dis* 2017;23:498–504.
- Jascholt I, Lai O, Zillikens D, Kasperkiewicz M. Periodontitis in oral pemphigus and pemphigoid: a systematic review of published studies. *J Am Acad Dermatol* 2017;76:975–978e3.
- Lo Russo L, Guiglia R, Pizzo G, et al. Effect of desquamative gingivitis on periodontal status: a pilot study. *Oral Dis* 2010;16:102–7.
- Carbone M, Broccoletti R, Gambino A, et al. Clinical and histological features of gingival lesions: a 17-year retrospective analysis in a northern Italian population. *Med Oral Patol Oral Cir Bucal* 2012;17:e555–61.
- Benzaquen M, Suter VGA, Gschwend M, Feldmeyer L, Borradori L. Mucous membrane pemphigoid of the oral lichen type: a retrospective analysis of 16 cases. *J Eur Acad Dermatol Venereol* 2019;33:e205–7.
- Fukuda A, Himejima A, Tsuruta D, et al. Four cases of mucous membrane pemphigoid with clinical features of oral lichen planus. *Int J Dermatol* 2016;55:657–65.
- Hubner F, Langan EA, Recke A. Lichen planus pemphigoides: from lichenoid inflammation to autoantibody-mediated blistering. *Front Immunol* 2019;10:1389.
- Sultan A, Stojanov IJ, Lerman MA, et al. Oral lichen planus pemphigoides: a series of four cases. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2015;120:58–68.
- Bagan J, Lo Muzio L, Scully C. Mucosal disease series. Number III. Mucous membrane pemphigoid. *Oral Dis* 2005;11:197–218.
- Buonavoglia A, Leone P, Dammacco R, et al. Pemphigus and mucous membrane pemphigoid: an update from diagnosis to therapy. *Autoimmun Rev* 2019;18:349–58.