

Case Report

Mucous membrane pemphigoid presenting as bleeding gums and burning sensation of mouth: a case report

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Abstract Dental practitioners may encounter various oral mucosal diseases. Oral lesions can be the early manifestation of many systemic diseases. Mucous membrane pemphigoid (MMP) is a chronic, auto immune vesiculobullous lesion involving the mucocutaneous structures. It is important for a dental surgeon to be aware of oral presentations of MMP. Early and accurate diagnosis of this rare clinical entity is essential for the effective management of the lesions which may reduce or lessen disease progression. Present case report highlights the clinical presentations of MMP affecting the oral mucosa along with diagnostic features.

Keywords: Burning sensation; gingival bleeding; mucous membrane pemphigoid; oral mucosa; vesiculobullous lesion.

Introduction

Mucous membrane pemphigoid (MMP) is a chronic, auto immune vesiculobullous lesion involving mucocutaneous structures (Vijayan *et al.*, 2016). It is heterogeneous in origin, characterized by auto antibodies that are directed against one or more components of the basement membrane (Xu *et al.*, 2013; Hasan, 2014). Linear deposition of IgM, IgG or C3 in the basement membrane zone causes separation of junctional epithelium giving rise to a sub-basilar split (Xu *et al.*, 2013; Darling and Daley, 2005; Schmidt and Zillikens, 2013; Scully and Laskaris, 1998). MMP is rare with incidence of 2-10 cases per 100,000 population and often unrecognized at early stage as their early presenting symptoms are non-specific (Xu *et al.*, 2013; Dharman and Muthukrishnan 2016). The lesion usually affects individuals above 40 years of age and mostly females (Hasan *et al.*, 2012). Diagnostic criteria by the first International Consensus on MMP (Xu *et al.*, 2013) is as follows: (1) Clinical feature representing a chronic inflammatory, blistering disease,

predominantly affecting any or all mucous membranes; (2) With or without skin involvement and with or without identifiable scarring; (3) Direct immunofluorescence (DIF) demonstrating continuous deposits of Ig G, Ig A and/or C3 in the epithelial basement membrane zone.

MMP is also termed as cicatricial pemphigoid, oral pemphigoid, ocular pemphigoid and benign mucous membrane pemphigoid (Xu *et al.*, 2013). The word cicatricial is derived from a Latin word that means scarring (Darling and Daley 2005; Lugović *et al.*, 2007). It involves the mucous membrane of the oral cavity, conjunctiva and sometimes larynx, oesophagus, genitourinary tract and anus. Skin may be affected in some cases (Neff *et al.*, 2008; Srikumaran and Akpek, 2012). Dentists can be the first one to diagnose this rare mucocutaneous lesion. We are reporting a unique case of MMP as only oral mucosa was involved.

Case report

A 75-year-old female patient presented to the Department of Oral Medicine and Radiology with a chief complaint of

bleeding gums and burning sensation on gums while taking hot and spicy food for the past 3 years. She gave history of repeated ulcers in the mouth since 3 years associated with bleeding and burning sensation, inability to eat and chew. The patient had consulted local doctors but there was no improvement in the symptoms. The patient's medical history was not contributory.

Intraoral examination showed poor oral hygiene with calculus and generalized periodontitis. The marginal, attached, and papillary gingiva appeared to be erythematous with areas of desquamation. Multiple erosions were noticed in the gingiva of maxillary, and mandibular anterior region, palatal mucosa and alveolar ridge in mandibular posterior teeth. Erosions were irregular in shape with erythematous border. Pseudomembrane covering the erosions was noticed in the palatal region and alveolar mucosa in the right mandibular posterior region (Fig. 1). The ulcer bled with light touch. Nikolsky's sign couldn't be elicited. Patient was referred for

dermatologic and ophthalmic evaluation. However, there was no cutaneous or ocular involvement. Considering the history and clinical findings a provisional diagnosis of pemphigus vulgaris and differential diagnosis of MMP was given.

An incisional biopsy was performed in the perilesional area from the palatal region and sent for histopathological examination and DIF. Histopathological investigation revealed linear fragments of stratified squamous epithelium with subepidermal bullae containing neutrophils along with haemorrhage. The epidermis showed scattered infiltration of neutrophils indicative of mucous membrane pemphigoid (Fig. 2). DIF on the excised mucosal lesion showed linear staining of basement membrane zone with IgM, IgG, C3 and fibrinogen. These features were suggestive of mucous membrane pemphigoid (Fig. 3). Patient was prescribed oral prednisolone (1 mg/kg/d) for 1 month and a topical corticosteroid (Triamcinolone acetonide 0.1%) 3 times a day for 1 month and was recalled after 1 month for follow-up.



Fig. 1 Multiple erosions in gingiva, palatal mucosa and alveolar mucosa (arrows). Pseudomembrane covering the erosions noticed in the palatal region and alveolar mucosa in the right mandibular posterior region.

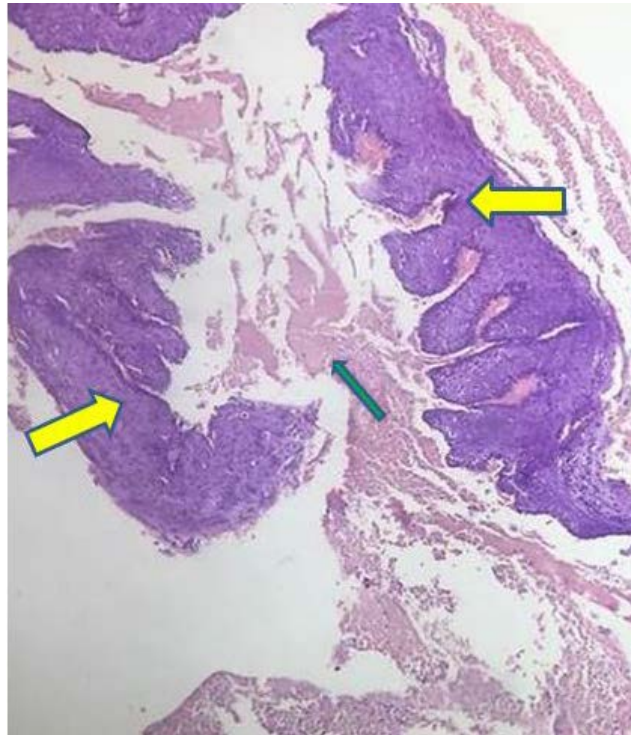


Fig. 2 Histopathological examination showing linear fragments of stratified squamous epithelium (yellow arrows) with subepidermal bullae (green arrow).

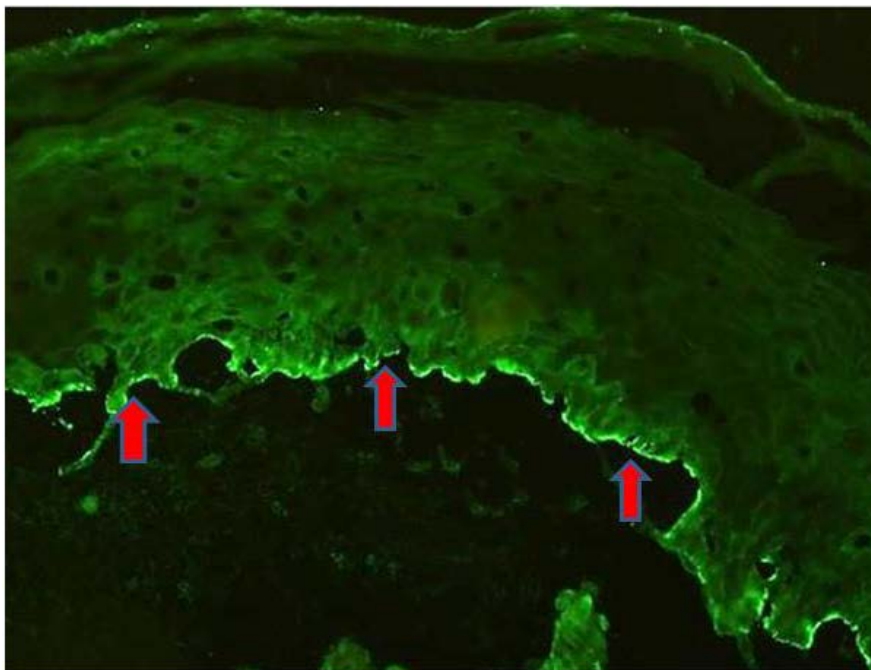


Fig. 3 Direct immunofluorescence (DIF) on the excised mucosal lesion showed linear staining of basement membrane zone with IgM, IgG, C3 and fibrinogen (red arrows).

Discussion

MMP was first reported by Wichmann in 1794, in a female patient with ocular and oral involvement (Hasan, 2014). It is associated with autoantibody-induced, complement mediated sequestration of leukocytes that results in release of cytokine and leukocyte enzyme. This is followed by detachment of the basal cells from the basement membrane zone along with complement mediated lysis of the basement membrane (Darling and Daley, 2005).

MMP is associated with human leukocyte antigen (HLA) major histocompatibility class II HLA-DQB1*0301. The auto antibodies associated with MMP are Bullous pemphigoid antigen 1 (BPAg1), Bullous pemphigoid antigen 2 (BpAg2), Collagen type I, Laminin- 6, Laminin-332 and Integrin subunits $\alpha 6/\beta 4$. Most commonly targeted auto antigen is BPAg2 which is a trans- membrane protein membrane (Xu *et al.*, 2013). MMP is associated with production of cytokines such as transforming growth factor beta (TGF β). A strong predominance of CD4+ T cell and Langerhans cell infiltrates in the conjunctiva indicates the role of cellular immunity in the pathogenesis of MMP (Xu *et al.*, 2013; Bernauer *et al.*, 1993).

MMP involves the oral mucosa in around 85% of the cases, ocular conjunctiva in 65% of the cases followed by nasal mucosa, skin, ano-genital areas, pharynx and larynx (Xu *et al.*, 2013; Chan, 2001). Scarring is a common finding in ocular and other mucosal lesions leading to complications such as blindness, laryngeal or pharyngeal stenosis and even death (Vijayan *et al.*, 2016). The most common manifestation of MMP is desquamative gingivitis. In many cases, desquamative gingivitis can be the only presenting manifestation. According to Laskaris *et al.* (1982), gingival involvement was in 63.6% cases of MMP. The bullae are often thick walled, can persist for about 24-48 hours before rupture. The present case did not present with intact bullae. Burning sensation on consuming spicy and hot food, bleeding of the gingiva are quite common

presentation associated with MMP. The present case also had burning sensation and gingival bleeding. (Vijayan *et al.*, 2016; Xu *et al.*, 2013). Irregularly shaped erosions with yellowish slough surrounded by an erythematous halo and covered with pseudomembranous coat is usually seen in MMP. The present patient also showed irregularly shaped erosions with yellowish slough (Hasan, 2014). Ocular involvement is the second most common, the earliest manifestation- subconjunctival fibrosis (Xu *et al.*, 2013). There was no ocular involvement in the present case.

The confirmatory diagnosis of MMP is established based on the histopathological examination and by immunofluorescence studies (Hasan, 2014). The favoured site of biopsy is area of vesicle or peri-lesional tissue and area of erosion. Biopsy of gingiva is avoided because chronic inflammation of gingiva can lead to improper diagnosis. MMP is characterized by junctional epithelium separation at the level of basement membrane which leads to sub-basilar split. The lamina propria shows the presence of chronic inflammatory infiltrates (Scully *et al.*, 1999). DIF test is considered as a gold standard method for the diagnosis of MMP due to its sensitivity and specificity (Hasan, 2014). DIF shows deposits of IgG and C3, in a linear manner in the basement membrane zone along the epithelial-mesenchymal junction (Schmidt and Zillikens, 2013). The present case had erosions in the oral mucosa for about 3 years and histopathological and DIF features were consistent with MMP.

A multidisciplinary approach is necessary for the management of MMP in reducing the disease-related complications (Vijayan *et al.*, 2016). The treatment depends upon the location, severity and rate of progression of the disease. The treatment strategies vary according to several factors such as age of the patient, severity of the lesion and the site involved. Patient education and motivation is very essential. Maintenance of good oral hygiene is beneficial (Hasan, 2014). The first international consensus on MMP (Vijayan *et al.*, 2016) had categorized the patients as - "low risk patients" and "high

risk patients". Low risk patients are ones with only oral mucosal and skin involvement and treated with topical corticosteroids. "High risk" patients are those who manifest with ocular, genital, nasopharyngeal, oesophageal and laryngeal mucosal involvement. Treatment is usually by prednisolone 1-2 mg/kg/day with gradual tapering of the dose. Other systemic therapies include dapsone at a starting dose of 50 mg/day, immunosuppressors like cyclophosphamide (0.5-2.0 mg/kg/day), azathioprine (1-2 mg/kg/day) methotrexate and cyclosporine (Xu *et al.*, 2013). Surgical management can be carried out in severe cases to prevent complications like blindness, airway stenosis and oesophageal strictures (Yilmaz *et al.*, 2010; Cafaro *et al.*, 2012).

Conclusion

Present report highlights the features of exclusive oral mucous membrane pemphigoid. Dentists play a vital role in diagnosis of MMP as oral mucosal involvement can be the early manifestation of this multi mucosal disease entity. The correct diagnosis requires detailed case history, comprehensive intraoral and extraoral examination, along with histopathological and immunofluorescence studies. As oral cavity is the most commonly affected site, early diagnosis and treatment can prevent the progression of disease and disease-related complications.

References

- Bernauer W, Wright P, Dart JK, Leonard JN, Lightman S (1993). The conjunctiva in acute and chronic mucous membrane pemphigoid. An immunohistochemical analysis. *Ophthalmology*, **100**(3): 339-346.
- Cafaro A, Broccoletti R, Arduino PG (2012). Low-level laser therapy for oral mucous membrane pemphigoid. *Lasers Med Sci*, **27**(6): 1247-1250.
- Chan LS (2001). Mucous membrane pemphigoid. *Clin Dermatol*, **19**(6): 703-711.
- Darling MR, Daley T (2005). Blistering mucocutaneous diseases of the oral mucosa - A review: Part 1. Mucous membrane pemphigoid. *J Can Dent Assoc*, **71**(11): 851-854.
- Dharman S, Muthukrishnan A (2016). Oral mucous membrane pemphigoid - Two case reports with varied clinical presentation. *J Indian Soc Periodontol*, **20**(6): 630-634.
- Hasan S (2014). Desquamative gingivitis - A clinical sign in mucous membrane pemphigoid: Report of a case and review of literature. *J Pharm Bioallied Sci*, **6**(2): 122-126.
- Hasan S, Kapoor B, Siddiqui A, Srivastava H, Fatima S, Akhtar Y (2012). Mucous membrane pemphigoid with exclusive gingival involvement: Report of a case and review of literature. *J Orofac Sci*, **4**(1): 64-69.
- Laskaris G, Sklavounou A, Stratigos J (1982). Bullous pemphigoid, cicatricial pemphigoid, and pemphigus vulgaris. A comparative clinical survey of 278 cases. *Oral Surg Oral Med Oral Pathol*, **54**(6): 656-662.
- Lugović L, Buljan M, Šitum M, Poduje S, Bulat V, Vučić M *et al.* (2007). Unrecognized cicatricial pemphigoid with oral manifestations and ocular complications. A case report. *Acta Dermatovenerol Croat*, **15**(4): 236-242.
- Neff AG, Turner M, Mutasim DF (2008). Treatment strategies in mucous membrane pemphigoid. *Ther Clin Risk Manag*, **4**(3): 617-626.
- Schmidt E, Zillikens D (2013). Pemphigoid diseases. *Lancet*, **381**(9863): 320-332.
- Scully C, Carrozzo M, Gandolfo S, Puiatti P, Monteil R (1999). Update on mucous membrane pemphigoid: a heterogeneous immune-mediated subepithelial blistering entity. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, **88**(1): 56-68.
- Scully C, Laskaris G (1998). Mucocutaneous disorders. *Periodontol 2000*, **18**: 81-94.
- Srikumaran D, Akpek EK (2012). Mucous membrane pemphigoid: recent advances. *Current Opin Ophthalmol*, **23**(6): 523-527.
- Vijayan V, Paul A, Babu K, Madhan B (2016). Desquamative gingivitis as only presenting sign of mucous membrane pemphigoid. *J Indian Soc Periodontol*, **20**(3): 340-343.
- Xu HH, Werth VP, Parisi E, Sollecito TP (2013). Mucous membrane pemphigoid. *Dent Clin North Am*, **57**(4): 611-630.
- Yilmaz HG, Kusakci-Seker B, Bayindir H, Tözüm TF (2010). Low-level laser therapy in the treatment of mucous membrane pemphigoid: a promising procedure. *J Periodontol*, **81**(8): 1226-1230.