

## Localized Oral Mucous Membrane Pemphigoid: Successful Treatment with Intralesional Triamcinolone Acetonide Injection

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### Abstract

Mucous membrane pemphigoid (MMP) is a rare, chronic and vesiculobullous disorder that classified as autoimmune disease. MMP can affect various mucous membranes but predominantly occurs in the oral cavity. In most of cases oral lesions may be initial manifestation or the only sign of the disease. It is predominantly seen in the fifth decade of life. It affects women more commonly than men. Children are rarely affected from this disease. MMP may cause extremely variable severity due to different clinical presentations as vesicles, erosions, pain, and occasional scarring. Oral lesions as gingival inflammation and scarring are not life threatening but lead to functional limitations. The primary goals of the treatment are to cease the progression of the disease, reduce the symptoms, and prevent the sequelae of tissue ulceration and consecutive scarring. The mild MMP lesions may be successfully managed with topical corticosteroids. However, the lesions that do not respond to local treatments or become widespread and also the diseases which show rapid progress can be treated with systemic glucocorticoids and immunosuppressive agents such as azathioprine, mycophenolate-mofetyl, cyclosporine, and dapsone, rituximab and intravenous immunoglobulin. In this report two cases of oral MMP treated successfully with intralesional triamcinolone acetonide are presented along with a review of literature.

**Keywords:** Mucous membrane pemphigoid; Topical steroids; Triamcinolone acetonide; Intralesional injection

### Introduction

Mucous membrane pemphigoid (MMP) is a rare, chronic and vesiculobullous disorder that classified as autoimmune disease. MMP affects frequently the mucosal surfaces of the mouth and also cutaneous involvement may be seen, approximately, one-quarter of patients. When it affects the gingiva, it is referred to as “desquamative gingivitis”. MMP is the most common group of autoimmune mucocutaneous diseases that affects the oral cavity<sup>[1-3]</sup>.

It is predominantly seen in the fifth decade of life. It affects women more commonly than men. Children are less frequently affected. MMP is usually associated with numerous target antibodies in the basement membrane and weaken the at-

tachment to the connective tissue. The MMP is a heterogeneous clinical and immunologic entity that is reflected in pathogenetic mechanisms, clinical presentations and response to therapy<sup>[4-7]</sup>.

MMP may cause extremely variable severity due to different clinical presentations as vesicles, erosions, pain, and occasional scarring. Oral lesions as gingival inflammation and scarring are not life threatening but lead to functional limitations. On the other hand, involvement of the conjunctiva as erosions with scarring and cicatrization may lead to blindness and the involvement of respiratory tract lesions in larynx, esophagus and lower airway may result in airway loss<sup>[1]</sup>.

The diagnosis of MMP is mainly based on the patients

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history, clinical examination and biopsy with histologic or direct immunofluorescent examination that showing deposition of IgG, IgA, and C3 in the basal membrane zone (BMZ). When performing a biopsy, it should involve the vesicle and surrounding tissue not the erosion itself. Cytology smears are not indicated. Separation of the intact epithelium from the underlying connective tissue should be seen on biopsy specimen with an often chronic inflammation in the connective tissue<sup>[8]</sup>.

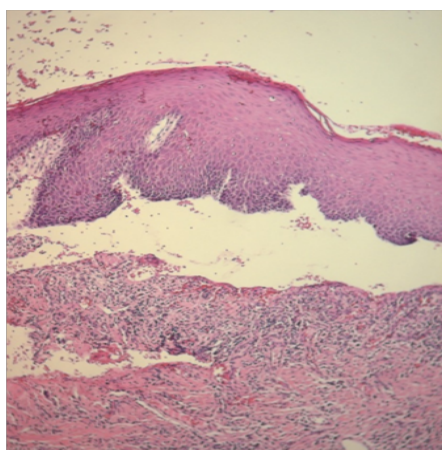
In this study two cases of oral MMP with special emphasis on their clinical features and treatments are presented along with a review of literature.

## Case Report

Case 1 was 64-year-old female patient was referred to the department of Oral and Maxillofacial Surgery with a complaint of burning sensation and pain of the right upper gums and palate for the past 6 months. She had no systemic disease or ongoing medical therapy at the referral time to our clinic. We revealed mild desquamation on the right posterior maxillary area (Figure 1). Gentle manipulation on the normal mucosa induced a positive Nikolsky's sign. An incisional biopsy was performed on this area and intact gingiva was submitted for histopathological examination. Biopsy specimens from the oral mucosa revealed detachment of epithelial basement membrane and subepithelial lamina propria with slight chronic inflammation, suggestive of MMP (Figure 2).



**Figure 1:** Intraoral examination of the first patient.



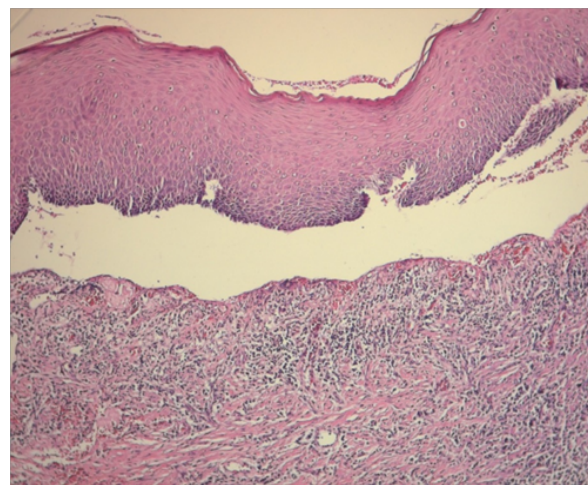
**Figure 2:** Histopathology revealed subepithelial cleft and basal cell degeneration, along with slight chronic inflammation. (H&E,x100).

Case 2 was a 61-year-old man who was referred to our

department with a chief complaint of pain and sensitivity of the mouth for 4 months which increases with intake of spicy food. The medical history was not significant and he was otherwise in good health. Oral examination revealed mild desquamation of the buccal mucosa (Figure 3). Also gentle pressure of the normal mucosa induced a positive Nikolsky's sign. An incisional biopsy was performed on this area and submitted for histopathological examination. Biopsy specimens from the oral mucosa revealed partial junctional separation at the level of the basement membrane, suggestive of MMP (Figure 4).



**Figure 3:** Intraoral examination of the second patient.



**Figure 4:** Histopathology showed the presence of stratified squamous epithelium supported by connective tissue stroma and partial junctional separation at the level of the basement membrane. (H&E,x200)

Both of the patients had an ophthalmologic and dermatological examination and no associated ocular, cutaneous or genital lesions were reported. Patients were initially treated with topical 0.1% triamcinolone acetonide per 3 - 4 times a day over a period of 4 weeks. The first patient showed no response and the second patient showed poor response to topical steroids; for this reason they were treated with intralesional triamcinolone acetonide injections (Figure 5). In the first case, complete healing without scar was obtained after 6 sessions. Whereas complete resolution without scar formation was observed after 3 sessions in the second case. At the end of the 2-year follow-up period both patients remained disease free (Figure 6 and 7).





**Figure 5:** Intralesional injection of triamcinolone acetonide in the second case.



**Figure 6:** Intraoral examination of the first patient at the end of the 2-year follow-up.



**Figure 7:** Intraoral examination of the second patient at the end of the 2-year follow-up.

## Discussion

MMP is a rare chronic autoimmune blistering disease that identified by deposition of IgA and/or IgG directed against proteins of the basement membrane complex. The activation of complement system by immunoglobulins attracts the leukocytes. Mainly neutrophils cause the release of proteolytic enzymes and subsequently cleave fibrils in the basement membrane that eventuate in blister formation<sup>[2,6]</sup>. In the literature MMP has been

termed by several names including cicatricial pemphigoid, benign mucous membrane pemphigoid, oral pemphigoid, and ocular cicatricial pemphigoid. In 2002, Chan<sup>[1]</sup> suggested the term of mucous membrane pemphigoid; because some serious complications, for instance ocular involvement may cause blindness or laryngeal scarring may result death<sup>[9]</sup>, make the term “benign” inappropriate and the disease does not always induce scarring, as in example of gingival involvement, the term of cicatricial does not involve all cases. Lastly site-specific terms exclude the patients with multiple mucous membranes involvement<sup>[1,2]</sup>.

MMP can affect various mucous membranes but predominantly occurs in the oral cavity. In most of cases oral lesions may be initial manifestation or the only sign of the disease<sup>[2,3,7]</sup>.

In the oral cavity MMP can be also manifested as desquamative gingivitis which is characterized by broad desquamation and/or erosion of the buccal side of attached gingival of anterior teeth. Additionally gentle pressure on the normal mucosa may induce a positive Nikolsky's sign<sup>[2]</sup> which was also present in our both cases.

Patients with MMP usually complain about pain, dysphagia, or peeling of the mucosa which adversely impact their quality of life<sup>[10]</sup>. Likewise both of our patients had complained of pain and discomfort that were especially increased during intake of spicy foods.

But most critical complication of MMP is scarring which is specifically poses important problem when the conjunctiva, esophagus, or larynx get involved<sup>[7]</sup>.

The primary goals of the treatment are to cease the progression of the disease, reduce the symptoms, and prevent the sequelae of tissue ulceration and consecutive scarring. The management of oral MMP can be challenging and differs based on the severity of disease<sup>[6]</sup>.

In general there is no approved management protocol for the oral MMP. Several treatments methods have been used but probably due to the rarity of the disease large-scale clinical drug trials could not been conducted<sup>[7]</sup>. The mild lesions may be successfully managed with topical corticosteroids. Right along with fluocinolone acetonide or clobetasol propionate, triamcinolone acetonide is the third indicated topical steroid for MMP but the form of ointment or aqueous solution is not sufficient to control the disorder. This synthetic glucocorticoid is more effective when interlesionally injection is desired hereby high concentration of the drug locally delivered with no systemic side effects<sup>[3]</sup>. MMP generally occurs in elderly people more than 50 years of age<sup>[7]</sup> which is similar to the presented patients. This age group can be highly associated with multiple medical problems that pose an obstacle for the systemic therapy. For that reason perilesional/intralesional triamcinolone injections may be an efficient choice between local and systemic therapy<sup>[3]</sup>. While our patients' lesions not respond to the topical corticosteroids; intralesional triamcinolone injections was preferred as the second line of therapy. Kalinska et al.<sup>[3]</sup> reported four patients with oral MMP who was successfully treated with multiple sessions (varied between 3 to 18) of perilesional and/intralesional triamcinolone injections.

However, lesions that not respond to local treatments or become widespread and also the diseases which show rapid progress can be treated with systemic glucocorticoids and immunosuppressive agents such as azathioprine, mycophenolate mofetyl, cyclosporine<sup>[6,11]</sup>.

Dapsone is a well-known drug that has been used in the treatment of the infectious diseases including leprosy and malaria for many years. But more recently it has become a worthwhile therapeutic agent in inflammatory diseases and found efficient in the adjunct therapy in MMP<sup>[7]</sup>. In the eighties Rogers et al.<sup>[12,13]</sup> and Matthews et al.<sup>[14]</sup> reported successful treatments of oral MMP with dapsone. In 1999 Ciarrocca and Greenberg<sup>[7]</sup> used dapsone in combination with topical corticosteroids which caused great improvement in patients with oral MMP. Al-Shehhi et al.<sup>[15]</sup> used dapsone (100 mg/day) combined with topical 0.05% clobetasol propionate cream for localized oral MMP. But due to insufficient improvement of the lesion after 6 months; they switched the therapeutic regimen to topical tacrolimus (0.1% solution) with oral prednisolone and after one month the lesion healed completely.

Recently there is an emerging trend to use rituximab (RTX) in patients with MMP in whom conventional therapy was failed. Although in the literature the majority of patients showed improvement after the use of RTX neither long-term follow-up was present nor optimal protocols were defined for specific subgroups of MMP. Besides, in most cases patients received concomitant immunosuppressive and anti-inflammatory therapy<sup>[16-18]</sup> which can cause serious adverse events including infections and death<sup>[19]</sup>.

Moreover intravenous immunoglobulin (IVIg) has been demonstrated as an effective adjuvant treatment for MMP. Yeh et al.<sup>[20]</sup> reported a significant decrease in the autoantibody titers which followed by clinical improvement in 13 patients with extensive MMP that showed no previous response to immunosuppressive therapy or had substantial adverse effects.

Also Letko et al.<sup>[21]</sup> stated IVIg therapy induced faster control of the acute inflammation by comparison with conventional immunosuppressive therapy in patients with MMP and no recurrences were recorded in IVIg therapy during the follow-up period. However, Iaccheri et al reported IVIg with systemic steroids and immunosuppressive agents failed to control ocular MMP<sup>[22]</sup>. A tetracycline type antibiotic, minocycline, alone or in combined with nicotinamide has also been reported in the treatment of MMP<sup>[23,24]</sup>. Although it has effective anti-inflammatory and immunosuppressive properties and shown as a safe alternative for MMP patients; several side effects including vertigo and gastralgia may cause withdrawal of the drug<sup>[6,25]</sup>.

Recently Carrozzo et al.<sup>[25]</sup> evaluated the therapeutic benefit of minocycline in patients with oral MMP. They reported a major response in 3 patients, a minor response in 4 and no response in 2 patients but also one patient showed permanent remission. More than half of the patients (55%) had to stop the drug because of side effects. Authors concluded that minocycline revealed temporary clinical benefits in oral MMP and patients without circulating autoantibodies against BP180 showed a better clinical response.

When clinical remission is achieved, medications should be slowly tapered to reduce the risk of disease flares. In case that discontinuance of the treatment is not achievable due to relapses, the least effective topical or systemic maintenance regimens should be implemented<sup>[6,26]</sup>.

In addition to pharmacological interventions, proper management of MMP requiring the multidisciplinary approach. Initially patient should be evaluated meticulously by an ophthalmologist whether the conjunctival involvement is present. Also-

based upon the suspected or known involvement sites clinical co-management between dentist and different physicians such as dermatologists, otolaryngologists, urologists, internists, gastroenterologists may be needed<sup>[6,27]</sup>.

## Conclusion

Perilesional injection with triamcinolone can be an efficient and safe choice in patients with oral MMP that showed no improvement with topical corticosteroids. It should be borne in mind that perilesional injection with steroids indicated especially in mild erosive lesions. The management of MMP should be individualized dependent on the severity, extent and progression of the disease. Also clinicians should be in contact with experienced physician in MMP for possible other mucosal involvements. Further clinical trials including different therapeutic regimens with longer follow up is needed.

**Conflict of Interest:** None.

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