INTRODUCTION

Benign Mucous Membrane Pemphigoid (BMMP), also called Cicatricial Pemphigoid (CP), is an uncommon, chronic immune mediated subepithelial vesiculobullous disease. The term cicatricial is derived from word ‘cicatrix’ meaning scar, as it heals with scarring. It is a part of the group of autoimmune subepidermal/subepithelial bullous disorders, recognized by the term “immune mediated subepithelial blistering diseases” (IMSEBD). This family of diseases constitutes a spectrum: at one end are bullous pemphigoid (BP) & pemphigoid - herpes gestationis (HG), which generally affects the skin, with minimal and infrequent involvement of the mucous membranes, while at the other end is cicatricial pemphigoid (CP), which mainly involves the mucous membranes most frequently of oral cavity & eyes along with less frequent involvement of mucous membranes of nasal cavity, pharynx, larynx, esophagus & genitalia & occasional involvement of the skin.

Wichmann (1794) first reported a female patient with ocular and oral involvement as well as skin lesions. In 1896, Thost introduced the original nomenclature chronic pemphigus of the mucous membrane & in 1911; he described the mucous membrane pemphigus with its salient features. On the basis of histologic studies in 1951, Lever distinguished CP from pemphigus vulgaris (PV). The disease was then referred to as benign mucous membrane pemphigoid (BMMP).

BMMP is usually of unknown cause but occasionally triggered by drugs (such as clonidine, indomethacin, D-penicillamine & some topical ocular medications). Other suggested etiological factors are viruses, UV light & genetic predisposition or occasional association with other autoimmune diseases. They are characterized by the in vivo linear deposition of immunoglobulins, complement or both, mainly IgG & C3 along the basement membrane zone (BMZ). There may be an immunogenetics background & an association with HLA DQB1*0301, which is especially notable in ocular pemphigoid. The pathogenesis of BMMP probably includes an autoantibody induced, complement mediated sequestration of leukocytes which results in release of cytokine & leukocytes causing detachment of basal cells from BMZ. However, BP180 epidermal antigen is a major
antigenic target of IgG autoantibodies produced by BMMP patients. BMMP autoantibodies localize to an extracellular site in lower lamina lucida & upper lamina densa region of lamina propria.

Dermatologic data suggest that BMMP is approximately 7 times less common than BP. On the other hand, it is up to 3 times more frequent than pemphigus, which itself has an annual incidence of 0.5 to 3.2 per 100000 people. There are no known racial or geographic predilections.

Most patients ranged from 23 to 75 years age; maximum being 50 to 60 years old. The female/male ratio was 1.8:1. The oral mucosal involvement is seen in all patients, the initial site of presentation being oral in 48% & ocular in 30%.

There are several variants of BMMP, each with distinctive clinical features, pattern of immunopathology and antigenic specificity of autoantibodies. They are oral pemphigoid, anti epiligrin pemphigoid, anti BP antigen mucosal pemphigoid, ocular pemphigoid & multiple antigens.

Commonly, patients with BMMP have oral, in particular, gingival lesions. It is one of the main known causes of desquamative gingivitis (DG). Hence, dentists could be the first health professionals to recognize this rare disease.

The clinical appearance is of gingival erythema & loss of stippling, extending apically from the gingival margins to the alveolar mucosa. The desquamation may vary from mild, almost insignificant small patches to widespread erythema with a glazed appearance. Chronic sorenness is common, being especially worse when acidic foods are eaten. The time between the onset of symptoms and diagnosis is relatively short, probably because of the patient's discomfort caused by bullae, ulcerations & subsequent pain. Vesicles or bullae may also occur elsewhere on the oral mucosa in BMMP & there can be a positive Nikolsky's sign.

The relatively tense oral blisters rupture quickly, leading to pseudomembrane covered, irregularly shaped erosions, which are the most common manifestation after DG. Erosions have a yellowish slough and are surrounded by an inflammatory halo. The hard and soft palate, buccal mucosa, alveolar ridge & tongue may also be involved, whereas lip lesions are uncommon.

Ocular manifestations have been quite common, ranging from 3 to 48 % and they may culminate in blindness. Eye involvement usually begins as chronic conjunctivitis with symptoms of burning, irritation and excess tearing. Scarring after repeated fibrosis can lead to the fusion of the sclera and palpebral conjunctivae (symblepheron) or of the superior and inferior palpebrae (ankyloblepheron). The conjunctivae may contract & invert the eyelid margins (entropion) leading to inversion of eyelashes onto the corneal surface with subsequent irritation (trichiasis). However, scarring is less common in the oral cavity.

The skin lesions are characteristically hemispherical & tense bullae which are usually asymptomatic until they rupture.

The diagnosis is based on the history, examination & biopsy with histologic and direct immunofluorescent (DIF) examination. The most appropriate area to biopsy is not the erosion, which will show loss of the epithelium one wishes to study, but a vesicle or perilesional tissue. Gingival biopsy is best avoided, as gingival chronic inflammation may lead to confusion.

Histologically, there is loss of attachment & separation of the full thickness of the epithelium from the connective tissue at basement membrane level. Epithelium, though separated, remains for a time intact and forms the roof of a bulla. The floor of the bulla is formed by connective tissue alone, infiltrated with inflammatory cells. A histopathologic feature distinguishing BMMP from BP is that the inflammatory infiltrate in former contains predominantly neutrophils with fewer eosinophils.
Direct immunofluorescence (DI) findings include linear IgG, C3 &, less commonly, other immunoglobulins deposited at the basement membrane zone. Investigation of presence of circulating antibodies in the patient's serum using indirect immunofluorescence (IDI) is not always reliable for diagnosis or monitoring of BMMP.4

In some patients, the disease is localized and has a slowly progressive course without complications; in others, it is devastating, with severe morbidity. Treatment should be individualized for each patient depending on disease severity, age and general state of health & associated medical problems. The main treatment is immunosuppressive & includes the topical & systemic corticosteroids, as well as other immunosuppressive agents such as dapsone, sulphapyridine & azathioprine.3-6, 9, 10, 12, 15

Topical corticosteroids remain the mainstay treatment of BMMP, especially for localized oral lesions, though some investigators advocate dapsone, tetracycline or mild to moderate strength systemic corticosteroids. For gingival lesions, topical corticosteroids are typically more effective when used in a vacuum formed custom tray or veneer. Candidiasis may complicate treatment, but it can be prevented by adding antimycotic therapy. If oral lesions continue to develop or extend or new oral lesions, progressive ocular disease or laryngeal or oesophageal lesions appear, treatment with a short plasma half-life systemic corticosteroid should be initiated, accompanied by systemic immunosuppressant & immunoglobulin. Topical antibiotics are advisable for resolution of eye lesions.9, 20, 21

Here, we present a case of a 27 year old male with typical oral, eye & skin lesions of benign mucous membrane pemphigoid who responded well to topical treatment.

**CASE REPORT**

A 27 year old male Hindu mill worker residing at Chandodziya, was referred from Skin Department of Civil Hospital, Sola to Oral Medicine & Radiology Department of Ahmedabad Dental College & Hospital (ADCH) for the complain of multiple painful ulcers in the oral cavity since a week.

Patient first noticed multiple painful ulcers in the oral cavity before 6 months, for which he was prescribed some topical ointment by a local general practitioner. The ointment provided some symptomatic relief but complete remission was not achieved. Then before a week, his condition got aggravated with appearance of multiple new ulcers in oral cavity and fluid filled vesicles on the upper lip. He also noticed fluid filled blisters on extensor surfaces of left forearm & leg which subsequently ruptured in few days. Before 3 days, he noticed a burning & itching sensation at medial canthus of right eye accompanied by continuous watering. So he visited a local dental practitioner, who diagnosed the condition as a viral infection and prescribed systemic acyclovir. With no relief, patient visited Civil Hospital, Sola before 4 days from where he was referred to ADCH.

Patient had no other significant medical or dental history. He reported inability to eat due to painful ulcers. He had habit of placing tobacco, betelnut & slaked lime quid in lower labial vestibule 5 to 6 times a day since last one year.

On extraoral examination, there was a laceration of palpebral conjunctiva at medial canthus of right eye with some scarring.
There was crusting of entire left half of upper lip. There were single, round, 5 mm diameter sized crusted lesions on extensor surface of left forearm as well as left leg.

On intraoral examination, patient had full complement of 32 teeth present with partially erupted 38 & 48. There were generalized extrinsic tobacco stains, more severe in relation with the labial surfaces of mandibular anterior teeth. The marginal and attached gingiva in mandibular anterior and right quadrants was erythematous and had a tendency to bleed as well as peel off on pressure.

There were multiple, round, 4 to 5 mm diameter ulcers with yellowish white floor and erythematous halo scattered over the dorsum & ventral surface of tongue as well as hard & soft palate.

There were large, irregular shaped ulcers in posterior half of right & left buccal mucosa.
On scraping the anterior border of the ulcer on left buccal mucosa, there was an extension of the ulcer to involve a normal mucosal surface anterior to the ulcer.

Based on the clinical findings, history & positive Nikolsky's sign, a provisional diagnosis of Benign Mucous Membrane Pemphigoid was placed. Bullous Pemphigoid, Erythema Multiforme (EM) & Epidermolysis Bullosa Acquisita were kept as differential diagnosis. An exfoliative cytology slide was prepared from affected areas on gingiva & buccal mucosa which showed chronic inflammatory cell infiltration but was negative for Tzanck cells.

The patient was given topical antiseptic & anaesthetic gel application along with topical steroid application with the objective of relief of symptoms. He was also advised topical sulfonamides for skin & eye lesions from skin department of Civil Hospital, Sola. The patient was recalled after a week for follow up and further investigations. However, on 1 week follow up, patient showed nearly complete remission of majority of oral & lip lesions as well as skin & eye lesions.
However, it does occur in males & occasional cases have been reported even in children & young adults, as in our patient who was a 27 year old male.

Oral & ocular lesions occur most commonly in BMMP with gingiva as the initial site of presentation. This is in accordance with the present case. Lip & skin involvement also occurs rarely in BMMP, which is in accordance to the present case.

There is a tendency for oral lesions to appear as vesicles, which rupture quickly to form ulcers in BMMP. Nikolsky’s sign may be positive for BMMP. This is in accordance with the present case.

Based on clinical findings, multiple mucosal involvements and positive Nikolsky’s sign, a provisional diagnosis of Benign Mucous Membrane Pemphigoid was placed. Such cases demand due attention and differentiation from all Immune mediated subepithelial blistering diseases (IMSEBD) based on histopathologic examination, direct & indirect Immunofluorescence testing & antigen testing. Hence, the differential diagnosis included Bullous Pemphigoid (BP), Erythema Multiforme (EM) & Epidermolysis Bullosa Acquisita (EBA). Oral lesions are more common in BMMP than in BP. The distinction continues to be based on the clinical presentation; if the disease is predominantly cutaneous with healing without scarring, a diagnosis of BP is made, whereas if it is predominantly mucosal which heals with scarring, a diagnosis of BMMP is more appropriate.

Erythema Multiforme most commonly presents at hands & feet & target or iris lesion is pathognomonic for this entity. Gingival involvement is rare in EM. Epidermolysis Bullosa Acquisita (EBA) also predominantly affects skin, especially over the trauma prone extensor surfaces, with scar & milia formation; presenting histopathologic & immunopathologic features

DISCUSSION

Benign Mucous Membrane Pemphigoid (BMMP) mainly involves the mucous membranes of oral cavity & eyes along with less frequent involvement of mucous membranes of nasal cavity, pharynx, larynx, esophagus & genitalia & occasional skin involvement. This was a case of Benign Mucous Membrane Pemphigoid in a young male. Literature suggests that it is more common in females with peak in fifth decade.

There was complete relief of symptoms & patient was able to eat comfortably. The patient is under routine follow up recalls with no reported recurrence within the two month follow up period.
indistinguishable from those of BMMP.\textsuperscript{8, 10, 15}

Classic histopathologic features include a subepithelial split with a chronic inflammatory infiltrate containing eosinophils in the lamina propria and immunostaining that shows deposits of IgG and C3 in a linear manner in the BMZ.\textsuperscript{3-7, 9, 12, 18}

However, being already in grave pain, the patient was not willing to undergo biopsy. As he responded well to topical therapy, further investigations were not advisable.

BMMP with oral &/or skin involvement is considered low risk case which responds to topical steroids. However, ocular, genital, oral & skin involvement falls in high risk category requiring systemic steroids along with dapsone & intravenous immunoglobulin for control of symptoms and rapid progression.\textsuperscript{3-6, 9, 10, 12, 15} However, the current case responded well to topical steroid & antibiotic therapy with satisfactory healing of oral & eye mucosal lesions as well as skin lesions after a week.

**CONCLUSION**

BMMP, being a part of a group of autoimmune subepithelial vesiculobullous diseases, has clinical & histopathologic similarities with a variety of diseases. Since the means of differentiation of all these diseases are special & costly investigations which are not routinely used, this entity demands thorough clinical & histopathologic evaluation combined with vigilant long term follow up of the patient to ensure prevention of further attacks. The gingival involvement often being the initial presentation of this entity, the dentist often plays a vital role in early detection & prevention of eye complications.

**REFERENCES**


