Chronic desquamative gingivitis was first described by Tomes and Tomes in 1894.[1] “Desquamative gingivitis” is a descriptive term, first introduced by Prinz in 1932 that is synonymous with the presence of erythema, desquamation, erosion, and blistering of attached and marginal gingiva.[2] Glickman and Smulow[3] stated that desquamative gingivitis may be a clinical feature common to a wide number of disorders. A classification was proposed based on etiologic considerations, together with histologic and immunologic findings.[4,5]

A. Dermatological diseases
- Cicatricial pemphigoid
- Lichen planus
- Pemphigus
- Psoriasis
- Bullous pemphigoid
- Epidermolysis bullosa acquisita
- Contact stomatitis.

B. Endocrine disturbances
- Estrogen deficiencies following oophorectomy and in postmenopausal stages
- Testosterone imbalance
- Hypothyroidism.

C. Aging

D. Abnormal response to bacterial plaque

E. Idiopathic

F. Chronic infections
- Tuberculosis
- Chronic candidiasis
- Histoplasmosis.

Overall, mucous membrane pemphigoid (MMP), oral lichen planus and pemphigus vulgaris account for the major causes of gingival desquamation. MMP is a rare, chronic autoimmune blistering disorder characterized by subepithelial bullae. The condition frequently involves mucous membranes, with rare skin involvement. Oral cavity is mostly affected and desquamative gingivitis is the most common manifestation. Hereby, we present an interesting case of MMP manifesting as desquamative gingivitis, along with a brief review of the literature.

Case Report

This was a case report of a 57-year-old female patient who reported to the out-patient Department of Oral Medicine and
Radiology, Saveetha Dental College and Hospitals, Chennai with a complaint of burning sensation and tenderness in the gums, which worsened on intake of spicy food since 9 months. The patient also noticed the appearance of blisters on her gums on and off which would heal subsequently without any medical intervention. Her medical history was non-contributory. There were no associated ocular, cutaneous or genital lesions. Intraoral examination revealed an erythematous and inflamed labial gingiva with interspersed areas of normal gingiva in relation to 11, 12, 21, 22. The marginal gingiva was scalloped in outline and had rolled borders with absence of melanin pigmentation [Figure 1]. There was a diffuse area of desquamation and erythema involving the buccal aspect of free, marginal and attached gingiva in relation to 24, 25, 26 and 27. Faint white strie were visible bordering the areas showing desquamation. The desquamated area showed loss of stippling. Single, isolated discrete hemorrhagic bullae, oval in shape, 1.5 × 1 mm in diameter was also appreciated on the buccal attached gingiva in region of 25. The bulla was relatively resilient to puncture [Figure 2]. Gentle manipulation of the normal mucosa induced a positive Nikolsky’s sign. The patient’s oral hygiene was poor and gingiva showed bleeding on probing with no attachment loss. After obtaining an informed consent from the patient, an incisional biopsy was taken from the buccal aspect of left maxillary gingival region (adjacent to the bullae region) for histopathologic and immunofluorescent studies. Histopathology showed variable thickness parakeratinized stratified squamous epithelium, subepithelial cleft and basal cell degeneration in few areas. Underlying connective tissue stroma revealed chronic inflammatory cell infiltrate, mainly plasma cells along with areas of hemorrhage [Figures 3 and 4]. Linear deposition of IgG and C3 at the dermo-epidermal junction was evident in direct immunofluorescence [Figure 5]. Differential diagnosis was made solely on the basis of clinical features. Dermatological pathologies like bullous pemphigoid, MMP, pemphigus vulgaris and bullous lichen planus were considered as the most probable differential diagnosis. Absence of skin lesions excluded the possibility of bullous pemphigoid. Presence of intact bullae and absence of erosions clinically and subepithelial cleft histopathologically ruled out pemphigus vulgaris. The striking presence of desquamative gingivitis in a 57-year-old female patient with an intact hemorrhagic bullae (without coexisting skin lesions), in association with
characteristic histopathological and immunofluorescent features confirmed the diagnosis of MMP. Thorough oral prophylaxis was done and the patient was counseled to maintain good oral hygiene. Thereafter, the patient was prescribed topical application of high potency steroids (Clobetasole propionate) thrice daily for 1 month and vitamin supplements (cap zincovit) once daily for 1 month. The patient was reviewed every 2 weeks for the first 1 month. The lesions improved considerably with topical steroids within 4 weeks of starting the treatment [Figures 6 and 7]. The patient was asked to stop the topical steroid application and reinforcement of oral hygiene instructions were given. Since the lesions may recur, the patient was under observation for 1 year and there was no recurrence.

Discussion

MMP is a heterogeneous group of autoimmune, chronic inflammatory, subepithelial blistering disease of mucous membranes, oral, ocular, genital, nasopharyngeal, esophageal, and laryngeal mucosa are frequently affected, with rare skin involvement. The condition belongs to a group of mucocutaneous autoimmune blistering disorders often collectively referred to as subepithelial bullous dermatoses. Previously, MMP was known as “benign MMP,” “cicatricial pemphigoid” and “ocular or oral–gingival pemphigoid.” However, now the term “MMP” is preferred.[7]

Wichmanns was the first to describe a case of MMP as early as late 19th century.[8] However, Thost presented the nomenclature and salient features of MMP.[9,10]

The exact etiology of MMP is not known. Known causative factors include severe mucosal inflammatory injury,[11] drugs (clonidine, indomethacin, D-penicillamine), [12] viruses, ultraviolet light and genetic predisposition such as HLA DQB1 * 0301.[13] Desquamative gingivitis, one of the clinical manifestation in MMP is commonly seen among post-menopausal stages in females. However, no direct relationship between MMP and smoking or menopausal status has been cited in the literature.[14] Autoantibodies against basement membrane proteins, together with complement (C3) and neutrophils cause a subepithelial split and resultant vesicle formation. MMP antigens are usually present in lamina lucida of basement membrane, but lamina densa may also be the primary site of involvement in some cases. The majority of cases of MMP demonstrate IgG directed against antigens on the epidermal side of the salt-split skin, which have been identified as BP180 (also called type XVII collagen). However, few cases of MMP may have antigens on the dermal side of the split (epiligrin/laminin 5).[15]

The epidemiological characteristics of MMP were unclear, with a reported incidence of 1.5-9.5 cases/100,000 inhabitants an year.[16] Middle aged adults are usually affected, although cases have also been reported children and the elderly, with a female-male ratio of 2.1.[17] The common sites of occurrence are mucous membranes of oral cavity, eye, nose, pharynx, larynx, esophagus, trachea, and anal canal as well as the mucosa of the genitalia. In patients with ocular MMP who were not treated or are inappropriately treated, scarring may lead to blindness. Laryngeal stenosis can lead to fatal asphyxia. Esophageal strictures may lead to dysphagia and may rarely rupture to result in mediastinitis.[18] Oropharyngeal MMP may present with hoarseness or dysphagia.[7]
The most frequent first site involved in MMP is the oral cavity. Desquamative gingivitis, vesiculobullous lesions, and ulcerations are the common intraoral features seen. The commonest intraoral site affected is the gingiva, and the lesions tend to heal with insignificant scarring. Desquamative gingivitis is the main oral feature of MMP and may be the sole presenting feature. Desquamative gingivitis is a fairly common disorder in which the gingivae are desquamated. Chronic soreness is commonly seen and intake of spicy foods may further worsen the condition. Erythematous gingiva with loss of stipping, extending apically from the gingival margins to the alveolar mucosa is a frequent observation. Severity may range from mild, almost insignificant small patches to widespread erythema with glazed appearance. Occasionally, gingival inflammation may occur in the absence of bacterial plaque, in the form of chronic desquamative gingivitis. Although pocket depth and attachment loss have not been found to be statistically significant.

Laskaris et al. reported gingival involvement in 63.6% of patients with MMP. Silverman et al. in a survey of 65 patients found gingival involvement in 100% of males and 92% of females. Gallagher and Shklar compiled the data of 120 patients and observed gingival involvement in almost all cases.

Vesicles or bullae may also occur elsewhere on the oral mucosa in MMP, and positive Nikolsky sign elicited by palpation with a finger, mouth mirror or periodontal probe is a fairly common observation. Pseudomembrane covered, irregularly shaped erosions constitute the second most common manifestation in MMP. Erosions have a yellowish slough and are surrounded by an inflammatory halo. Persistent extensive erosions may be present in the buccal mucosa and especially the palate, but they cause little discomfort unlike pemphigus vulgaris. However, the oral lesions usually heal without scarring.

In the present case, the affected patient was a 57-year-old female who presented with exclusive oral involvement without any other mucosal or cutaneous involvement. There was widespread erythema and inflammation of maxillary anterior labial gingiva. However, the palatal gingiva was unaffected. Desquamative gingivitis affecting the marginal and attached gingiva was appreciated with respect to left maxillary gingival region, along with the presence of blood filled bullae. Gentle manipulation induced a positive Nikolsky’s sign. The features reported in the present case were consistent with the previous literature reviews.

The definitive diagnosis can only be established based on the histopathological data and immunofluorescence studies. The preferred site of biopsy should be a vesicle or peri-lesional tissue and not the erosion, which will show loss of the epithelium one wishes to study. Gingival biopsy is best avoided, as gingival chronic inflammation may lead to confusion. Histologically, MMP is characterized by junctional separation at the level of the basement membrane and resultant sub-basilar split. Chronic inflammatory infiltrate in the lamina propria contains eosinophils, lymphocytes, and neutrophils. Direct immunofluorescence (DIF) testing is a sensitive and specific test, and is considered to be the gold standard method for diagnosing MMP. DIF shows deposits, usually of IgG and C3, in a homogeneous linear manner in the basement membrane zone along the epithelial-mesenchymal junction. Circulating antibodies can be detected by indirect immunofluorescence and immunoblot assays. Indirect immunofluorescence using salt-split mucosa provides more sensitive assay.

Histopathological features in the present case, showed subepithelial cleft and basal cell degeneration, along with band of intense chronic inflammatory cell infiltrate consisting predominantly of plasma cells and areas of hemorrhage. In our case, DIF showed linear deposition of IgG and C3 at the dermo-epidermal junction.

There is no standard treatment protocol for the management of patients with MMP. The treatment strategies vary according to the preference of the physician, the age of the patient, the severity of the disease and the site involved. Patient’s education and motivation should be done, as plaque induced gingivitis may worsen or aggravate the course of the disease. Good oral hygiene and use of a soft bristle toothbrush may partly alleviate the patient’s discomfort. An anti-plaque agent such as 0.2% chlorhexidine mouthwash twice a day may also have beneficial effects. Systemic drugs or agents are reserved for skin or mucosal locations other than oral sites, such as the conjunctiva. Oral MMP may be more difficult to manage than other subgroups of the disease. Secondary infections, constant trauma from chewing and the use of a tooth brush, may delay the healing process. This in turn may lead to malnutrition. Topical corticosteroids seem beneficial for milder lesions of MMP. However, systemic corticosteroids, antimitabolites (cyclophosphamide, azathioprine, mycophenolate mofetil, methotrexate), antibiotics (tetracyclines), and dapsone play a role in treatment of recalcitrant oral lesions. Other treatment regimen includes intravenous immunoglobulins, plasmapheresis, and Low level laser therapy (LLLT). LLLT has anti-inflammatory effects, causes pain relief and accelerates regeneration of damaged tissues. LLLT results in biostimulation or biomodulation effects, causing cellular alteration by irradiation at a specific wavelength.

The patient in the present case underwent thorough oral prophylaxis and was treated with topical steroids and vitamin supplements for 1 month. The lesions showed considerable improvement after steroid application. Regular follow up was done and the lesions showed no signs of recurrence.

Conclusion

Dentists could be the first health professionals to recognize this multi-mucosal involvement disorder. Correct diagnosis of the condition entails taking a detailed history, coupled with a thorough intraoral and extraoral examination, along with histopathology and Immunofluorescence studies. The gingival lesions are usually treated by improved oral hygiene measures and topical corticosteroid therapy.

Acknowledgment

I gratefully acknowledge the faculty and staff at Saveetha Dental College and Hospitals, Chennai.
Hasan: Mucous membrane pemphigoid with gingival desquamation

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Source of Support: Nil, Conflict of Interest: None declared.
