Case Report

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Asymptomatic Mucous Membrane Pemphigoid: A Case Report

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ABSTRACT

Background: Benign mucous membrane pemphigoid (MMP) is an autoimmune disease characterized by chronic vesiculo-bullous eruptions, predominantly on mucous membranes but occasionally on the skin. The diagnosis is hard to achieve due to similarity in clinical picture with other vesiculo-bullous lesions such as pemphigus or bullous pemphigoid, thereby, posing a diagnostic dilemma for the clinician. Histopathology can confirm the diagnosis; however, corticosteroids can be started to relieve the symptoms while confirmatory reports are not available as it is common treatment for most mucosal lesions.

Keywords: Mucous Membrane Pemphigoid, Histopathology, Corticosteroids.

INTRODUCTION

Desquamative gingivitis is a manifestation of a variety of diseases. It is characterized by epithelial desquamation, erythema, ulceration, and/or the presence of vesiculobullous lesions of gingiva and other oral tissues. This phenomenon can be associated with number of dermatoses,most commonly lichen planus,pemphigus vulgaris cicatricial pemphigoid(benign mucous membrane pemphigoid) and bullous pemphigoid.[1] In aged individuals, desquamative gingivitis often affects their routine life because of associated pain and discomfort.

The term pemphigoid applies to a number of cutaneous, immune-mediated, sub epithelial bullous diseases characterized by a separation of the basement membrane zone. The term is used because clinically it often appears similar (the meaning of the '-oid' suffix)to pemphigus[2] The pemphigoid includes bullous pemphigoid, mucous membrane pemphigoid and pemphigoid (herpes) gestations.[3] Among these conditions, bullous pemphigoid and mucous membrane pemphigoid, also known as benign mucous membrane pemphigoid or cicatricial pemphigoid have received considerable attention. Current molecular findings on these two diseases clearly indicate that they are separate entities. [4] However, considerable histological and immunopathological overlap exists between the two diseases such that their differentiation may be impossible based on the set two criteria. In many cases, the clinical findings are probably the best cognitive element to discriminate them. The term bullous pemphigoid is preferred when the disease has no scarring and mainly affects the skin. The term cicatricial pemphigoid commonly used when scarring occurs and the disease is mainly confined to the mucous membrane. [5]

Oral mucosal involvement in mucous membrane pemphigoid is often the first and usually the only site of disease involvement.[6] Desquamative gingivitis, vesiculo bullous lesions and ulcerations are the common intraoral manifestations. Epithelial sloughing and exposure of painful bleeding surfaces beneath (positive Nikolsky's sign) is most commonly observed. Period of exacerbation and remission are common and lesions may remain unrelenting for several years. [7] The gingival lesions are by far the most common intraoral sites

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affected and the lesions tend to heal with insignificant scarring. [6]

CASE REPORT

Presented here in, is a unique case report in which there was only involvement of the gingiva which remained asymptomatic for years without involvement of the other parts of the oral cavity and the other parts of the body.

A 53-year-old male patient, a bank manager, came to our dental clinic complaining of carious teeth which he wanted to get filled. It was the patient's first dental visit He did not complain of bleeding or pain. His medical history was of good general health and he was not taking any medications. His personal history and working condition in the bank was recorded to rule out any involvement of stress. At the time of initial presentation, the patient had noticed changes in the gingiva but did not have any complaints regarding the same. On further enquiries about the changes in the gingiva, he reported the appearance of occasional swelling in the gingiva on applying digital pressure. The swelling subsided or the superficial layer would have separated from the underlying tissue. Even during this period, the patient was asymptomatic. The patient reported a normal diet and had not avoided any spicy food because of the changes in the gingiva He was using the same tooth paste which he had been using since childhood. His personal history revealed that he was not a smoker, was not consuming alcohol and brushing his teeth twice daily. He did not complain of any skin lesions in any other part of the body. However, the patient was referred to the skin specialist and ophthalmologist to rule out any involvement of the skin and eye. In between these periods, the patient was transferred to different places as he was employed in a nationalized bank and did not visit our clinic. The patient visited our dental clinic again in 2016 for the replacement of missing teeth. Gingival examination conducted, during this visit revealed similar findings as were seen 3 years ago; again, the patient was asymptomatic regarding his gingival condition. The patient again visited our clinic in 2017 when he was 57 years old for the cementation of a loose crown; gingival examinations revealed similar findings as were seen 4 years prior and the gingiva was asymptomatic.

During his first visit, intraoral examination showed diffuse erythematous changes in the gingiva, without any involvement of the buccal mucosa, palate or floor of the mouth. The surface appeared smooth and shiny. On application of digital pressure, the superficial epithelium separated and left exposed and underlying erythematous area (positive Nikolsky's sign). The patient did not complain of any pain while eliciting this sign. The provisional diagnosis of pemphigoid was given with differential diagnosis of pemphigus and lichen planus being considered. (Figs 1–3). There was grade 1 bleeding on probing. The patient had very good oral hygiene. Hard tissue examination revealed carious teeth (16,class II disto-occlusal [D.O.]; 18, class II mesio-occlusal[M.O.]; 27, class II, D.O.; 17, class I; 34 and 35, class I, Deep caries).The patient was informed of his gingival condition and the need for biopsy. He was initially reluctant to consent to the procedure because the condition was asymptomatic. Even though patient had not noticed any skin or eye changes. He was referred to a skin specialist and ophthalmologist to rule out skin and eye involvement. On consultation with the ophthalmologist and dermatologist skin and eye involvement were ruled out. The patient returned after few days and at his visit biopsy of the gingival lesion was performed. Supragingival scaling and polishing was done. He was advised to use soft tooth brush to avoid trauma to the gingiva. Topical or systemic steroids treatment was deferred due to asymptomatic nature of the lesions. Unfortunately, however the patient visited only twice thereafter due to nature of his job. The patient visited our dental clinic 1 year after and the gingiva appeared the same as it was 5 years ago but patient gave a history of remission and exacerbation. During period of exacerbation the patient noticed the appearance of bullae which subsided without any intervention. However the gingival lesions remained asymptomatic.

Histopathological analysis of the gingival lesion showed acanthotic parakeratinized stratified Squamous epithelium; the epithelium was completely separated from the underlying connective tissue stroma at places. The epithelium was not showing any inter-or intracellular edema or acantholysis. The detachment of the epithelium from the underlying connective tissue was suggestive of epithelial bulla. The underlying

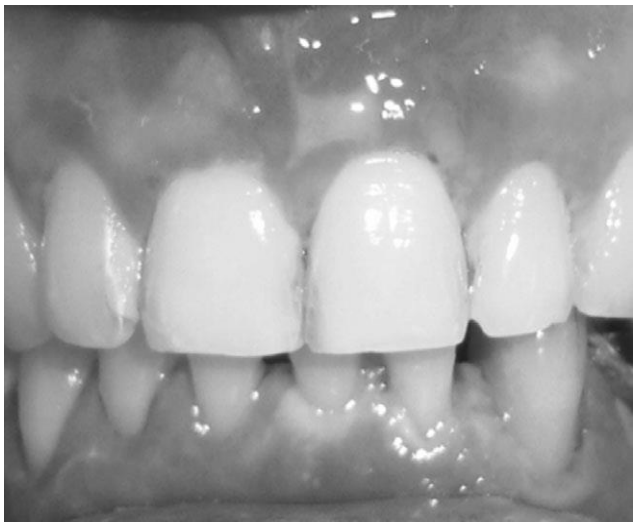

Fig 1: Front view of maxillary anterior region of Desquamative gingivitis associated with mucous membrane pemphigoid.

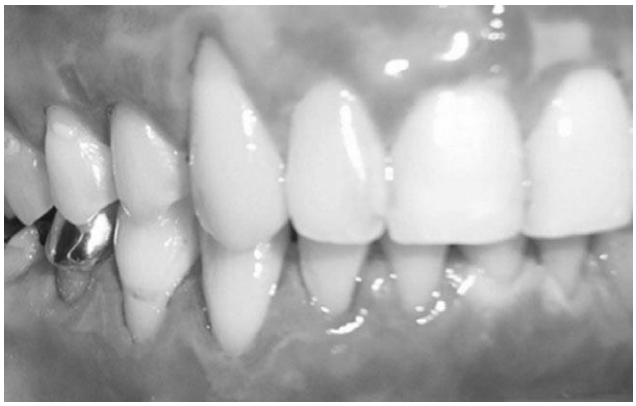

Fig 2: Right buccal view of maxillary anterior region of desquamative gingivitis associated with mucous membrane pemphigoid.

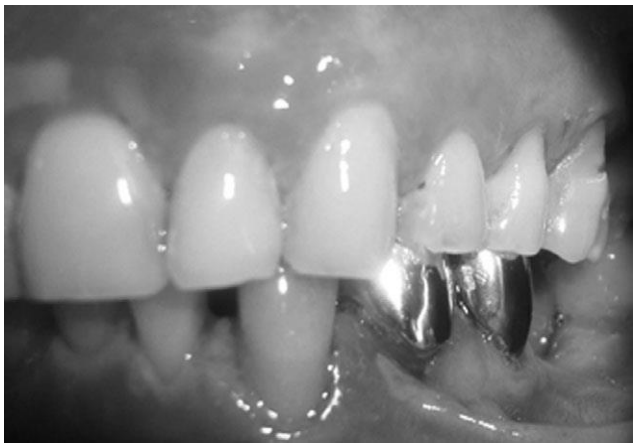

Fig 3: Left buccal view of maxillary anterior region of desquamative gingivitis associated with mucous membrane pemphigoid

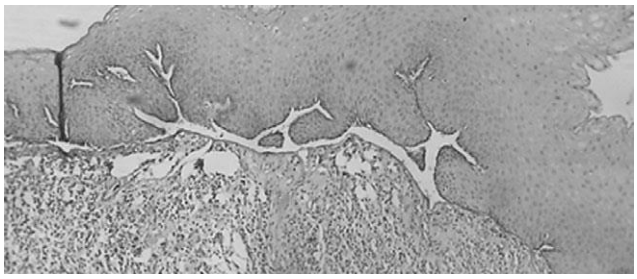

Fig 4: Light microscopy of hematoxylin–eosin stained specimen of gingival lesion at 10 magnifications

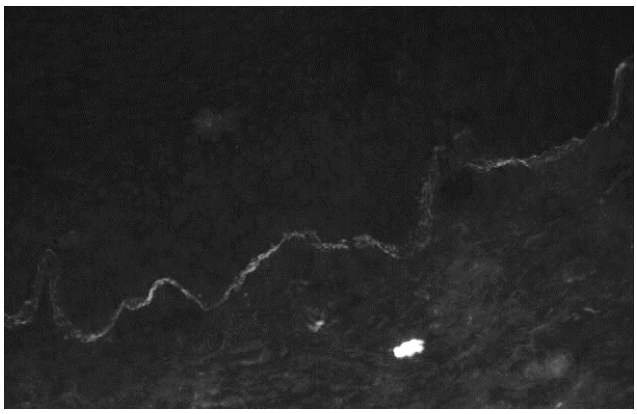

Fig 5: Direct immunofluorescence shows linear deposition of component C3 and immunoglobulin Ginthe basement membrane zone.

connective tissue stroma was highly edematous, with numerous capillaries filled with red blood cells and a moderate infiltration of chronic inflammatory cells with occasional neutrophils and eosinophils. The case was diagnosed "pemphigoid", and biopsy was suggested for immunofluorescence examination to confirm the histological and clinical diagnosis. (Fig. 4) Direct immunofluorescence (DI) and indirect immunofluorescence microscopy was done. Direct immunofluorescence revealed linear deposits of complement component C3 and immunoglobulin(IgG) in the basement membrane zone (BMZ) and it was negative for IgM, IgA and fibrinogen (Fig. 5). Indirect immunofluorescence was negative. Because there was no intra epithelial clefting, DI was negative intercellularly and indirect immunofluorescence was negative, pemphigus was ruled out. Erythema multiform usually shows target lesions on the skin, which are most often associated with hemorrhagic crusting of the vermillion border of the lip. Moreover, clinical lesions seen in our case were asymptomatic, unlike in erythema multiforma. Lichen planus was not considered because of

absence of saw tooth reteridges and negative DI findings for fibrinogen. Thus, the case was diagnosed as "mucous membrane pemphigoid".

DISCUSSION

Although a variety of terms have been used over the decades to design this condition group of experts from both medicine and dentistry met in1999 and came to a consensus that "mucous membrane pemphigoid" would be the most appropriate name for the disease. Cicatricial pemphigoid" is another commonly used term to design at such lesions, and is derived from the word cicatrix, meaning scar.[7] Other commonly used terms include "benign mucous membrane pemphigoid", "ocular pemphigus", "childhood pemphigoid" and "mucosal pemphigoid".5Mucous membrane pemphigoid is the most common of the autoimmune blistering conditions, associated with auto antibodies directed against BMZ target antigens. Auto antibodies of the IgG subclass, particularly IgG4, are associated with this condition. However, IgA antibodies have been detected. In mucous membrane pemphigoid, one or more of several heterogeneous antigens (BP180,BP230, epiligrin [laminin-5]) and others within the basement membrane adhesion complex may be targeted resulting in an immunoresponse. In cases of mucous membrane pemphigoid the most consistent or allusions are gingival, with other sites in the oral cavity ultimately becoming involved. The present case was diagnosed as mucous membrane pemphigoid and differentiated from pemphigus by histopathological features, namely, sub epithelial cleft in and no intraepithelial clefting. DI was not positive intracellularly and only gingival involvement was found over the 5-year follow up. Gingival lesions in these conditions are usually extremely erythematous, and the appearance of vesicles and ultimate erosions that develop are usually exceedingly painful. In the present case, even though patient reported appearance of the bullae and erosions after minor trauma, he remained strangely asymptomatic. Pemphigoid-like lesions have been identified in patients taking systemic medications such as captopril, carbamazepine, clonidine, furosemide, penicillamine and practolol. Such medications are commonly prescribed for aged individuals for systemic aliments. It has also been observed that paraneoplastic pemphigoidis associated with internal malignancy [8–14]. In the present case report, a thorough systemic history and biochemical evaluation ruled out the possibility of association of pemphigoid with such conditions and also ruled out the involvement of other mucosal areas including ocular.

Immunofluorescent examinations performed in cicatricial pemphigoid have shown different results. Daniels and Quadra-white reported [17] (51%) linear basement membrane zone pattern of IgG, 10 (33%) IgA, 12(36%) IgM and 32(97%) C3.[15] In the present study, we found a linear BMZ pattern for the C3 component only. Laskaris and Angelopaulus [16] reported 26 of 33 cases with linear BMZ for C3. These authors also pointed out that the immunofluorescence patterns were indistinguishable from those observed in bullous pemphigoid. In the present study, gingival lesions were asymptomatic; biopsy and immunofluorescence were done initially to determine the underlying dermatoses. This was necessary because there are case reports of the gingival lesions beginning as a sole manifestation and over a period of time there is appearance of skin, ocular and other mucous membrane involvement. Thus, an initial biopsy would be helpful in treatment if any systemic involvement occurred over a period of time.

Corticosteroids are typically used to control mucous membrane pemphigoid. [17] Topical steroids for mild disease and maintenance are commonly followed. Very high doses are occasionally required to achieve significant results for some cases of recalcitrant gingival mucous membrane pemphigoid. A custom made, flexible mouth guard may be used to keep the topical medication in place, [18] which helps in the constant bathing of the medications to the gingiva and also avoids the unnecessary contact of the medications to the other parts of the oral cavity. Periods of exacerbation and remission are common with this lesion and some may remain unrelenting for many years. [7] In the present study, lesions remained asymptomatic despite occurrence of bullae and an erythematous area There were periods of remission and exacerbation. During both these periods, the lesions were asymptomatic, and therefore allowed us to follow up the case without any prescription of

the topical steroids or systemic steroids for the period of 5 years. The patient was also told to visit the dermatologist and ophthalmologist to rule out the development of skin or the ocular lesions. Scrupulous oral hygiene and follow-up oral prophylaxis was done whenever the patient visited our dental clinic.

This is a rare case report presented to show gingival lesions associated with mucous membrane pemphigoid seen over a period of 5 years, which remained asymptomatic without any involvement of the skin, ocular or other mucosal areas. Follow up of desquamative gingivitis lesions treated with only maintenance of oral hygiene, without any medication (either topical or systemic steroids) and regular referral thereafter other dermatologist and ophthalmologist in older-aged individuals to rule out the involvement of other parts of the body is always necessary. With age and the aging process, the patient will usually be on multiple medications, so adverse drug reactions by potentially inappropriate medications are possible. [19] Careful assessment and proper prescription of medications prevents such old-aged individuals suffering from unwanted effects of these medications.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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