ORAL MUCOUS MEMBRANE PEMPHIGOID; A CASE REPORT AND REVIEW

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Abstract

Pemphigoid is a set of chronic, blistering mucocutaneous autoimmune illnesses, which are characterized by tissue-bound autoantibodies that are directed against one or more basement membrane constituents. Although clinically identical to pemphigus, pemphigoid has a distinct prognosis and microscopic features. Most patients exhibit oral lesions. However, additional locations, including the skin, conjunctiva, nasal, oesophageal, laryngeal, and vaginal mucosa, may also be affected. We present a distinct case of oral pemphigoid in a 48 year old male patient with varying clinical presentations, as well as review of literature on Pemphigoid.

***Key words**: Pemphigoid, Autoimmune Disease, Subepithelial split*

Pemphigoid in general consists of a group of subepithelial vesiculobullous disorders, such as Bullous pemphigoid, Gestational pemphigoid, Mucous Membrane Pemphigoid (MMP), Dermatitis herpetiformis, and Linear IgA disease. These are all immune-mediated subepithelial blistering diseases[1].

Mucous membranes are the major target of MMP, an autoimmune, chronic inflammatory subepithelial blistering condition. Auto antibodies like IgG, C3, IgA, and IgM are directed against various antigens which include bullous antigens 1 and 2, laminin and unidentified basal membrane zone antigens in hemidesmosomes. It frequently affects elderly women, whose ages range from 50 to 80 years. Oral mucosa, ocular mucosa, oropharynx, larynx, and vaginal region are the most commonly affected areas.[2]

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The mucosal scarring that develops after the erosions and blisters heal, is the distinguishing hallmark of MMP. It was previously known as cicatricial pemphigoid primarily because the ocular mucosa frequently exhibited scarring. Scarring, blindness, dysphagia, laryngeal stenosis, and anal or urethral strictures are long-term consequences of MMP. Desquamative gingivitis, vesicles, erosions coated with pseudo membranes, and ulcers are intraoral characteristics which are seen in MMP.[3] We are reporting a case of MMP that was present on oral cavity extensively.

CASE PRESENTATION

A 48-year old male patient reported to the department of Oral medicine and radiology, Malabar dental college and research centre, Edappal with chief complaint of blisters in mouth which when ruptures leaves painful ulcers and peeling of gingiva since last 2 months. It was accompanied by burning sensation while patient was having hot and spicy foods. He had visited a general practioner for ulcers and topical antiseptic gel was prescribed but on application it did not have any effect on ulcers.

Extraoral examination revealed no ocular, cutaneous, or genital lesions. On intraoral examination, generalized gingival erythema was noted with labial gingiva showing loss of stippling from the attached gingiva until the mucogingival junction. (Figure 1)

Fig 1- Generalized gingival erythema with recession and loss of stippling

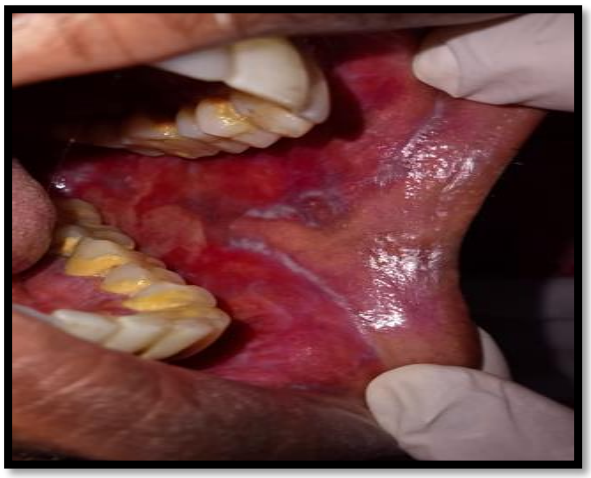

Fig 2- White diffuse patch with greyish areas on buccal mucosa

A diffuse patch was also seen on the left buccal mucosa with respect to 35,36 and 37 region. Keratinization was seen on both sides of buccal mucosa with smooth surface which was whitish in color with diffuse margins. (Figure 2) Application of lateral pressure caused bleeding in gingiva and epithelium was peeled off from the upper labial mucosa. The oral mucosa was tender on palpation. Based on clinical history and presentation, the lesion was provisionally diagnosed as Pemphigus and lesions like Pemphigoid, Bullous lichen planus and allergic stomatitis were considered as differential diagnosis.

Incisional Biopsy of the lesion was carried out and tissue was sent for histopathological examination to the department of Oral and Maxillofacial Pathology of Malabar Dental College (Figure 3).

Fig 3- Gross specimen

Histopathologic study revealed a stratified squamous epithelium supported by connective tissue stroma (Figure 4). Epithelium was hyperplastic with short rete ridges Focal areas of separation between the epithelium and connective tissue noted at the subepithelial level.(Figure 5) Connective tissue stroma was densely populated with mixed inflammatory cell infiltration. Moderate vascularity was also noted. On the basis of above histopathological examination, the lesion was diagnosed as MMP.

DISCUSSION

First case of Mucous Membrane Pemphigoid was reported by Wickmann in a female in 1794.[4] MMP represents a group of chronic, blistering ,mucocutaneous autoimmune diseases predominantly affecting the mucous membrane of mouth, oropharynx, conjunctiva, nasopharynx, esophagus and genitalia. Tense blisters and erosions are seen on head and neck or at sites of trauma in case of cutaneous involvement. MMP is known by different names including Cicatrical

pemphigoid or Benign mucous membrane pemphigoid or oral/ocular cicatrical pemphigoid. This condition has a heterogeneous origin in which tissue bound autoantibodies are directed against one or more components of the basement membrane. Pemphigoid clinically appears to be similar to pemphigus but varies by prognosis as well as microscopic features. MMP follows less severe course than pemphigus.[5]

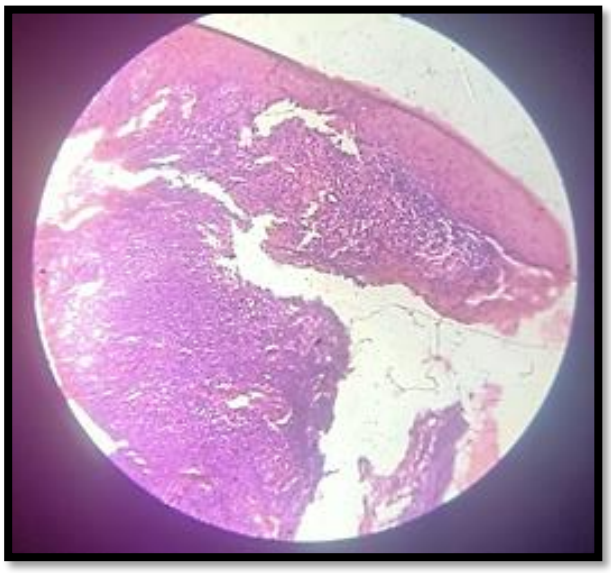

Fig 4- Hyperplastic epithelium with underlying dense connective tissue showing heavy inflammatory cell infiltrate (10x)

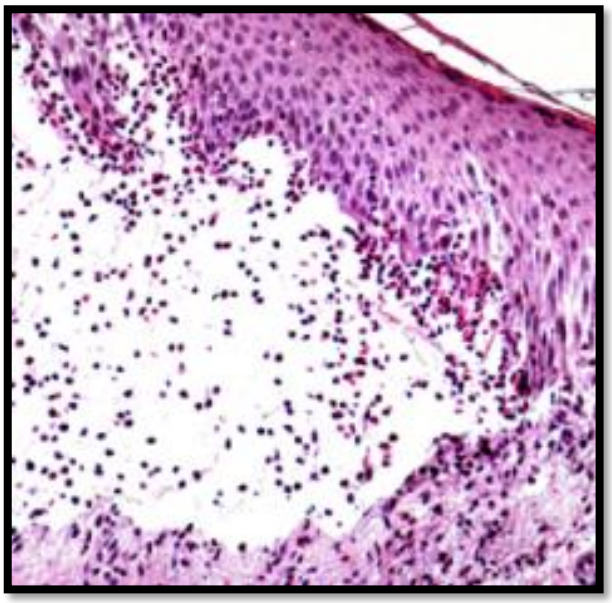

Fig 5-Subepithelial split in between epithelium and connective tissue (40X)

CLINICAL FEATURES

MMP has a female predilection and occurs usually after the fifth decade of life. It has a female to male ratio of 2:1. A recent study from the United Kingdom demonstrated that ocular MMP accounted for 61% of the cases of newly diagnosed cicatricial conjunctivitis and the incidence was calculated as 0.8 per million population.[5]

Sites involved are oral cavity, conjunctiva, genitalia, vulva and mucosa of nose, larynx and oesophagus. Skin lesions occurs particularly involving genitalia and near the body orifices in 25% cases. Lesions heal by scar formation.[6]

Ocular involvement is a serious complication of this condition which can even lead to complete blindness due to obliteration of palpebral fissure, with opacity of cornea.[7] Ocular lesion begins as subconjunctival fibrosis and on progression , conjunctiva becomes inflamed and eroded . Later, symblepharons occur which will lead to adhesions between upper and lower eyelids themselves. Lesions in larynx, though seen rarely , is manifested as airway obstruction and sudden change in vocalization .[6]

ORAL MANIFESTATIONS

MMP typically appears as a vesiculobullous lesion in oral cavity. Oral lesions mostly involve gingiva and palate as well as tongue, labial and buccal mucosa. Commonly seen manifestations are either in the form of erythematous, pseudomembranous or erosive lesions and even intact blisters in some cases. Gingiva is most commonly affected intraorally.

The salient clinical sign seen in MMP is Desquamative gingivitis manifested as erythematous gingiva and stippling loss that extends from gingival margins to alveolar mucosae often showing a glazing appearance. Patients often complain of tender gums with bleeding and associated dysphagia.[8]

Vesicles, bullae or blisters filled with either fluid or blood can also be present which may rupture leaving erosions or tender ulcers covered by pseudomembrane with yellowish slough. Eroded lesion will be surrounded by an inflammatory halo. Nikolsky's sign is usually positive in MMP.[7] Scar formation occurs rarely in oral lesions. Our case also had similar clinical features with peeling of epithelium when pressure was applied on its surface.

Histopathologically, vesicles and bullae are subepidermal rather than suprabasilar. Acantholysis is not seen. Chronic inflammatory infiltrate of plasma cells, eosinophils and lymphocytes are noted in connective tissue.[7]

INVESTIGATIONS

Biopsy is the gold standard in diagnosis of Pemphigoid lesions. In Current scenario, direct and indirect immunofluorescence provides final confirmation.

Intraoral biopsy of the lesion shows split between surface epithelium and underlying connective tissue along with mild chronic inflammatory infiltrate in connective tissue.

Direct immunofluorescence is positive in nearly 90% cases whereas indirect immunofluorescence is positive only in 5-25% cases. Perilesional tissue always gives the accurate diagnosis rather than an ulcerated one. A continuous linear band of immunoreactants at basement membrane zone is seen through direct immunofluorescence studies of perilesional mucosa.[9]

MANAGEMENT

Management mainly aims on suppressing extensive blister formation, promoting healing, and preventing scar formation. After confirming the diagnosis through light microscopy and/or immunofluorescence, patient should be referred to an ophthalmologist to rule out any ocular involvement. Treatment should always be based on lesion's distribution, disease activity as well as therapeutic response.[7]

Topical corticosteroids can be applied for oral lesions which is discontinued once the lesion suppresses. Good oral hygiene measures along with flexible mouth guard as a carrier for steroid medication is helpful in those with only gingival lesions. If the condition is mild to moderate, then systemic corticosteroids should be combined with topical ones. Cyclophosphamide, Dapsone, Tetracycline, Minocycline and Niacinamide are used systemically with a dosage of about 0.5 g to 2g daily. In severe and refractory cases, immunosuppressants, biologic therapies including intravenous immunoglobulin are preferred.[8]

MMP can be controlled with treatment but in some cases it can progress despite management. Routine eye examination should also be done to prevent complications like blindness. Appropriate wound care is also particularly important to promote healing and minimize scarring. A team of dentist, ophthalmologist and dermatologist plays the major role in alleviating the symptoms of MMP.

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Conflict of Interest: *None Decl*ared