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Current Update On Mucous Membrane Pemphigoid

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ABSTRACT

Mucous membrane pemphigoid is a rare mucocutaneous disorder that has a predilection for the mucous membranes. Oral cavity is the chief site of involvement and desquamative gingivitis is the main presenting manifestation. Other mucous membranes like ocular, nasal, tracheal, laryngeal, pharyngeal and genital mucosa may also be affected. The disorder affects females in the middle age group. Histopathological and immunofluorescent features are highly diagnostic for the disease. Steroids are the mainstay of treatment, along with other immunosuppressive agents. This paper aims to present a recent update on mucous membrane pemphigoid taking in account its etio-pathogenesis, clinical and oral features, diagnostic aids and treatment protocols.

Keywords: Mucous membrane pemphigoid, Desquamative gingivitis, Nikolsky sign, corticosteroids.

INTRODUCTION

Mucous membrane pemphigoid (MMP) is a chronic autoimmune, inflammatory, sub epithelial, blistering disorder. The condition predominantly affects the mucosal membranes, with or without clinically apparent scarring[1] MMP constitutes a part of subepithelial bullous mucocutaneous disorders. MMP was earlier referred to as "cicatricial pemphigoid", "benign MMP," and "ocular or oral–gingival pemphigoid." Currently, the disorder is named as Mucous membrane pemphigoid (MMP)[2]

Mucous membrane pemphigoid was first reported by Wichmanns[3] and Thost first decribed the essential characterstics and nomenclature of the disorder[4,5]

Etiopathogenesis

MMP is an autoimmune disorder with an unknown etiology. Variety of inflammatory trauma to mucosa[6] medications (clonidine, D-penicillamine, indomethacin)[6] viral agents, UV light, and occasional occurrence with other autoimmune diseases are some of the predisposing factors[7] Racial or

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geographic predilections are unknown, but there is a possibility of an immunogenetic background that is associated with HLA DQB1*0301[8,9] The most frequently presenting feature in MMP is desquamation of gingiva and frequently occurs in post-menopausal women. There is no cited literature supporting the association of MMP and post menopausal condition or habit of smoking[10]

MMP is an autoimmune disorder. The basement membrane complex proteins are primarily targeted by the autoantibodies (usually IgG). The immunoglobulins formed attract and trigger the leukocytes (chiefly neutrophils) which liberate proteolytic enzymes. These proteolytic enzymes cause blister formation byattaching to thebasement membrane zone fibrils[11] The salt split skin test demonstrates IgG autoantibodies bound toantigens on the epidermal side, however, occasional cases have shown the presence of IgG autoantibodies on the dermal side[12] The autoantibodies bound to the dermal side precipitate the glycoprotein epiligrin and bind to the basement membrane of the lower portion of the lamina lucida at its interface with the lamina densa. [13,14] There is also a mention about cell mediated immunity and cytokines in the etio-pathogenesis of MMP[15]

Epidemiological characterstics

MMP is reported with an incidence of 1.5-9.5 cases per 100,000 inhabitants every year[16] Various data analysis suggest that Bullous pemphigoid is 7 times more common than MMP[17] A number of immunofluorescence studies have shown 3 times more frequent occurrence of MMP as compared toPemphigus[18-20] There is a predilection for middle aged adults and the condition infrequently affects children and old age individuals. The condition predominantly affects females (M:F-2:1)[21]

Clinical and oral manifestations

Mucous membranes are chiefly affected by the condition. The condition frequently affects the oral mucosa, followed by ocular, pharyngeal, laryngeal, nasal, esophageal, tracheal and genital mucosa. Oral mucosal involvementoccurs in more than 90% cases and ocular lesions are seen in 60-70% cases[22,23] Only about 25% of patients may report cutaneous lesions.

The most frequently occurring manifestations in the oral cavity are desquamation of gingiva,vesicles and bulla formation, and ulcerations. Gingiva is the most frequently affected intraoral site[24,25] and healing with scarring is characteristically seen. Desquamative gingivitis is a salient intra-oral feature of MMPand may be the only manifestationin few cases[26] The patient usually gives a long history of gingival soreness. Chronic superficial gingival erosions and isolated epithelial tags may be contributory to the diagnosis[27] The common presenting manifestations are tender gums with bleeding on slight provocation, mucosal peeling with difficulty in swallowing (dysphagia)[28]

Fluid filled blisters develop or sometimes due to mild to moderate trauma blisters may be blood-filled. A positive Nikolsky's sign is characteristically seen in MMP. When tangential pressure is applied to erythematosus area or to apparently normal mucosa adjacent to lesional tissue, it results in blister formation[29] These flaccid blisters eventually rupture producing denuded tender ulcers that show slow healing. A variable pattern of severity occurs in MMP, and ranges from infrequent blisters to continuous severe blister formation and ulceration. Gingival lesions usually do not demonstrate scarring, although healing with scarring in other oral lesions is associated with diminished functions[30]Intact bullae is infrequently seen intraorally, and fibrin covered shallow erosions with irregular marginis a common manifesting feature in MMP[31]Adhesive apertures may develop between various parts of oral cavity in advanced and severe MMP. Ankyloglossia or limited tongue protrusive movements may be seen in cases of frenal involvement[32]

Ocular mucosa is the second commonest site of involvement in MMP. Ocular lesions show scarring conjunctivitis withfibrotic changes in the subconjunctival tissues.Fornix foreshortening and formation of adhesion between bulbar and palpebral conjunctiva (symblepharon) is also seen in MMP[23,33] Initial lesions show non-specific features and remain confined to one eye. Advanced stage is characterized by conjunctival fibrosis, severe entropion, trichiasis, symblepharon, dry eye syndrome, corneal erosions and ulcerations, keratitis and even ultimately result in blindness[33]

Life threatening asphyxia may occur in stenosis of larynx. Difficulty in swallowing (dysphagia) may be seen in cases of esophageal webs. Occassionally rupture of esophageal webs occurs and cause mediasinitis[9] Pharyngeal involvement in MMP may cause hoarseness or dysphagia[1]

Diagnosis

Histopathological and immunofluorescence findings form the standard diagnostic aids[34] The chosenbiopsy location should be a vesicle or the tissue surrounding the lesion. Gingival biopsy should be avoided, as gingival inflammation may be induced and will result in improper diagnosis.

The characteristic histopathologic feature in MMP isa sub-epithelial split caused due to disruption at the basement membrane. Eosinophil, neutrophil and lymphocytes predominate the inflammatory cells in the lamina propria[35]

Direct immunofluorescent testing (DIF), being both a specific and sensitive test is regarded as principal diagnostic aid for MMP[1] Linear deposition of immunoreactants, chiefly IgG, IgA or complement proteins (C3), along the epithelial / sub epithelial basement membrane zone of a mucous membrane is highly diagnostic for MMP. Indirect immunofluorescence using salt-split mucosa provides more sensitive assay[36]

Treatment

Topical corticosteroids, either alone or in association with systemic corticosteroids form the mainstay of treatment[37] Promising and dramatic responses have been achieved with Dapsone[38-40] Patient should be subjected to regular blood profile testing as prolonged dapsone use may induce hemolytic anemia. Immunosuppressive drugs such as methotrexate, azathioprine, levamisole, cyclophosphamide, and mycophenolate mofetil are also used as a treatment protocol in MMP[41-43] MMP has also been treated with a tetracycline derivative or a combination of tetracycline and niacinamide[44-46] Maintaining dental hygiene and avoidingpredisposing factorsis important in the management of patients with MMP[47] Intravenous immunoglobulins, plasmapheresis, and Low level laser therapy (LLLT) constitute the recent development in the management strategies of MMP.

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