Medical Management of Vesiculobullous Lesions in Oral Cavity

Tamizh Paavai. Tha1, Dr. Dhanraj2

1Bachelor of Dental Surgery, Saveetha Dental College and Hospitals, Chennai, Tamil Nadu
2Professor, Department of Prosthodontics, Saveetha Dental College and Hospitals, Chennai, Tamil Nadu

Abstract: The oral cavity may be a potential source of diagnostic information. Oral manifestations of vesiculobullous disease may occur independently or precede cutaneous involvement by a year or more. The vesiculobullous disorders that occur commonly in the oral cavity are pemphigus vulgaris, cicatricial pemphigoid, erythema multiforme, IgA disease and bullous pemphigoid. This review article summarises their oral presentation, diagnosis and medical management.

Keywords: Vesiculobullous, medical, pemphigus, oral, lesion, treatment

1. Introduction

In oral medicine, dermatologic diseases have special attention as oral mucosal lesions may be a clinical feature or the only sign of various mucocutaneous diseases. Dentists are often the first to be consulted by patients who develop acute oro-facial pain and the skin lesions associated with oral lesions could be neglected by dentists due to lack of information and/or improper diagnosis. Maintenance of oral hygiene, discomfort that results in poor hydration and nourishment, and secondary infection must be addressed to assure disease control and patient comfort.

Vesiculobullous lesions are a distinct group of oral disorders characterized by formations of vesicles or bullae. Vesiculobullous lesions that involve the oral cavity are common features of a wide variety of diseases. The dental practitioner attempting to diagnose the oral ulcers and lesions is often confronted with several diseases having similar, if not identical clinical appearances. Also, the clinical identification of intact vesicle and bulla in the oral cavity is really a challenge due to regular irritation and the friable nature of the oral mucosa that makes the diagnosis of vesiculobullous lesions even more difficult as the differential diagnosis of the disease also includes ulcerative, immunological, neoplasms and systemic diseases.

This review analyses the various features of some of the common vesiculobullous lesions that occur in the oral cavity such as pemphigus vulgaris, erythema multiforme, cicatricial pemphigoid, IgA disease and bullous pemphigoid with their latest medical management modalities.

2. Pemphigus Vulgaris

Pemphigus is a severe, blistering mucocutaneous autoimmune disorder. Pemphigus vulgaris, as an autoimmune mucocutaneous disease, creates bullous lesions in mucous and cutaneous membranes by producing IgG autoantibodies against keratinocytes antigens[1].

Oral lesions are common and any mucous membrane such as that of esophagus, larynx and pharynx[2]. Intraorally, bullae formation which rupture to form large erosions with ragged borders are seen. Nikolsky’s sign is often present and desquamative gingivitis may also be observed[3].

Similar to other autoimmune diseases, if not promptly treated, the process of pemphigus vulgaris would be progressive providing the opportunity for the spreading of epitopes. It seems that adequate treatment at the onset of the disease leads to better outcomes in terms of controlling the disease and preventing recurrences. The main object in pemphigus treatment is development of low steroid regimens or an intervention without using systemic corticosteroid therapy[4].

Commonly used treatments include corticosteroids and immunosuppressive drugs. There is still no standard treatment for pemphigus vulgaris data is not available from randomized trials using different drugs and methods. Recently, newer agents such as intravenous immunoglobulin therapy, rituximab, immunoadsorption using the Glo-Baffin adsorber system and immunoadsorption for rapid removal of desmoglein-reactive autoantibodies[5].

The diversity of these drugs and treatment methods, together with their choosing a suitable treatment for pemphigus today[6].

3. Mucous Membrane Pemphigoid

Mucous membrane pemphigoid (MMP) or cicatricial pemphigoid is a chronic autoimmune subepithelial disease that primarily affects the mucous membranes of patients over the age of 50 years, resulting in mucosal ulceration and subsequent scarring. Mucous membrane pemphigoid is caused by autoantibodies, usually of the IgG class, that are directed against proteins of the basement membrane complex. The antigens associated with mucous membrane pemphigoid are most frequently present in the lamina lucida portion of the basement membrane. The subepithelial lesions of mucous membrane pemphigoid may involve any mucosal surface, but they most frequently involve the oral mucosa.

In the oral cavity, gingiva is the most frequently affected site that is seen as erythema, sloughing and occasional bullae formation. Positive Nikolsky’s sign, which depicts desquamation manifests clinically as desquamative gingivitis. Patients often complain of painful gingiva that

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bleed with mild provocation. The untreated lesions have periods of exacerbation and remission; but lesions may also be seen for long durations with minimal improvement when treatment is administered[9].

The management of a patient with mucous membrane pemphigoid is complicated by the chronic nature of the disease and the fact that affected individuals tend to be elderly and have multiple medical problems. In addition, there is the potential for patients with mucous membrane pemphigoid to develop severe complications, including blindness from conjunctival lesions, and even to die as a result of severe esophageal or laryngeal scarring. Several forms of therapy have been advocated for the management of oral lesions of mucous membrane pemphigoid. When the lesions are confined to the oral mucosa, systemic corticosteroids will suppress their formation, but the clinician must weigh the benefits against the hazard from side effects of the drug. Unlike pemphigus, mucous membrane pemphigoid is not a fatal disease, and long-term use of steroids for this purpose must be carefully evaluated, particularly because most cases are chronic, most patients are elderly, and treatment is required for a long period of time. Patients with mild oral disease should be treated with topical and intra-lesional steroids. When topical therapy is not successful, several drugs have been used to treat several oral lesions. These include systemic corticosteroids, antimetabolites, antibiotics, and dapsone. Dapsone has been in clinical use for almost 50 years. It is effective in a variety of infectious diseases, including malaria and leprosy. Recent studies have shown that dapsone in combination with corticosteroids is the most useful treatment[10].

4. Erythema Multiforme

Erythema multiforme (EM), described as concentric “target” lesions, can be caused by infections, autoimmune disease, neoplasms, drugs, or medications. Although erythema multiforme is considered to be a self-limiting condition, it overlaps with a more severe variant: Stevens Johnson syndrome. The pathophysiology is not clearly known although it has been shown that 43% of the cases of erythema multiforme, Stevens Johnson syndrome, and toxic epidermal necrolysis that are severe enough to require hospitalization are caused by drug reaction. The common culprits are phenobarbital, nitrofurantoin, trimethoprim/sulfamethoxazole and ampicillin[11].

The oral lesions are characterized by the formation of blisters which rupture to produce erosions and ulcerations with grayish pseudomembranes and a haemorrhagic crust[12]. The lips are commonly affected and the mucosal lesion have a parboiled appearance. They exhibit positive Nikolsky’s sign and healing occurs within two to three weeks recurrence has been reported in 25% of the cases of erythema multiforme[13].

Management of erythema multiforme involves determining the etiology when possible. The first step is to treat the suspected infectious disease or to discontinue the causal drug. Mild cases of erythema multiforme do not require treatment[14]. Oral antihistamines and topical steroids may be used to provide symptom relief[15]. In patient with existing or recent Herpes Simplex Virus infection, early treatment with oral acyclovir (Zovirax) may lessen the number and duration of cutaneous lesions[16][17].

Azathioprine (Imuran; 100 to 150 mg per day) has been used successfully in patients for whom other treatments have failed[18]. Recurrent erythema multiforme also has been treated with cyclosporine (Sandimmune)[19].

IgA DISEASE

IgA disease is a chronic condition that mainly occurs in adults[20] and are observed as small, tense subepithelial bullae with polymorpho nuclear leukocyte or as large mononuclear cells[21]. In the oral cavity they usually manifest as desquamative gingivitis[22].

Their direct immunofluorescence is similar to that seen with childhood cicatricial pemphigoid and dermatitis herpetiformis. In case of chronic condition, the oral lesions present are observed as tense bullae on an inflated erythematous base that is also associated with pruritis and a burning sensation. The oval shaped bullae that may improve or regress with puberty are usually treated with corticosteroids or dapsone[23].

During initial stages the patients are treated with dapsone and are subjected to a gluten free diet[24].

5. Bullous Pemphigoid

It is a chronic, autoimmune disorder which commonly affects skin and mucous membrane of elderly people is characterized by formation of tense bullae that heals without scarring. The mucosal lesions frequently involve the oral cavity[25]. Unlike cicatricial pemphigoid wherein mucous membrane is initially where lesion occur in bullous pemphigoid they occur on the skin.

The oral lesions tend to rupture to form painful, eroded surfaces. The common sites in the oral cavity include palate, floor of the mouth, tongue and buccal mucosa. Desquamative gingivitis may also be observed[26].

They are mainly diagnosed with the help of histopathological feature and direct immunofloresence wherein circulating immunoglobulins are present. Serum antigen detection of antigens such as 230-kDa and 180-kDa is also used as adiagnostic tool[27,29].

The treatment options most frequently used are systemic corticosteroids alone or in combination with other immunosuppressive agents[29][30]. In recent times, systemic dapsone, cyclosporine, sulfapridine as well as a combination of tetracycline and niacinamide have demonstrated therapeutic effect[31-35].

6. Conclusion

Although it is clear that many vesiculobullous disease may be considered medical conditions, dentists as well as other dental health care providers may be called upon to manage these diseases alone or in conjunction with other
health care providers. Vesiculobullous lesions of the oral cavity often present with common clinical manifestations complicating a definitive diagnosis. Diagnosis is facilitated with the histological evaluation of tissue specimens using routine histopathology as well as immunofluorescence. Better understanding of the causation and pathogenesis of vesiculobullous diseases has allowed for the development of more successful treatment modalities and therapeutic interventions.

References