Oral Mucous Membrane Pemphigoid With Positive Nikolsky's Sign: A Case Report

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Abstract- Mucous membrane pemphigoid (MMP) is a rare inflammatory, autoimmune, and subepithelial vesiculobullous disease in which tissue-bound autoantibodies are produced against one or more components of the basement membrane. Oral lesions of the pemphigoid begin in the form of vesicles or bullae that often involve throughout the mouth but may be confined to specific areas, especially the gingiva, in a pattern known as desquamative gingivitis. The positive Nikolsky's sign is characteristic of pemphigus vulgaris, in which a blister can appear on the normal-appearing skin if exerting lateral pressure, and is very rare in the mucosa and other vesiculobullous diseases. Here we report a case of mucous membrane pemphigoid that developed as desquamated gingivitis in a 46-year-old woman with positive Nikolsky's sign in the gingival mucosa. In the histopathologic view, a subepithelial cleft was observed. The results of direct and indirect immunofluorescence tests and related therapeutic interventions are also presented. Positive Nikolsky's sign can be observed in the mucosa as well as in the mucous membrane pemphigoid in addition to pemphigus vulgaris, and vesiculobullous lesions should be diagnosed based on the sum of clinical, histopathological, and immunofluorescence findings.

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Introduction

Dentists may experience various oral mucosal diseases. Oral lesions can be the primary manifestation of many systemic diseases (1). Mucous membrane pemphigoid is a rare inflammatory autoimmune subepithelial blistering disease under epithelial (2) in which tissue-attached autoantibodies are produced against one or more components of the basement membrane (3). Early and accurate diagnosis of this rare clinical condition is essential for the effective treatment of lesions that may reduce disease progression (1). The disease usually affects the elderly. Women are more likely to be infected than men (3).

Oral lesions are seen in most patients, but other areas, such as the conjunctiva, nose, esophagus, larynx, and vaginal lining, as well as the skin, maybe involved (3). Oral lesions of pemphigoid begin as vesicles or bullae that may sometimes be clinically identified. After a while, these blisters usually rupture and leave extensive map-like mucosal erosions or ulcers (3). The disease is often seen diffusely throughout the mouth but may be limited to specific areas, especially the gums. Gingival involvement creates a pattern of clinical response called desquamative gingivitis (3). The positive Nikolsky's sign is a characteristic of pemphigus vulgaris, in which bullae (blister) can appear on the skin that appears to be normal if firm lateral pressure is applied (3). This sign is very rare in the mucosa and other vesiculobullous diseases other than pemphigus vulgaris. (4). Here we report a case of mucous membrane pemphigoid that developed as desquamative gingivitis in a 46-year-old woman and had a positive Nikolsky's sign on the gingival mucosa.

Case Report

The 46-year-old female patient complained of burning gums and white scales on her upper jaw gums and presented to the Department of Oral Diseases. The

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patient also mentioned a history of similar lesions a year ago and said that there was a blister-like lesion on his scalp, but since the lesions had healed after a while, he did not follow up during this time. However, after the recurrence of the lesions, and having concerns in this regard, follow-ups have begun to find the diagnosis of the lesion. In reviewing the medical history, the patient did not report a history of systemic disease. Also, there were no similar lesions in other areas of the mucosa or skin by oral examination and questioning of the patient. He did not take any special medication. On oral examination, white scales similar to desquamative gingivitis were observed on the gums of the anterior and posterior maxillary areas of the patient, which were removed by application of the gauze on these scales, and the erythematous gingival mucosa appeared below it. With finger pressure or a dental mirror, hemorrhagic blisters formed on the gums (Figure 1).

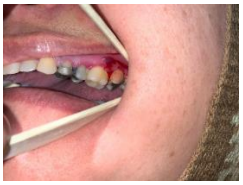

Figure 1. A hemorrhagic blister formed after applying pressure by a dental mirror on the gingiva in the context of desquamative gingivitis

The patient was referred to a periodontist for lesional biopsy with clinical suspicion of conditions causing desquamative gingivitis, including pemphigus vulgaris, mucous membrane pemphigoid, and erosive lichen planus. At the time of the biopsy, the hemorrhagic blister was induced with the minimum pressure on the gingiva. On histopathological examination of the submitted sample, a sub-basilar cleft containing red blood cells was observed under the parakeratinized stratified squamous epithelium of the oral mucosa. The roof of the cleft was the epithelium of the oral mucosa, and the floor was underlying lamina propria. The presence of granulation tissue containing abundant acute and chronic inflammatory cells was evident (Figure 2).

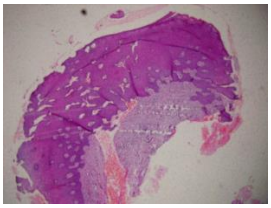

Figure 2. Sub-basilar cleft below the stratified squamous epithelium of oral mucosa filled with red blood cells (100X magnification)

This sub-basilar cleft could be matched with one of the following histopathological diagnoses: 1. Mucous membrane pemphigoid, 2. Angina bullosa hemorrhagica, 3. bullous lichen planus, and 4. linear IgA bullous dermatosis. Direct and indirect Immunofluorescence tests were performed to confirm the diagnosis. Direct immunofluorescence testing on healthy fresh tissue around the lesions showed a focal linear deposition of the IgG immunoglobulin as well as of the complement component 3 (C3) along the junction of the epithelium and lamina propria. The result of the indirect immunofluorescence test was negative. Therefore, based on the combination of clinical, histopathological, and immunofluorescence characteristics, the final diagnosis of mucous membrane pemphigoid was made for the patient. After confirming the diagnosis, the patient was referred to an ophthalmologist to check for eye lesions, but fortunately, no eye involvement was observed after specialized examinations. Topical treatment with topical corticosteroids (adcortyl ointment four times a day) was started in combination with nystatin for the patient. Gingival lesions improved after about two weeks after treatment. The patient took ointment on an alternate day for maintenance therapy, which was followed by taking twice a week. After about six months of treatment, no recurrence of the lesions was observed, and there is no sign of progressive disease, and lesions in other areas of the mucosa or skin were not found.

Discussion

As mentioned, mucous membrane pemphigoid usually involves the elderly (3). Our patient was 46 years old and did not match the general age of the disease. In terms of gender, our case is consistent with the higher incidence of women in mucous membrane pemphigoid.

Differential diagnosis of desquamative gingivitis (as seen in our patient) includes mucous membrane pemphigoid, erosive lichen planus, and to a lesser extent, pemphigus vulgaris (3).

The most common complication of this disease is ocular involvement (3). Fortunately, no eye involvement was observed in the patient after referring to an ophthalmologist and performing specialized examinations. Although it is possible for other areas of the mucosa to become infected, our patient did not experience any other mucosal involvement.

Skin involvement in mucous membrane pemphigoid is not common and occurs in about 20% of patients as

firm blisters (3). Our patient also mentioned a history of blistering lesions on the scalp, although there was no such lesion at the time of referral.

A characteristic feature of pemphigus vulgaris is that a bulla (blister) can form on the apparently normal skin in the event of firm lateral pressure, which is called a positive Nikolsky's sign and is useful in the clinical diagnosis of pemphigus. (3). Other blistering conditions that show positive Nikolsky's sign include pemphigus foliaceus, paraneoplastic pemphigus, stevens-johnson syndrome, staphylococcal scalded skin syndrome, toxic epidermal necrolysis, oral lichen planus, mucous membrane pemphigoid, and epidermolysis bullosa (4).

Although the classic Nikolsky's sign is seen on the skin, there have been two case reports which reported its appearance on mucous membranes of other tissues. In one case, Nikolsky's sign was induced on the esophageal mucosa of a patient with pemphigus vulgaris. In another, Nikolsky's sign was induced on the cervical mucosa in 13 of 16 patients with pemphigus. However, this is very rare (4).

Direct immunofluorescence studies of the mucosa around the lesion show a continuous line of immune responses in the basement membrane in about 90% of patients. Immune deposits are mainly composed of IgG and C3, although IgA and IgM may also be identified (3). In our patient, this continuous linear band consisting of IgG and C3 was also seen. These immune reactants play a role in the pathogenesis of the formation of subepithelial vesicles by weakening the binding of the basement membrane by various mechanisms, including the activation of complement and recruitment of inflammatory cells, especially neutrophils. Indirect immunofluorescence is positive in only about 5 to 25 percent of cases, indicating a relative lack of circulating autoantibodies (3). In this patient, the result of the indirect immunofluorescence test was negative.

Other relatively rare conditions can histopathologically mimic pemphigoid. These conditions include linear IgA bullous dermatosis, angina bullosa hemorrhagica, and acquired epidermolysis bullosa acquisita. Linear IgA bullous dermatosis is characterized by linear deposition of only IgA along the basement membrane area. It also mainly affects the skin and can usually be differentiated from mucous membrane pemphigoid based on clinical findings (5). In angina bullosa hemorrhagica, painful blood-filled blisters usually involve the soft palate of middle-aged or elderly people. Although the subepithelial cleft is seen on histopathology, no hematologic or immunopathological abnormalities are identified. A history of trauma or inhaled corticosteroids is also seen in many patients. In epidermolysis bullosa acquisita, autoantibodies are produced against type VII collagen, the main component of anchoring fibrils (in pemphigoid, they are produced against various components of the basement membrane or hemidesmosomes). Although oral lesions are present in approximately 50% of cases, such lesions are uncommon in the absence of skin lesions. A special procedure is also performed to differentiate epidermolysis bullosa acquisita from other immunobullous diseases with a subepithelial cleft. A sample of the patient’s perilesional skin is incubated in a concentrated salt solution, which separates the epithelium from the connective tissue and forms an artificial blister. The immunohistochemical evaluation shows the deposition of IgG autoantibodies on the blister floor (connective tissue side), where type VII collagen is located. This finding contrasts with most forms of mucous membrane pemphigoid, in which autoantibodies are usually confined to the roof of the blister (3).

There is no single good treatment for patients with mucous membrane pemphigoid. Treatment should be personalized depending on the distribution of lesions, disease activity, and response to treatment. If only oral lesions are present, sometimes the disease can be controlled by using one of the stronger topical corticosteroids on the lesions several times a day. Once the control is achieved, the drug can be stopped, although the lesions will certainly recur again. Sometimes an alternate-day application can prevent the disease from getting worse. In cases of local corticosteroid failure, systemic treatments are available (3). The use of low-level lasers has also been used successfully in the treatment of gingival lesions in patients with mucosal pemphigoid (6).

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