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CASE REPORT

Global Dentistry

Pemphigus Vulgaris and Mucous Membrane Pemphigoid: A Comparison between Clinical Cases

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Abstract

Background: *Pemphigus vulgaris (PV) and mucous membrane pemphigoid (MMP) are autoimmune bullous inflammatory dermatoses. The former is characterized by the abnormal production of IgG autoantibodies against desmogleins of the epithelial cell surface desmosomes, and the latter against components of the basement membrane. Both are characterized by vesicles and/or blisters that rupture to form ulcerations, being diseases of low incidence, but with high morbidity and sometimes lethal. PV is more common than MMP and in the oral region it mainly affects the palate, gingiva, ventral tongue, and labial mucosa, involving adults of both sexes in the same proportion. MMP affects older people and can involve skin and mucous membranes locally and also systemically. However, when delimited, the gingiva is the most affected site. Aim: To describe two cases comparing two types of autoimmune vesiculobullous diseases: pemphigus vulgaris and mucous membrane pemphigoid.*

Case report 1: *A 72-year-old man came to the clinic with a complaint of burning mouth 14 days before. On examination, three ulcerated lesions were observed in the left and right retromolar region and soft palate.*

Case report 2: *A 71-year-old woman complained of blisters on her gums three months before, with frequent peeling, burning and pain. In both cases, the positive Nikolsky's sign was the initial diagnostic hypothesis of MMP or PV. Incisional biopsies were performed, and the histopathological reports confirmed, respectively, PV and MMP.*

Conclusion: *The study contributes to the differential diagnosis between diseases, assisting health professionals in the proper management of these conditions.*

Keywords: *pemphigus, benign mucous membrane pemphigoid, oral pathology, pathology*

Introduction

Pemphigus vulgaris (PV) and mucous membrane pemphigoid (MMP) are immune-mediated diseases, clinically characterized by bullous, ulcerated, and eroded lesions [1]. MMP is more common in middle-aged women [2] and PV affects equally both genders, mainly between the fourth and sixth decades of life [3].

PV is characterized by the production of autoantibodies against desmosomal proteins found in the epithelial junctions of the lining tissues [4], causing a distance from one cell to another, marking the phenomenon of acantholysis. MMP, on the other hand, is characterized by the formation of auto antibodies against the normal components of the basement membrane of the epithelium [5].

The blisters in the PV are fragile and break quickly, forming painful erosions that bleed easily, being covered by hematic crusts [3]. In the MMP, there is the presence of vesicles or blisters, which after rupture form a painful ulcerated area [6].

Oral lesions are the first manifestations in PV, which are randomly spread through the mucosa. However, they are more frequent in the palate, labial mucosa, ventral tongue and gums [7]. MMP lesions mainly affect the oral, ocular, pharyngeal and laryngeal, genital and esophageal mucous membranes, however, in most cases, the involvement of the gingival mucosa is more common, in the clinical form of desquamative gingivitis[5].

Although PV and MMP are clinically similar, they have different prognosis and the differential diagnosis must be made on the basis of clinical, histopathological and immunopathological findings so that the appropriate treatment can be established. The purpose of this article is to describe two cases comparing two types of autoimmune vesiculobullous diseases: pemphigus vulgaris and mucous membrane pemphigoid.

Case Reports

First Case

A 72-year-old man attended the Stomatology specialization course with a burning mouth complaint 14 days before. On clinical examination, three ulcerated lesions were observed on the left and right retromolar regions and the soft palate (Figure 1). A positive Nikolsky's sign was observed in the lesions. An incisional biopsy of the retromolar region was performed with histopathological report of pemphigus vulgaris (Figure 2).

Second Case

A 71-year-old woman complained of blisters on her gums three months before, with frequent peeling, burning and pain. On clinical examination, an eroded, erythematous, and peeling area was observed in the gingiva (Figure 3). A positive Nikolsky's sign and histopathological report of mucous membrane pemphigoid was observed (Figure 4).

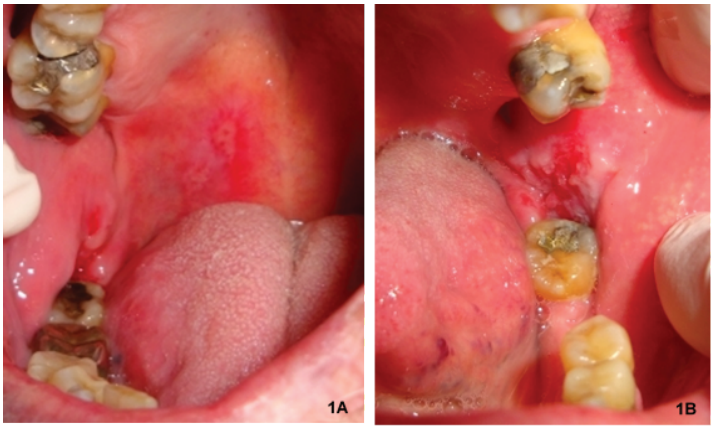

Figure 1.*Clinical presentation:* A Ulceration in the right retromolar region and erosion in the soft palate; B Ulceration in the left retromolar region.

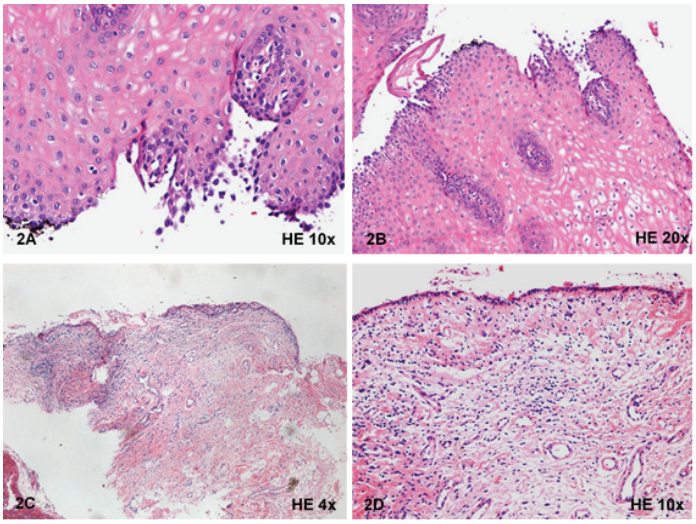

Figure 2. *Histopathological characteristics: A* Intraepithelial cleft showing the keratinocytes of the spinous layer; B Magnification increase showing acantholytic epithelial cells (Tzanck) in the cleft; C Connective tissue with no lining epithelium; D Detail showing the basal cells of the epithelium preserved and adhered to the submucosa.

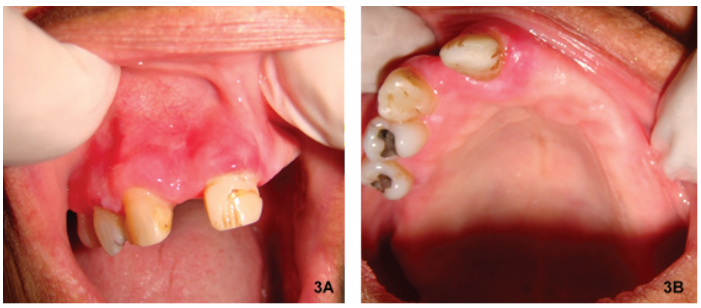

Figure 3. *Clinical presentation:* A Upper erythematous and erosive vestibular gingiva; B Palatal view of the erythematous region.

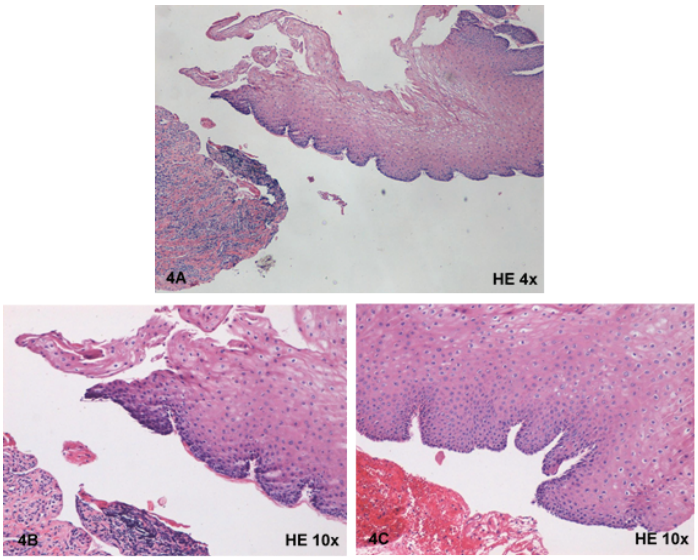

Figure 4. *Histopathological characteristics:* A 4x magnification showing the total separation between epithelium and connective tissue; B Subepithelial cleft; C Hemorrhagic content in the cleft and epithelium totally separated from the conjunctiva.

Discussion

PV and MMP are similar vesiculobullous diseases of autoimmune origin. They are differentiated according to the location of the blister in the histopathological examination, which are, respectively, intraepithelial and subepithelial [8].

PV is caused by autoantibodies, which results in the dissolution of intercellular bonds within the epidermis and mucosal epithelium [8], being considered the most common variant when involving both mucosa and skin, mainly on the scalp, axilla, face, groin, trunk and pressure points. This pathology affects men and women equally and has a greater incidence between the fourth and sixth decades of life. The formation of blisters occurs due to the presence of IgG antibodies against the intercellular adhesion structures, desmogleins, which results in acantholysis. Clinically, the main complaint is pain in the oral mucosa due to the presence of superficial and irregular erosions and ulcerations distributed at random [9,10]. The blisters have a thin and friable roof, which can be easily ruptured, being, hardly observed by the examiner.

MMP is also caused by autoantibodies (IgG, IgA and/or C3) that are deposited on the basement membrane of the epidermis [2,9], being considered a rare disease compared to PV. It is characterized by the predominance of mucous membranes - oral, ocular, nasopharyngeal, esophageal, laryngeal and genital - with healing success. This pathology has a higher incidence in middle-aged women, in a 2:1 female-to-male ratio [9,14]. Clinically, oral lesions begin with blisters that can be identified by the examiner, with a thicker and more resistant roof than the PV [10] ones and, therefore, more difficult to break. Despite being infrequent, MMP presents an important severity, and rapid and effective treatment is essential to stop the progression of the disease, since in later cases, patients may develop esophageal and laryngeal stenosis, and blindness [15].

Thus, it is possible to observe that both pathologies are similar autoimmune bullous skin diseases, making histopathological analysis essential to confirm the diagnosis. In addition, despite presenting terribly similar lesions, these conditions have different prognosis, having PV a worser one.

For the differential diagnosis, the literature indicates the studies of direct immunofluorescence of the perilesional mucosa as it´s

the gold standard exam to confirm diagnosis. In the MMP there is a linear deposition of immunoglobulins (IgG, IgA or IgM) or C3 in the suprabasal region, and in the PV there is a deposition similar to an immunoglobulin network (IgG or IgM) or C3 in the intercellular areas of the squamous epithelium [14].

As for the histopathological characteristics, in PV there are acantholytic cells (Tzanck cells) in the intraepithelial cleft - intraepithelial blisters. The connective tissue is missing the lining epithelium, and the basal cells of the epithelium are preserved and adhered to the submucosa. The immediate suprabasal acantholytic blister is characteristic of PV and the only layer of intact basal cells that forms the base of the blister is compared to a "row of headstones". In MMP, on the other hand, there is the total separation between epithelium and connective tissue - subepithelial and non-acantholytic blisters - and the presence of a mild chronic inflammatory infiltrate in the superficial submucosa [8].

The type of treatment of both diseases is based on the severity of the oral lesions [11]. MMP, when mild, can be managed with topical or systemic corticosteroids, such as dapsone or methotrexate [13]. If severe, it´s required systemic therapy with a loading dose (30mg to 50mg per day) for a week to eliminate the lesions, and then, later, try to keep the patient on low maintenance doses (5mg per day) to control the disease [14]. In PV, the initial treatment is more aggressive with systemic corticosteroid therapy in combination with immunosuppressants (azathioprine). This type of treatment is related to the reserved prognosis of the disease due to the risk of side effects [15]. In general, a common risk factor to both conditions are the long-term use of systemic corticosteroids that can lead to hyperglycemia, adrenal suppression, weight gain, osteoporosis, peptic ulcers, mood swings and infections [15]. In addition to corticosteroid therapy, some authors also report the off-label use of anti-TNF and anti-CD20 as promising in satisfactory results [13].

Therefore, it is noted that both bullous skin diseases require essential multidisciplinary management for a quick diagnosis and a better assessment of the extent and severity of the disease [12,13].

Conclusions

PV and MMP are similar diseases in both the pathophysiological and clinical aspects. Therefore, the differential diagnosis between them by histology analysis of the perilesional tissue is essential.

Microscopically, PV has an intraepidermal involvement, in which a separation of the epithelium is observed above the basement membrane, which remains connected to the connective tissue. On the other hand, in MMP there is a separation between the surface epithelium and the underlying connective tissue of the basement membrane. Consequently, the disease involvement is deeper. In this context, an early diagnosis is necessary, since the prognosis between diseases is different. While in MMP the usual evolution is benign with frequent and self-limited recurrences, in PV, if left untreated, it can progress to sepsis and death.

The strategy in both treatments is based on topical or systemic corticosteroid therapy, depending on the patient clinical condition and the severity of the disease. Thus, this study contributes to a review of literature to assist health professionals in the early diagnosis of these conditions, and also, favoring mainly the appropriate choice of therapy and, consequently, the improvement of their prognosis.

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