Pemphigus vulgaris

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Abstract

Pemphigus vulgaris is a chronic autoimmune mucocutaneous disease that initially manifests in the form of intraoral lesions, which spread to other mucous membranes and the skin. The etiology of pemphigus vulgaris is still unknown, although the disease has attracted considerable interest. The pemphigus group of disease is characterized by the production of autoantibodies against intercellular substances and is thus classified as autoimmune diseases. Most patients are initially misdiagnosed and improperly treated for months or even years. Dental professionals must be sufficiently familiar with the clinical manifestations of pemphigus vulgaris to ensure early diagnosis and treatment, since this in turn determines the prognosis and course of the disease. This article presents a case report with unknown etiology along with an overview of the disease.

Keywords: Autoimmune disease, bullae, mucous membrane, pemphigus vulgaris

Introduction

Pemphigus is a group of potentially life-threatening autoimmune diseases characterized by cutaneous and/or mucosal blistering. Pemphigus can be classified into six types: Pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, pemphigus foliaceus, paraneoplastic pemphigus, and IgA pemphigus. [1] Pemphigus vulgaris, which has multiple clinical variants, is an autoimmune blistering disorder of skin and mucous membranes, usually affecting the elderly, with a strong immunogenetic link and showing oral lesions as an initial manifestation in 50% of cases. [2] This life-threatening illness affects only 1–5 patients per million populations per year. The peak incidence of pemphigus vulgaris occurs between the fourth and sixth decades of life with a male-to-female ratio of 1:2. [3] Clinically, the oral lesions are characterized by blisters that rapidly rupture, resulting in painful erosions. While any area in the oral cavity can be involved, the soft palate, buccal mucosa, and lips are predominantly affected. [4] The diagnosis depends on biopsy confirmation of intraepithelial vesicle formation, acantholysis, and the presence of Tzanck cells. [3] This article discusses the case report of pemphigus vulgaris with unknown etiology along with overview of disease [Figures 1 and 2].

Case Report

A 45-year-old woman was referred to the Department of Oral Pathology and Microbiology with a month long history of painful oral ulcers. The patient reported that the lesions caused considerable discomfort and affected her normal oral function. Application of glycerin at the site of ulcer formation along with multivitamin supplements showed no improvement. Personal and family histories were uneventful.

On intraoral examination ulcers were noted on buccal mucosa, buccal vestibule, and attached gingivae, but no ulcers were noted on tongue. No skin lesions were seen [Figure 3]. Generalized gingivitis was seen along with generalized attrition of teeth and gingival recession. Orthopentamogram (OPG)

Figure 1: Extraoral photograph
Figure 2: Right buccal mucosa showing ulceration

Figure 3: Erythema on attached gingivae

Figure 4: OPG showing horizontal bone loss

Figure 5: Photomicrograph shows suprabasilar split and vesicle (×10)

Figure 6: Tzanck cells can be seen in intraepithelial vesicle (×10)

Figure 7: PAS positive basement membrane and suprabasal layer of cells (×10)
showed horizontal bone loss [Figure 4]. Incisional biopsy was performed which confirmed the diagnosis of pemphigus on H and E and PAS staining.

Histopathological examination
Histopathological examination showed acantholysis in the suprabasal region showing the hallmark of ‘suprabasilar split’. Intraepithelial vesicle also showed Tzanck cells. Connective tissue stroma showed loose collagenous stroma with dense inflammatory cells [Figure 5].

Discussion
In pemphigus vulgaris, lesions at first comprise small asymptomatic blisters, although these are very thin-walled and easily rupture giving rise to painful and hemorrhagic erosions. In most cases (70–90%), the first signs of disease appear on the oral mucosa. While lesions can be located anywhere within the oral cavity, they are most common found in areas subjected to frictional trauma, such as the cheek mucosa, tongue, palate, and lower lip. The ulcerations may affect other mucous membranes including the conjunctiva, nasal mucosa, pharynx, larynx, esophagus, and genital mucosa, as well as the skin where intact blisters are commonly seen.[5] Increased salivation and problems with chewing and swallowing are the major subjective complaints.[6]

The etiology of pemphigus vulgaris is still unknown although the disease has raised much concern. The pemphigus-group diseases are characterized by the production of autoantibodies against intercellular substances and, therefore, classified as autoimmune diseases. The presence of a viral infection may also be involved in autoantibody production.[7] In some cases, it may have a strong genetic basis as it has been reported more frequently in certain racial groups, for example, the Ashkenazi Jews and those of Mediterranean descent. Strong associations with certain HLA Class II alleles have been demonstrated in pemphigus vulgaris. Other initiating factors reported include certain foods (garlic), infections, neoplasms, and drugs. The drugs commonly implicated are those in the thiol group, in particular captopril, penicillamine and others such as rifampicin.

In pemphigus vulgaris, autoantibodies are produced against desmosomes (adhesion proteins), specially desmoglein 3 (Dsg 3). Another important component of desmosomes is termed desmoglein 1 (Dsg 1). The latter is the target of the autoantibody formation in pemphigus foliaceus that affects the cutaneous site only. Dsg 3 is predominantly expressed in oral epithelium while both Dsg 1 and Dsg 3 are expressed in the skin (although Dsg 1 is expressed more intensely in the superficial layer while Dsg 3 is found more abundantly in basal and suprabasal layers). Dsg 1 and Dsg 3 are components of desmosomal cadherin responsible for holding the cells of the epithelium together. The loss of the adhesive function among the spinous cells due to anti-Dsg 3 antibodies results in bullae formation immediately in the suprabasal region in pemphigus vulgaris.[8]

The principal dermal and mucosal changes involve the loss of coherence among layers of keratinocytes. This is manifested, in the early stages of disease, by the wrinkling of apparently healthy skin under pressure and subsequent exposure of a lesion, which is called a direct Nikolsky’s sign. The primary lesion is a thin-walled bulla, several centimeters in size, containing clear fluid, developing on both normal and erythematous skin. Under pressure it releases its content through the surrounding epidermis and further increases in size. This is an indirect Nikolsky’s sign. Healing is very slow, but no scars will remain. On the oral mucosa, bullae filled with fluid are also present but no inflammation develops. When the epithelial wall of the bulla ruptures and becomes detached, a flat painful lesion arises. Lesions are either uncovered or covered with whitish fibrin pellicles penetrated with leukocytes. In other cases, oral lesions show clinical and morphological features of aphthae.[9]

Acantholysis, the loss of coherence of epidermal cells and their subsequent detachment, is the main histological finding. Light microscopy shows that this process starts by the development of oedema among keratinocytes situated above the stratum basale. In the next stage, a suprabasal crevice develops that widens to give rise to a bulla. In cellular material scraped from the base and sides of a bulla, typical acantholytic cells can be found by cytological examination (Tzanck test). Immunofluorescence methods are used to detect IgG antibodies in the intercellular space of the epidermis or epithelium and circulating antibodies in serum [Figures 6 and 7].

Conclusion
Pemphigus vulgaris is a rare cause of chronic ulceration of the oral mucosa. The mouth may be the only site of involvement for a year or so and this may lead to delayed diagnosis and inappropriate treatment of a potentially fatal disorder.

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