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CASE REPORT

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Oral pemphigus vulgaris: dentists take-home message

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Abstract

Pemphigus is a life-threatening disease but timely recognition of oral lesions is critical to prevent serious cutaneous and fatal complications.

KEYWORDS

pemphigus vulgaris, oral pemphigus, Oral vesiculobullous lesions

1 | INTRODUCTION

Pemphigus is a rare group of life-threatening vesiculobullous diseases affecting the skin and mucous membrane.[1] Its global incidence rate was estimated around 0.2–3 per 100,000 person years and expressed typically during the 5th and 6th decade of life with a male-to-female ratio of 1:2.[2] The most common variant of this condition is pemphigus vulgaris (PV) accounting for 80% of the cases.[3] The term "*pemphix"* is derived from the Greek root word "blister or pustule" and "vulgaris" from the Latin word "common".[4] It is characterized by the development of flaccid intraepithelial bullae that easily rupture creating areas of painful erosions and ulcerations. In many patients, PV manifests first in the oral cavity followed by skin lesions.[5] Oral PV tends to involve areas exposed to mechanical irritation; hence, the buccal mucosa is considered the most common site followed by the palatal and lingual mucosa.[3] Given that the oral cavity may present as the first site of involvement, it is essential that dentists are able to recognize this condition and refer appropriately. Untreated generalized PV can be fatal; therefore, early diagnosis and treatment of oral lesions could ultimately improve the prognostic outcome. This is a case report of a 47-year-old male presenting with oral pemphigus, highlighting the importance of prompt diagnosis to reduce the morbidity of the condition.

2 | CASE HISTORY/EXAMINATION

A 47-year-old Asian male was admitted to the department of Oral and Maxillofacial Surgery for acute exacerbation of chronic oral ulceration resulting in considerable discomfort with swallowing and affecting his dietary intake. History revealed intraoral blister formation preceding painful ulcers which were aggravated on consuming any type of diet for the duration of 3 months. This well-built gentleman did not show any signs of cutaneous or other mucosal surfaces involvement. On intraoral examination, multiple areas of irregular superficial ulcerations and erosions presented bilaterally on the buccal mucosa along the occlusal plane, extending posteriorly to the retromolar trigon, faucial pillars, and the soft palate (Figure 1). These lesions were described as well-defined raw hemorrhagic erosions within an erythematous background and not attached to the underlying structures. Nikolsky's sign showed a positive reaction. Based on the

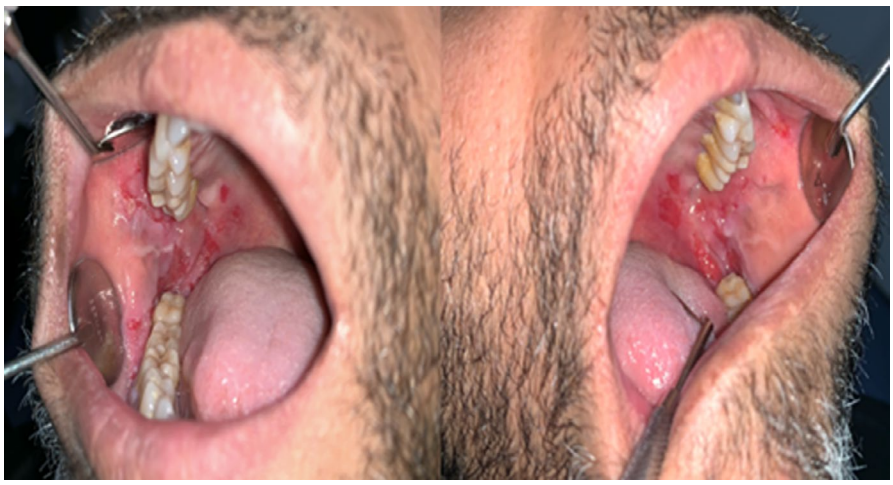

FIGURE 1 Intra-oral photograph demonstrating ulcerative lesions present on bilateral buccal mucosa along the line of occlusion

clinical presentations and examination, a provisional diagnosis of oral vesiculobullous lesions was suspected.

3 | DIFFERENTIAL DIAGNOSIS/ INVESTIGATION

Given the long list of differentials, patients with oral pemphigus could be misdiagnosed and incorrectly treated by dental professionals. The most frequent differential diagnosis includes recurrent aphthous ulceration, Behçet disease, erosive lichen planus, oral candidiasis, and erythema multiforme.[6] These conditions could be distinguished with careful history and clinical examination; for example, erythema multiforme is characterized by target-shaped skin lesions and involvement of the lips. In youngsters, oral pemphigus should be differentiated from acute herpetic gingivostomatitis, impetigo, linear IgA disease, and epidermolysis bullosa. Mucous membrane pemphigoid is a common differential for PV especially for patients over 60 years old, and it is usually presented by intermitted eruptions of tense subepithelial bullae affecting multiple mucosal sites with occasional skin involvement. The latter condition can be distinguished histologically by direct immunofluorescence studies demonstrating a linear deposition of IgG, IgA, and C3 along the basement membrane.[1] Incisional biopsies were performed on perilesional sites of the right buccal mucosa. These were sent for histopathological examination and direct immunofluorescence testing. Histological findings demonstrated suprabasilar acantholytic clefts with intercellular edema and loss of intercellular desmosomes in the lower epithelium. Occasional giant cells (Tzanck cells) and focal influx of neutrophils and eosinophils were evident in the epithelium. The papillary layer of the connective tissue was edematous with marked infiltration of chronic inflammatory cells in the subepithelial and perivascular regions (Figure 2).

Direct immunofluorescence demonstrated prominent deposition of IgG in the intercellular areas of the epithelium

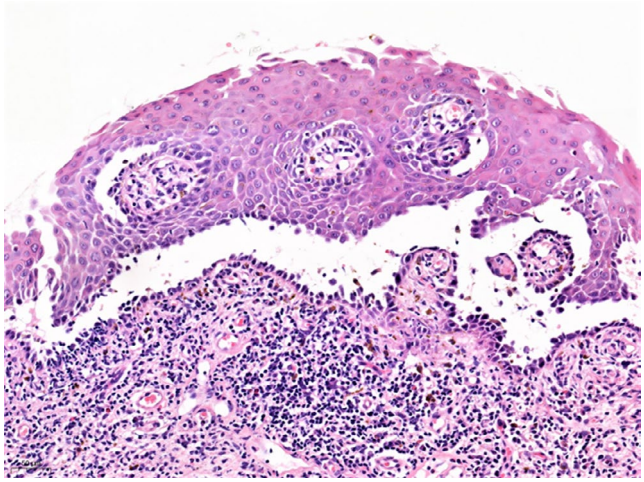

FIGURE 2 Biopsy of the buccal mucosa demonstrating acantholysis and supraepithelial clefting with occasional, freely floating Tzanck-like cells

(Figure 3). Based on the above findings, a final diagnosis of pemphigus vulgaris was confirmed.

4 | TREATMENT

The treatment was targeted to control the severity of disease and prevent relapses. This gentleman was commenced on systemic steroids (prednisolone) at an initial dose of 0.5 mg/kg/day (60 mg). Topical analgesic mouthwashes and ointments were also prescribed for symptomatic relief. On the first follow-up, the patient noted around 50% reduction of symptoms with partial resolution of the lesions and the surrounding mucosa. The periodontal health was monitored with the dentist including sessions of oral hygiene instructions, regular scaling, and root surface debridement. Following 3 months, further improvement was noted and the dose of prednisolone was tapered to 15 mg. After 6 months, this dose was gradually tapered down and the lesions were almost completely healed.

5 | OUTCOME AND FOLLOW-UP

Almost complete resolution of all intraoral lesions has taken place in this case with no evidence of skin lesions on regular 6-month follow-up and the patient was discharged after 1 year to the care of the general practitioner (Figure 4).

6 | DISCUSSION

Pemphigus is defined as a group of life-threatening, autoimmune blistering diseases of the skin and mucous membrane. It is characterized by acantholysis (loss of keratinocyte cell adhesion) and bullous formation. There are five major variants of this condition: PV, pemphigus foliaceus, pemphigus vegetans, paraneoplastic pemphigus, and drug-induced pemphigus. Pemphigus vulgaris is the most common type contributing to more than 80% of the cases.[3] This condition almost always affects the oral cavity, and it is the first sign of presentation in 70% of the cases before spreading to the skin and other mucosal surfaces.[6] Clinically, the lesions manifest as thin-walled blisters anywhere in the mouth, especially at areas subjected to frictional trauma, for example, buccal mucosa, tongue, palate, and lower lips. These vesicles easily rupture leaving areas of denuded and hemorrhagic erosions. Given the common presentation of intraoral ulcers, many patients could be initially misdiagnosed as gingivostomatitis, aphthous stomatitis, erythema multiforme, or erosive lichen planus and improperly managed for long periods.

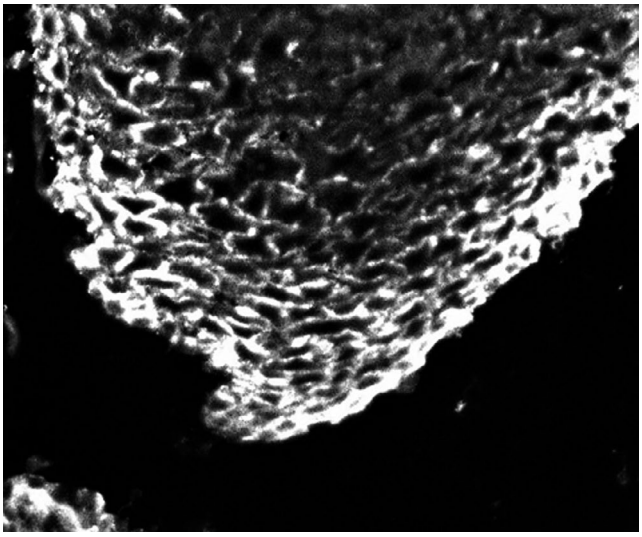

FIGURE 3 Direct immunofluorescence staining demonstrating an intercellular deposition of IgG and C3 producing a 'chicken wire' pattern

In the present case, oral lesions of the buccal mucosa and soft palate were the first manifestations of the disease, and the definitive diagnosis was based on the histological and immunofluorescence studies.

In PV, the underlying mechanism accountable for the development of intraepithelial bullae is the binding of autoantibodies (IgG) to desmosomes (adhesion proteins), especially desmoglein 3 (Dgs3). These antigen-antibody complexes deactivate the adhesion function of Dgs3 resulting in separation of suprabasilar cells (acantholysis) and blister formation. Antibodies targeting Dgs3 are deposited at the periphery of the epithelial cells giving the appearance of "chicken wire" when viewed with direct immunofluorescence. Furthermore, circulating IgG against Dgs3 can be detected in the serum using indirect immunofluorescence assay.[7]

A key aspect of the patient management is early diagnosis to allow low doses of medications to be administered for shorter periods to control the disease. Institution of prompt treatment plan could inhibit progression to other mucosal and cutaneous sites and prevent fatal complications. Without appropriate management, PV could be fatal due to loss of the epidermal barrier leading to dehydration and secondary bacterial infection.[8]

Generally, PV is managed with topical and systemic steroids. Guidelines set by the British Association of Dermatologists (BAD) recommend treatment of PV in 2 phases: induction phase to control the disease and maintenance phase for consolidation and treatment tapering.[9] Local treatment including ointments and mouthwashes can be used

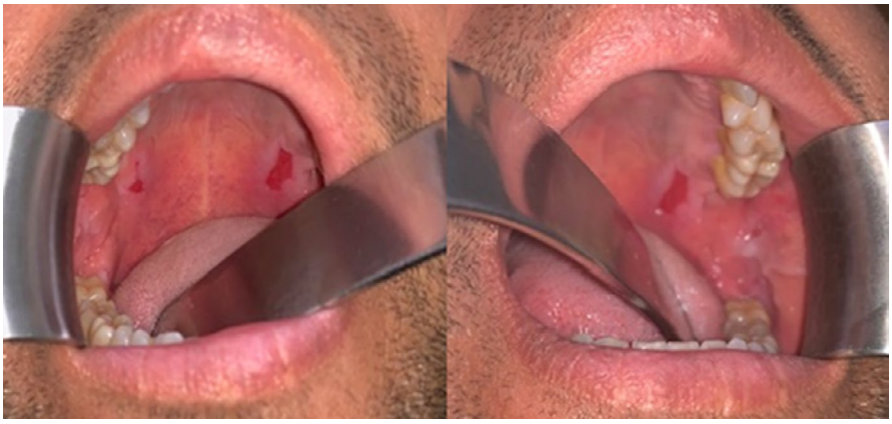

FIGURE 4 Intra-oral photograph demonstrating a reduction in the size of the lesions with partial resolution of the surrounding erythema and inflammation

alone or in conjunction for managing the symptoms particularly in patients with low titer of circulating autoantibodies, for example, 0.1% triamcinolone acetonide in orabase, 0.05% clobetasol propionate, or 0.05% halobetasol. In refractory lesions, intralesional injection of triamcinolone acetonide (20μg/L) or paramethasone can be administered every 7–15 days; however, if symptoms do not ameliorate, the treatment should be withdrawn.[3,6]

In patients with extensive oral ulceration or cutaneous involvement, systemic corticosteroids are initiated immediately. Prednisolone dose of 0.5–1 mg/kg is recommended which is gradually reduced to the lowest therapeutic dose to minimize its side effects. Moreover, steroid sparing drugs such as cyclophosphamide and azathioprine are added to the regimen if long-term steroids are needed to control the complications of steroid therapy.[9]

As a complement to local or systemic treatments, general dental practitioners could implement various treatments to enhance the patients' well-being. This includes maintaining strict oral hygiene, periodontal treatment, dietary advice, close inspection of prosthetic restorations, and application of anti-candida medications for patients on long-term steroids.[3,10]

6.1 | Take home messages

- Pemphigus vulgaris is a serious and potentially life-threatening autoimmune disorder affecting the skin and mucous membrane.
- The majority of cases present with oral lesions as the first sign of the disease.
- Dental professionals must be sufficiently familiar with the clinical manifestation of this condition to ensure early diagnosis and treatment which in turn would determine the prognosis of the disease.
- Accurate clinical examination together with other diagnostic modalities such as routine biopsy and immunofluorescence studies is essential in differentiating pemphigus vulgaris from other vesiculobullous lesions.

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CONFLICTS OF INTERESTS

None declared.

AUTHOR CONTRIBUTIONS

Aya Al-Harbawee[1] involved in investigation, drafting manuscript, and revision; Karim Kassam[2], Ankur Nilesh Patel[2], Hannah Cottom[2], and Mr Leo Cheng[2] involved in investigation and revision.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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