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Oral Pemphigus Vulgaris: A Case Report and Literature Review

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Abstract Pemphigus vulgaris (PV) is a rare chronic autoimmune mucocutaneous blistering disease characterized by the production of autoantibodies targeting desmogleins, key components of intercellular adhesion of keratinocytes. This process leads to the loss of intercellular adhesion, culminating in the development of intraepithelial bullae and erosions. PV manifest as intraoral lesions that subsequently spread to other mucous membranes and the skin. While the exact etiology remains elusive, several triggering factors have been identified. Oral lesions of PV are often misdiagnosed and mistreated, emphasizing the need for early recognition by dental professionals. This case report aims to contribute to the existing literature by illustrating representative clinical features of PV, diagnostic approach, and therapeutic challenges associated with our case.

Keywords: *pemphigus vulgaris, oral ulceration, autoantibodies, autoimmune*

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1. Introduction

Pemphigus Vulgaris (PV) is a rare autoimmune disorder characterized by the formation of blistering lesions on the skin and mucous membranes [1]. This condition arises from the production of autoantibodies targeting desmogleins, which are essential components of intercellular keratinocytes. The resultant loss of cell adhesion leads to the formation of blisters and erosions, causing significant morbidity for affected individuals. Despite being a relatively uncommon disease, PV poses substantial challenges in terms of diagnosis, management, and the impact it has on patients' quality of life. Given the clinical overlap with other oral pathologies, PV should be considered in the differential diagnoses of vesiculobullous lesions [2,3]. A comprehensive understanding of diagnostic and therapeutic approaches is crucial for effective management. This case report and literature review aims to provide a comprehensive update of PV, highlighting its etiology, clinical manifestations, diagnostic approaches, current treatment modalities, and potential avenues for future research.

2. Case Report

A 61-year-old male patient sought consultation at the Oral Medicine clinic with a notable presentation of oral and skin manifestations of a suspected autoimmune disorder. The patient was presented with extensive oral ulcerations involving the buccal mucosa bilaterally extending to the soft palate shown in Figure 1 and Figure 2.

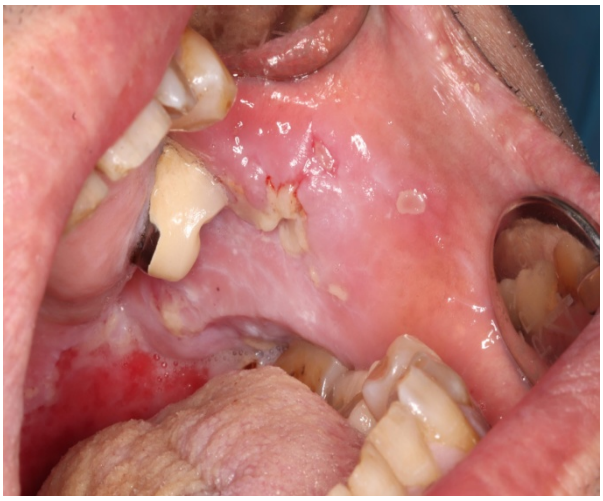

Figure 1. (Left buccal mucosa and soft palate) Extensive oral ulcerations involving the left buccal mucosa extending to the soft palate

The lower lip mucosa shows widespread ulcerations with fragile epithelium that peeled off easily on examination (Figure 3 and Figure 4). The oral lesions presented were accompanied by pain and difficulties with speech, eating and swallowing. The left thumb presented with an inflamed lump with clinical signs of infection (Figure 5). The diagnostic approach for this case involved a biopsy specimen from the lower lip mucosa morphologically demonstrating an

intramucosal blister. The specimens showed notable intercellular edema with loss of intercellular attachments in the basal layer (Figure 6). Suprabasal cells separate from the basal cells to form clefts and blisters. Blister cells contain occasional acantholytic cells with notable edema and perivascular polymorphic inflammatory infiltrates including plasmalymphocytic cells with neutrophils and eosinophils (Figure 7). Immunofluorescence studies supported the histopathological diagnosis of PV with an ELISA score of 60.83 for DsG1 and 172.56 for DsG3.

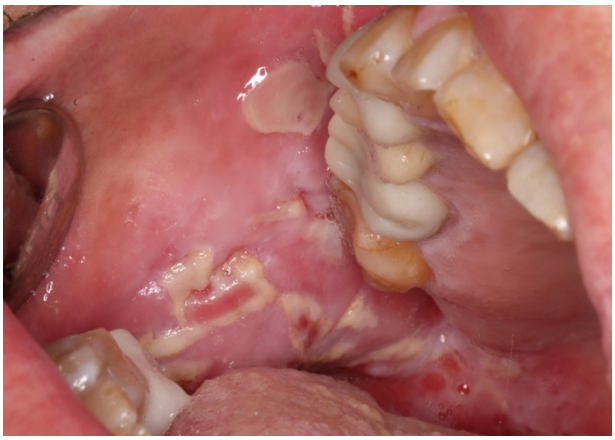

Figure 2. (Right buccal mucosa and soft palate) Extensive oral ulcerations involving the right buccal mucosa extending to the soft palate

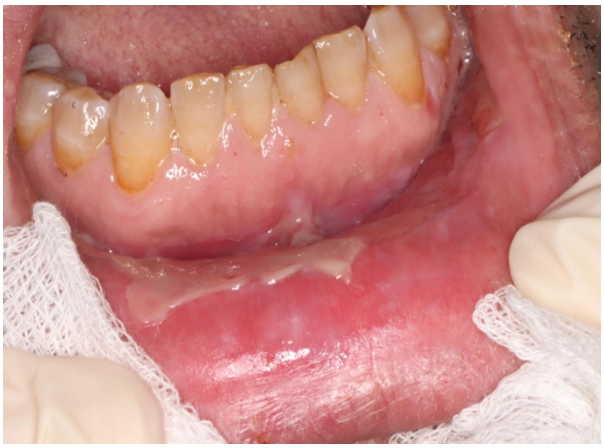

Figure 3. (Lower lip mucosa) Epithelial sloughing

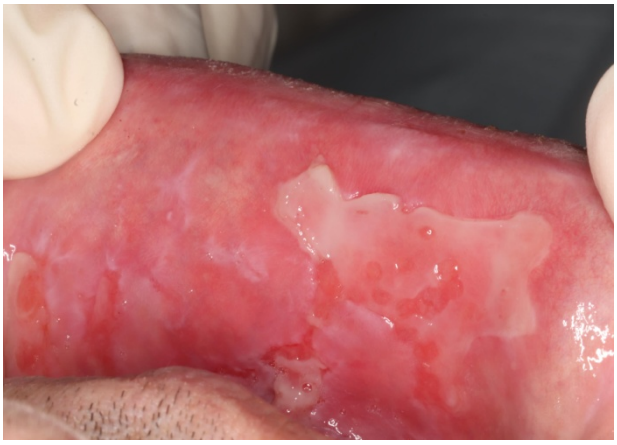

Figure 4. (Lower anterior vestibule) Extensive ulceration, erythema and epithelial sloughing involving the lower lip mucosa and vestibule

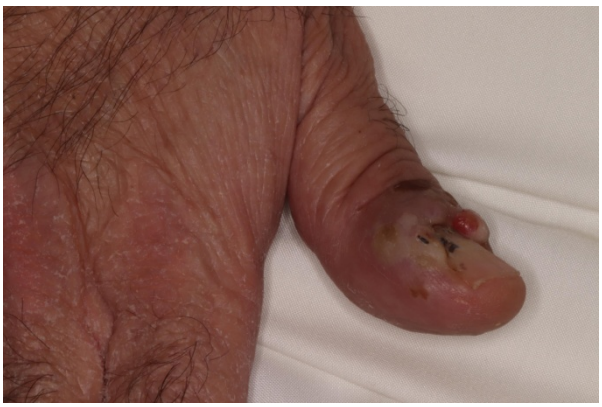

Figure 5. (Left thumb) Inflammatory lump and clinical infection

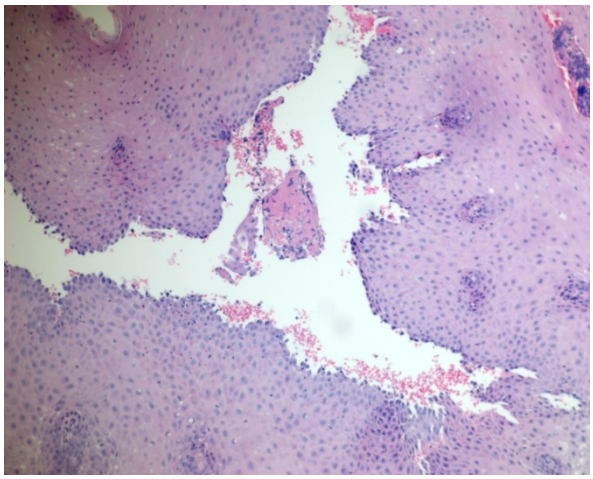

Figure 6. (x20 magnification) Photomicrograph of biopsy specimen showing intercellular edema with loss of intercellular attachments from the basal cells to form clefts and blisters

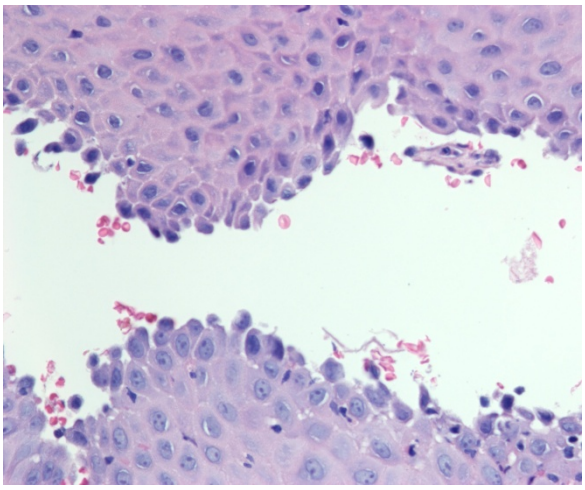

Figure 7. (x40 magnification) Photomicrograph of lower lip mucosa showing loss of intercellular attachments in the basal layer

3. Discussion

PV is a life-threatening mucocutaneous disorder affecting both the skin and mucous membranes [1,2]. It clinically presents as widespread, deep vesicles and ulcerations at any mucosal site. Extensive mucosal erosions with ruptured blistering are often seen. Oral

manifestations of PV usually precede involvement at other sites [4,5]. Cutaneous or dermal manifestations are less common, with oral lesions frequently being the primary clinical presentation of PV [5]. The global prevalence of PV is approximately 2.83% per million population per year [6]. However, the incidence varies based on various factors especially geographic location and ethnic populations. In Europe, literature reports suggest an incidence ranging from 0.76 to 16 per million population per year [5,7]. In India, the prevalence is lower than the global average, ranging from 0.09% to 1.8% [5,7]. PV is associated with a prolonged clinical course, significant morbidity, and mortality [8]. Left untreated, the mortality rate reaches 50% after two years and approaches 100% at the end of five years, with causes of mortality including extensive skin involvement, septicemia, bronchopneumonia, electrolyte imbalance, and secondary systemic infections [8,9].

3.1. Pathogenesis and Immunological Mechanisms

It is well-established that PV is primarily mediated by autoantibodies targeting desmoglein 3 (Dsg3) and, to a lesser extent, desmoglein 1 (Dsg1) [2], which are cell adhesion molecules critical for maintaining epithelial integrity. The pathogenicity of these autoantibodies, their production, and the complex interplay with genetic (HLA II Alleles) and environmental factors are areas of ongoing research. Understanding the precise mechanisms by which autoantibodies disrupt desmosomal adhesion and induce blister formation is crucial. This knowledge can potentially lead to the development of targeted therapies that specifically inhibit pathogenic autoantibody production or interfere with downstream signaling pathways [10,11,12,13,14].

3.2. Clinical Manifestations and Histopathology

PV predominantly manifests with painful, flaccid blisters on the skin and mucous membranes. The lesions are often fragile and prone to rupture, contributing to erosions and ulcerations. Direct immunofluorescence microscopy of perilesional biopsy is a key diagnostic tool, demonstrating the presence of IgG and C3 deposits at the epidermal cell surface [2,13,15].

3.3. Clinical Management and Therapeutic Strategies

Our report underscores the importance of multidisciplinary collaboration in managing PV. Early diagnosis remains paramount, as delayed intervention can lead to severe complications. A definitive diagnosis relies on clinical features, histopathologic examination, and immunological tests, facilitating appropriate and timely therapeutic intervention [16]. Numerous reported cases of pemphigus vulgaris with both oral and cutaneous manifestations are compiled in Table 1.

High-dose corticosteroids [17], often in combination with immunosuppressive agents like azathioprine or mycophenolate mofetil, have been the mainstay of treatment for many years. Emerging therapies, such as rituximab [5], an anti-CD20, plasmapheresis and intravenous immunoglobulins [18] offer promising alternatives and are increasingly used in cases of refractory or intolerant disease.

Table 1. Summary of cases of pemphigus vulgaris with both oral and cutaneous manifestations

Author(s) and year	Patient's age and gender	Oral manifestation	Cutaneous manifestation
Vijay P et al., 2016 [21]	40 years old Female	Ulcerative and eroded lesions located on the tongue and buccal mucosa present intermittently for one year	Simultaneous occurrence of reddish-brown, eroded, and ulcerated lesions on the arms and trunk
Ahankare P. et. al., 2019 [5]	44 years old Male	Fifteen days history of diffuse erythematous lesions accompanied with ulceration on the hard palate extending from maxillary tuberosity to retromolar area and soft palate of the right side accompanied with difficulty in swallowing	Raw eroded and crusted areas with central erythematous zone were present on the chest and the back region
Ramineni HB et al., 2015 [22]	24 years old Female	One month history of numerous oral ulcers that did not respond to medications	Generalized widespread fluid filled vesicles proceeded oral lesions
Vasudevan V et al., 2008 [23]	49 years old Male	Multiple ulcers in the right and left of buccal mucosa as well as the floor of the mouth	Multiple ulcers located on the scalp, back, trunk, and extremities
Temilola D et al., 2018 [15]	54 years old Female	Nine months duration of painful oral ulcers proceeded by vesicles involving hard palate, soft palate, buccal mucosa, and gingiva	Ocular complications occurred few weeks after oral symptoms, followed by the development of small red lesions on the outer surfaces of both thighs
Aggarwal A and Jain S, 2019 [24]	53 years old Female	Linear erosion located on buccal mucosa, labial mucosa, and gingiva	Widespread ulcerative lesions on the anterior of the neck below the chin region
Rath SK et al., 2012 [25]	36 years old Female	Three months duration of oral and gingival ulcers associated with burning sensations	Three weeks duration of minor skin eruptions on the face, back, and extremities
Dağistan S. et. al., 2008 [26]	35 years old Female	Painful and uncomfortable ulcers located on the buccal and palatal mucosa as well as the ventral aspect of the tongue	None

The modalities discussed above have shown significant improvement and remission in disease symptoms. Furthermore, it is important to note that corticosteroids remain the primary treatment for Pemphigus Vulgaris

(PV). Recent research has largely focused on identifying the most effective steroid-sparing agent, though the evidence remains inconclusive. Azathioprine and mycophenolate mofetil (MMF) are considered first-line steroid-sparing treatments.

In cases of recalcitrant PV, where other treatments are ineffective, Rituximab has proven to be extremely effective. Systemic treatment for PV has been successful in reducing the incidence of adverse events and morbidity, showing a marked improvement over past treatment [19]. Consequently, the long-term efficacy and safety profiles of all the treatment modalities mentioned warrant further investigation [20].

Following lesion remission, a maintenance regimen becomes essential to control the disease and mitigate drug-related side effects, with the duration of medical treatment contingent on the extent of lesion involvement [5]. Thus, there is an emergent need for personalized treatment approaches, as the severity of PV can vary widely among individuals. Tailoring therapeutic regimens to a patient's disease activity, comorbidities, and preferences is crucial to optimize outcomes and minimize side effects.

3.4. Quality of Life and Psychological Impact

Beyond the physical symptoms, PV has a significant impact on patients' quality of life [27]. The chronic nature of the disease [28], the often-extensive blistering, and the side effects of immunosuppressive medications [29] can lead to substantial psychological distress [30]. Addressing these aspects of patient care is integral to comprehensive management [31]. Supportive care, patient education, and psychosocial interventions play vital roles in improving the well-being of PV patients [33]. Recognizing the psychosocial burden and providing access to mental health resources should be incorporated into the treatment paradigm [33].

3.5. Future Directions

Ongoing research efforts are directed towards understanding the molecular mechanisms underlying PV, identifying novel therapeutic targets, and developing more targeted treatment approaches with fewer side effects. Additionally, advancements in precision medicine may pave the way for personalized treatment strategies based on individual patient profiles.

4. Conclusion

Pemphigus vulgaris represents a complex autoimmune disorder with significant implications for affected individuals. The rarity of the disease and its multifaceted nature underscore the importance of continued research to enhance our understanding of its pathogenesis and improve diagnostic and therapeutic strategies. Collaborative efforts between clinicians and researchers are crucial to addressing the challenges posed by PV and ultimately improving the quality of life for patients diagnosed with this autoimmune blistering disorder.

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