

# Oral pemphigus vulgaris

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## Abstract

Pemphigus is a group of potentially life-threatening autoimmune mucocutaneous diseases characterized by epithelial blistering affecting cutaneous and/ or mucosal surfaces. Pemphigus affects 0.1-0.5 patients per 100,000 population per year. Oral lesions of pemphigus are seen in up to 18% of patients at dermatology out-patient clinics, but despite the frequency of oral involvement, and novel therapeutic approaches, there are surprisingly few recent studies of either the oral manifestations of pemphigus or their management, and delays in diagnosis are still common. Most patients are initially misdiagnosed and improperly treated for many 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. Pemphigus has been reviewed in the oral literature in the past decade<sup>4</sup>, but several advances in the understanding of the etiopathogenesis, pemphigus variants, and management warrant an update. Here, we report a case of pemphigus vulgaris that was misdiagnosed in its earliest stage. Oral ulceration may arise from a variety of causes. This case illustrates that, although rare, pemphigus vulgaris may need to be included in differential diagnosis.

**Key words:** Chronic ulcerations, Immunofluorescence, Oral pemphigus, Systemic corticosteroids

## INTRODUCTION

Pemphigus is a group of potentially life-threatening diseases characterized by cutaneous and mucosal blistering<sup>1</sup>. There is a fairly strong genetic background to pemphigus with linkage to HLA class II alleles. Pemphigus vulgaris (PV), the most common and important variant, is an autoimmune blistering disease characterized by circulating pathogenic IgG antibodies against desmoglein 3 (Dsg3), about half the patients also having desmoglein1(Dsg1) auto-antibodies<sup>2</sup>. Oral lesions are initially vesiculobullous but readily rupture, new bullae developing as the older ones rupture and ulcerate. Biopsy of perilesional tissue, with histological and immunostaining examinations, is essential to the diagnosis. Serum autoantibodies to either Dsg1 or Dsg3 are best detected by both normal human skin and mucosa or by enzyme-linked immunosorbent assay (ELISA)<sup>3,4</sup>. Before the introduction of corticosteroids, pemphigus vulgaris was typically fatal mainly from dehydration or secondary systemic infections<sup>5</sup>. Current treatment is mainly involving the use of systemic corticosteroids with adjuvant drugs like mycophenolate

mofetil, azathioprine, Intravenous immunoglobulins (IVIG) rituximab, cyclophosphamide etc.

## CASE-REPORT

A 40 year old female patient complained of burning sensation in the mouth since two months. There was history of noticing it first over the right side of mouth which gradually increased in severity and spread to other parts of the mouth. Patient gave history of noticing areas of slightly raised loosely held mucosa, which peeled off in a day to give rise to large red ulcerated areas associated with pain and burning sensation. The ulcers were gradually increasing in size. Burning sensation increased in intensity while eating and swallowing with associated history of bleeding which stopped spontaneously on its own. There was no history of pus or watery discharge. There was no history of other associated symptoms such as loss of appetite, fatigue or loss of weight. No such lesions were noted anywhere else in the body.

Patients past medical, dental, family and personal histories were non-contributory. General physical examination revealed that she was moderately built and nourished with all her vital signs within normal limits. On local examination, soft tissue revealed diffuse large areas of superficial ulcerations extending from the region of premolars up to the retromolar area. The ulcers were

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shallow with sloping borders and surrounding tissue tags. The floor of the ulcers were irregularly covered by food debris and psuedomembrane. Similar ulcerated and erythematous areas were noted over the upper and lower, anterior and posterior vestibular regions, dorsal and ventral surfaces of tongue, soft palate, floor of the mouth and oro-pharynx (Figure 1, 2). Gingiva showed marginal erythema with superficial ulcerations over attached gingiva. On palpation of soft tissue all the findings regarding number, size, shape, extent and surface were confirmed. Bleeding was noted on palpation from the ulcerated areas. The submandibular lymph nodes were palpable and tender bilaterally. Nikolsky's sign was positive. There was no hepatosplenomegaly.

A provisional diagnosis of pemphigus vulgaris was made. The results of blood tests and hepatic and lipid screening tests were normal. List of differential diagnosis include pemphigoid, linear IgA disease, bullous lichen planus and paraneoplastic pemphigus. Incisional biopsy of the intact bulla showed suprabasal bulla containing acantholytic cells and few inflammatory cells. Adjacent epidermis showed supra basilar acanthosis. A final diagnosis of oral pemphigus vulgaris was made and patient was prescribed systemic corticosteroids with betamethasone and Benzzydamine hydrochloride mouthwashes. The patient was also put through periodontal sessions, which include oral hygiene instructions and scaling/root planning. There was marked improvement in two weeks with most of the mucosal lesions were healing and no new lesion appeared (Figure 3, 4, 5). Patient was lost for follow up after three weeks.



**Figure 1:** Ulcerations over the palatal regions



**Figure 2:** Ulcerations noted in tongue and floor of the mouth



**Figure 3:** Post treatment photograph after two weeks of steroid therapy



**Figure 4:** Post treatment photograph after two weeks of steroid therapy



**Figure 5:** Post treatment photograph after two weeks of steroid therapy

## DISCUSSION

Pemphigus is an autoimmune mucocutaneous disease characterized by intraepithelial blister formation. This results from a breakdown or loss of intercellular adhesion, thus producing epithelial cell separation known as acantholysis. Widespread ulceration following rupture of the blisters leads to painful debilitation, fluid loss, and electrolyte imbalance<sup>5,6</sup>. Before the use of corticosteroids, death was not an uncommon outcome for patients with pemphigus vulgaris. Four types of pemphigus are recognized: pemphigus vulgaris, pemphigus foliaceus, paraneoplastic pemphigus and drug induced reactions. These differ in the level of intraepithelial involvement in the disease; pemphigus vulgaris and pemphigus vegetans affect the whole epithelium, and pemphigus foliaceus and pemphigus erythematosus affect the upper prickle cell layer/spinous layer. Only pemphigus vulgaris and pemphigus vegetans involve the oral mucosa. Pemphigus vegetans is very rare and is generally considered a variant of pemphigus vulgaris<sup>6</sup>. All forms of the disease retain distinctive presentations both clinically and microscopically but share a common autoimmune etiology. Evident are circulating autoantibodies of the IgG type that are reactive against components of epithelial desmosome-tonofilament complexes. The specific protein target has been identified as desmoglein 3, one of several proteins in the desmosomal cadherin family. The circulating autoantibodies are responsible for the earliest morphologic event: the dissolution or disruption of intercellular junctions and loss of cell-to-cell adhesion.

In pemphigus vulgaris, lesions at first comprise small, asymptomatic blisters. These are very thin-walled and

easily rupture giving rise to painful and hemorrhagic erosions. In most cases, the first signs of disease appear on the oral mucosa. The lesions can occur anywhere within the oral cavity, but mostly found in the areas subjected to frictional trauma, such as the cheek mucosa, tongue, palate, and lower lip. The ulcerations may affect other mucous membranes such as conjunctiva, nasal mucosa, pharynx and genital mucosa. In the present case, the oral lesions were seen mainly in the palate, cheek mucosa and labial vestibule. The diagnosis is generally based on the oral manifestations, while confirmation is done by the histological findings, which shows the presence of intraepithelial blisters, acantholysis, and Tzanck cells<sup>7,8</sup>.

Direct immunofluorescence of the tissue specimens reveals IgG or IgM and complement fragments in the intercellular space<sup>2</sup>. In our case, a biopsy of the intra-oral lesions and smear were obtained. The sections were stained with hematoxylin-eosin, and the principal histological characteristics were evaluated. In 2014 Nguyen et al reported a case of pemphigus on the lateral border of the tongue and showed the importance of local therapy and its potential to induce long-term remission<sup>8</sup>. According to study on 155 patients on immunosuppressive therapy 94 patients developed secondary infections<sup>9</sup>. Some studies have showed that low-level laser therapy can provide immediate and significant analgesia in patients with pemphigus vulgaris<sup>10</sup>. Systemic corticosteroids are the most useful drugs in the treatment of pemphigus vulgaris and continue to be the mainstay of therapy for this disease. Their use rapidly induces remission in the majority of patients but the clinician must weigh the benefits against the hazard from side effects of the drug<sup>9,10</sup>.

## ORAL CORTICOSTEROIDS

The oral route of administration of corticosteroids is the one most preferred, and prednisone is the medication most frequently used. The initial dose of corticosteroid is usually 0.75 to 1 mg/kg/day, this dose may be increased by 25- 50% every 5-7 days if found insufficient in controlling the disease. The disease may be tentatively classified based on the severity of the lesion as mild, moderate and severe and can be treated at different levels based on this.

Bystryn regimen recommends the following regime: Mild disease is treated with a trial of topical corticosteroids, followed by low-dose (20 mg/day) oral steroids. About 50% of the patients receiving this treatment regimen are ultimately able to discontinue all therapy. Moderately severe pemphigus is managed with 60 – 80 mg/day of

prednisone<sup>11</sup>. For severe disease, the Bystryn regimen recommends 80 mg of prednisone administered daily. If necessary, the dose is increased by 50% every four to seven days until control is achieved, as demonstrated by the absence of new lesions and the disappearance of itching. This dose is maintained until there is 80 – 90% clearance of lesions. Reduction of the dose by 50% is recommended at two-week intervals<sup>10,11</sup>. Various other treatment options include tacrolimus, mycophenolate mofetil, cyclosporin, dapsone and plasmapheresis for recalcitrant cases. Treatment with these drugs require close monitoring of patients for various side effects.

## CONCLUSION

Pemphigus vulgaris is a rare chronic autoimmune cutaneous–mucosal disease that is often diagnosed late, even when oral lesions occur. If not treated promptly, the disease has a high morbidity rate, and it may be fatal in 5% to 10% of cases. The diagnosis is confirmed through pathological examination and direct immunofluorescence testing in the healthy perilesional mucosa. The therapeutic regimen, based on corticosteroid therapy as well as adjuvant treatments, helps to decrease painful symptoms. Current research is directed to finding substitutes for general corticosteroid therapy so as to lower the rates of iatrogenic morbidity.

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