

# Intergrated Clinical Approach on an Atypical Case of Pemphigus Vulgaris – A Dental Professional’s Role.

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## Abstract

Pemphigus is a group of potentially life threatening chronic mucocutaneous autoimmune blistering disease of the stratified squamous epithelia. It includes Pemphigus vulgaris, Pemphigus foliaceus, Paraneoplastic pemphigus and variants like Pemphigus vegetans, Pemphigus erythematosus, Fogo selvagem, Herpetiform pemphigus and Drug-induced pemphigus [1]. The oral lesions are the first manifestation of the disease and resist resolving even with therapy. Precise diagnosis and prompt treatment by the dental professionals will ensure good prognosis of the disease at its earliest stages as undiagnosed cases lead to death due to complications like pneumonia, septic shock and dermatological infections. We report here a disparate case of Pemphigus vulgaris, refractory to initial treatment and treated successfully by pulse therapy with a multidisciplinary approach of Department of Dermatology and Department of Oral Medicine by integrating knowledge and comprehensive healthcare, improving the quality of life of patient.

**Keywords :** Pemphigus, Corticosteroids, Pulse therapy

## Introduction

Pemphigus vulgaris is the most common form of Pemphigus derived from the Greek word ‘*pemphix*’ originally given by Wichman in 1971 which means blister or bubble [2], and Latin word ‘*vulgaris*’ which means common [3]. It is a blistering disease with formation of bullae and vesicles in the skin and the mucous membrane. The average incidence of 2-10 cases per one million inhabitants in some areas of the world and a prevalence of 0.1-0.7 per one hundred thousand inhabitants, preferentially affects women, and most of the patients are 50–60 years of age at disease onset [4].

## Case Report

A 45 year old female patient reported to the department of Oral Medicine and Radiology with a chief complaint of severe oral ulceration associated with burning sensation for a period of two weeks. History revealed that the patient developed difficulty in consuming hot and spicy food which increased in severity. The patient revealed history of irritation and redness in the eyes and nose for past one week. The past medical history revealed that

she was diagnosed with rheumatoid arthritis and was under Siddha medication for two months.

On general examination the patient was moderately built and moderately nourished. The extra oral examination revealed erythema in bilateral ocular mucosa and nasal mucosal membrane with no initial skin lesions [Fig:1a,b,c,d]. The intra oral examination reveals extensive erosions and ulcerations in bilateral buccal mucosa, upper lip, lower lip, dorsal and ventral surface of tongue, floor of the mouth, hard palate and soft palate with mild bleeding in the areas surrounding the erosions in the lips, tongue and bilateral buccal mucosa [Fig:2a,b,c,d]. The ulcers were multiple with irregular margins, freely movable base, without induration and lymph nodes appeared normal.

The clinical presentation and history of sudden onset of the oral lesions with no history or clinical evidence of vesicle or bullae led to the provisional diagnosis of Erythema multiforme and differential diagnosis of Pemphigus vulgaris, Pemphigus vegetans and Cicatricial pemphigoid. The biochemical and haematological investigations were within normal limits. The patient was counselled regarding the nature and progression of the disease, dietary habits and treatment regimen. Initially topical anaesthetic gel (2% Lignocaine) thrice daily, medium potency topical corticosteroid gel (0.1% Triamcinolone acetonide) thrice daily, systemic corticosteroid (Prednisolone 30mg in three divided doses) and nutritional supplements was given for three days. The patient was reviewed on the third day and seventh day

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Figure 1: Clinical presentation of the case during first visit (extra oral)

- a) Mild erythema in the right lower ocular mucosal membrane
- b) Left Ocular mucosa appears normal.
- c) Mild erythema in right nasal mucosa.
- d) Mild erythema in left nasal mucosa.



Figure 3: Clinical presentation of the case during seventh day

- a) Reduction of ulceration in upper and lower lip, absence of hemorrhage in tongue.
- b) Reduction of hemorrhage from the ventral surface of the tongue.
- c) Reduction of Ulceration in the left buccal mucosa.
- d) Reduction of Ulceration in the right buccal mucosa.

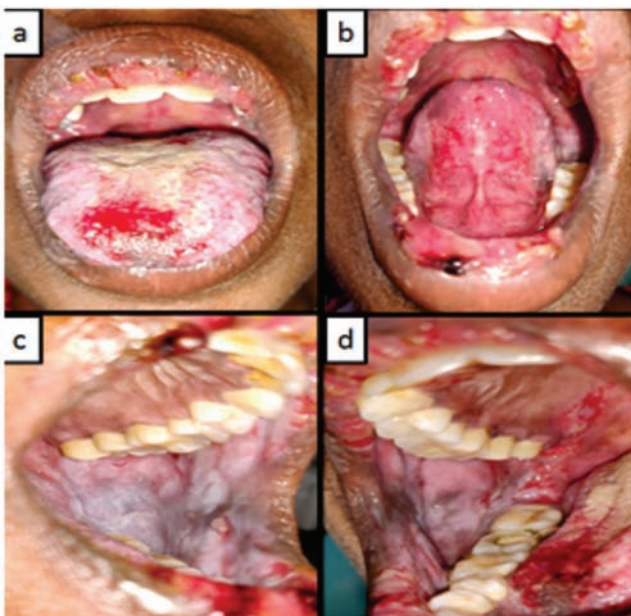


Figure 2: Clinical presentation of the case during first visit

- a) Erosion and ulceration in upper and lower lip, hemorrhage in the tongue.
- b) Hemorrhage in ventral surface of the tongue.
- c) Ulceration in the left buccal mucosa.
- d) Ulceration in the right buccal mucosa.



Figure 4 : Photomicrograph of H&E stained histological section under 4X magnification showing acantholysis and suprabasilar split

[Fig: 3a, b, c, d], the symptoms were reduced and signs of healing present and hence the patient was advised to continue the regimen and the dose was tapered (Prednisolone 20 mg in two divided doses). However exacerbation of symptoms was present as the steroid dosage was tapered and the incisinal oral mucosal

biopsy was made from the left buccal mucosa and the histopathological section revealed stratified squamous epithelium, foci showing acantholysis and suprabasal bullae with a few desquamated cells and basal layer in tombstone arrangement, underlying mucosa shows congested blood vessels correlating with Pemphigus Vulgaris [Fig: 4a, b, c, d]. Treatment regimen was altered and systemic steroid dosage was up scaled to 30 mg everyday (three divided doses) and high potency topical steroid 0.05% Clobetasol Propionate gel (thrice daily) was advised. The oral lesions successfully responded to the high potency topical Corticosteroid, the patient started developing papular, pruritic lesions in the scalp, forehead and neck and exhibited positive Nikolskysign which was not positive initially. The skin lesions were refractory to the systemic steroid therapy and hence the case was discussed in detail with the department of dermatology for the management of skin lesions through a multidisciplinary approach. Pulse therapy was initiated and systemic Prednisolone and Dexamethasone (cumulative dose 513.5 mg – Dexamethasone for 6 consecutive days once daily and Prednisolone for 4 consecutive days thrice daily in split doses) was given for three consecutive days. The skin lesions showed signs of healing and the patient was continued with the pulse therapy. The skin lesions and oral mucosal lesions were completely resolved by the end of first week of pulse therapy and the patient is under constant follow up [Fig: 5a, b, c, d].

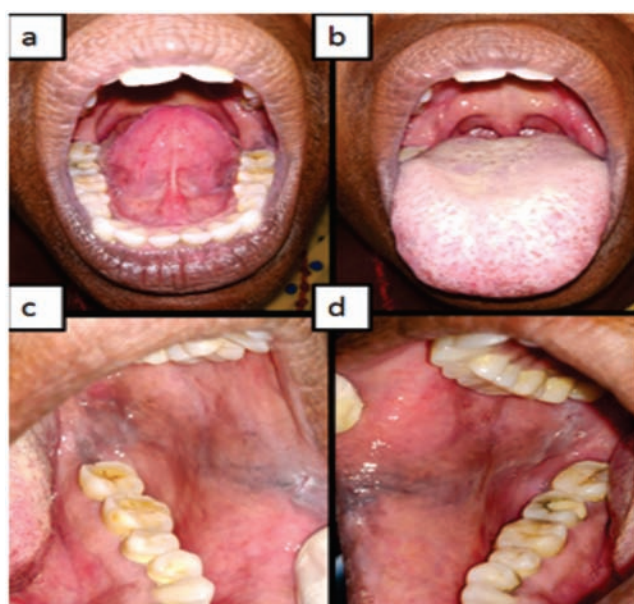


Figure 5: Clinical presentation of the case during the end of first week of pulse therapy

- Floor of the mouth appears normal and healed.
- Tongue appears normal and healed.
- Left buccal mucosa appears normal and healed.
- Right buccal mucosa appears normal and healed..

## Discussion

Pemphigus vulgaris is an autoimmune blistering disease with Immunoglobulin G autoantibodies produced against the epidermal cell surface calcium binding transmembrane glycoproteins desmoglein 3 and desmoglein 1 which are the components of cadherin cell adhesion molecule family located in cluster of chromosome 18 in desmosomes. The pathogenesis involves the production of activated B-cells and IgG with stimulation by IL-4 by T-helper 2 cells [1].

The clinical manifestation primarily involves cutaneous, mucosal erosions and flaccid bullae. The bulla representative of pemphigus is essentially thin walled and arises from the mucosa or skin. The oral mucous membrane, conjunctival mucosa, laryngeal, oesophageal and pharyngeal mucous membrane are usually involved. Intact bullae is uncommon in oral cavity, the bullae ruptures and leads to a large denuded painful erosion associated with sloughing [5]. The loss of epithelium by rubbing unaffected skin is termed as Nikolsky's sign [2]. The histopathological analysis on the early stages of vesiculation shows separation of cells in the stratum spinosum layer leading to loss of cohesion between cells called as acantholysis which progresses to form suprabasilar split. The basal cells are attached to the lamina propria leading to the appearance of 'tombstone'. The clumps of cells in the vesicular fluid is called as the Tzanck cells [2]. The bullous stage predominantly shows acantholysis and leukocytes with marked RNA content in the acantholytic cells [2]. The direct immunofluorescence detects IgG which is bound to the keratinocyte and the indirect immunofluorescence on monkey oesophagus reveals IgG. Enzyme Linked Immuno Sorbent Assay can be used to distinguish between anti-DSG1 antibodies and anti-DSG3 antibodies [5].

The mainstay of treatment is tailored in decreasing the severity of the lesion, decreasing the morbidity and improvising the health. Corticosteroids is commonly used in the treatment of Pemphigus vulgaris, topically and systemic. Corticosteroid act by anti inflammatory, immunosuppressive effects, alteration of leukocyte function and humoral functions at lower dosages and intercalate with the cell membrane, causes immunosuppression, inhibits prostaglandins, inhibits leukotrienes and nuclear factor kappa B at higher dosages [6]. Mild local lesions are treated using topical corticosteroids like Triamcinolone acetonide and Clobetasol propionate [7]. Recalcitrant cases are treated with pulse therapy involving administration of Corticosteroids in the suprapharmacologic dosages in an intermittent manner [8] to enhance the therapeutic effects and to reduce the adverse reactions. Newer

modality of treatment involves regimens with combination of Prednisolone with Dexamethasone, Azathioprine, Rituximab, Mycophenolate Mofetil, Cyclophosphamide, Dapsone, Methotrexate and Infliximab. Adjuvant therapy involves usage of Immunoglobulin Tumor Necrosis Factor alpha, anti CD-20 antibody and B cell depleting agents [4, 9] and paraneoplastic pemphigus is treated with multidisciplinary approach [10]. Other newer techniques used are immunoabsorption, plasmapheresis and extracorporeal photochemotherapy [9].

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