Case Report

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Oral Pemphigus Vulgaris: Case Report

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ABSTRACT

Background: Pemphigus is a blistering disorder caused by autoantibodies that result in the dissolution of intercellular attachments within the epidermis and mucosal epithelium. Though rare, without treatment it may be life-threatening, and its pathobiology provides important insight into the molecular mechanisms of keratinocyte adhesion. Pemphigus vulgaris, by far the most common type (accounting for more than 80% of cases worldwide), involves the mucosa and skin. It is one such lesion where oral lesions are preceded by cutaneous lesions. Hence, dental professionals must be efficient to recognize the clinical features of pemphigus vulgaris to ensure early diagnosis and treatment, so that it determines the favorable prognosis and course of the disease. Here in this article, we report a case on oral pemphigus vulgaris.

Keywords: Pemphigus vulgaris, Autoimmune disease, Keratinocytes.

INTRODUCTION

Pemphigus is a serious chronic skin disease characterized by the appearance of vesicles and bullae. Pemphigus is derived from Greek word Pemphix meaning bubble or blister. Pemphigus was originally named by Wichman in 1791. The disease commonly affects the skin and mucous membranes.[1] Pemphigus Vulgaris (PV) is a chronic mucocutaneous disease which usually manifests first in the oral cavity, which later may spread to the other parts of the body. It is characterized by the development of flaccid, easily ruptured intraepithelial bullae on apparently normal skin and mucous membranes.

The oral cavity is frequently affected in the course of this disease. Although any part of the oral mucosa may be affected, areas exposed to mechanical irritation are most commonly involved.[2] Here, we describe a case of oral pemphigus vulgaris and a brief note on its management.

CASE REPORT

A 75 year old female patient visited the department of Oral Medicine and Radiology of SVS Institute of Dental Sciences, Mahabubnagar with a chief complaint of burning sensation and difficulty in eating for the past 2 months from the time of visit. The patient reported that the lesions caused considerable discomfort and affected her normal oral function. On examination the patient presented neither with any skin lesions nor involvement of other mucosal sites. The patient is a known diabetic and is on medication and there was no other relevant medical history.

On intra-oral examination, multiple diffuse erosive lesions were found bilaterally on the buccal mucosa with similar lesions on posterior part of the palate [Figures 1a-c]. Apart from the inspectory findings, erosions were tender on palpation. No discharge was elicited from the erosions neither its base was indurated. There was no fixity to underlying structures. A punch biopsy was

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performed from the most representative site of the lesion under local anesthesia (LA) with due consent of the patient, and the tissue was subjected for histopathological examination.

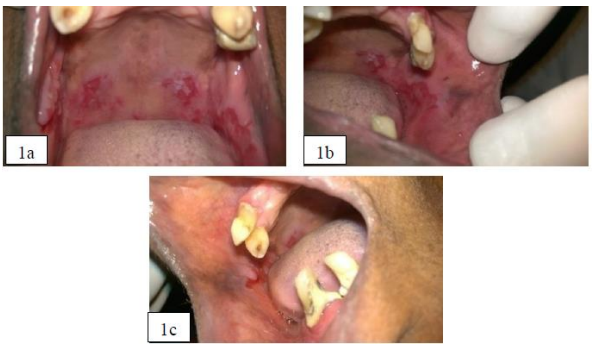

Figure 1a: Erosive lesion on soft palate, **1b** and **1c**: Similar lesions on left and right buccal mucosa respectively.

On histopathological examination there was hyperplastic parakeratinized stratified squamous epithelium with broad elongated rete ridges. The superficial epithelium showed intracellular edema and ulceration. The epithelium also exhibited suprabasilar split with separation of parabasal layers from the basal cell layer of the epithelium. There was loss of intercellular bridges between the epithelial cells resulting in acantholysis, because of which clumps of epithelial cells were found lying free in the intraepithelial split. The underlying connective tissue was fibrocellular with dense chronic inflammatory cell infiltrate made of lymphocytes and dilated vascular channels engorged with RBCs (Figure 2a-b). Based on the clinical and histopathological findings, the case was diagnosed as PV and the treatment was instituted with regular follow-up.

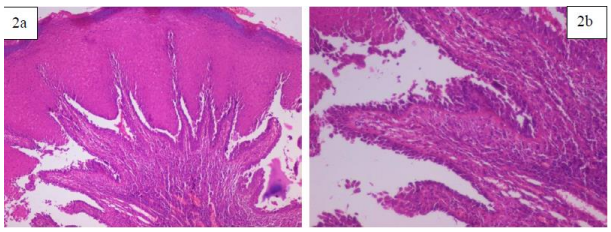

Fig. 2a: Evident suprabasilar split with the separation of parabasal layers from the basal layer under 10x. **2b:** Acantholysis with clumps of epithelial cells seen in the intraepithelial blister under 40x.

The patient was commenced on systemic prednisolone at an initial dose of 20mg/day along with topical corticosteroid, 0.05% kenocot (3 times a day) and antibiobiotic amoxicillin (500mg 3 times a day) for 1 week. Partial healing of the lesion was noted after 1 week of commencement of the treatment. The systemic prednisolone dosage was increased to 40mg/day as the lesion has not healed completely and the patient was asked to continue with the application of the topical steroid and was on regular follow up.

DISCUSSION

PV is a chronic autoimmune mucocutaneous disease that frequently appears first in the oral cavity and can progress to involve other sites. The reported incidence is 0.1-0.5 cases per 100,000 individuals worldwide per year. No gender predilection was noted but few studies have shown a slight female predominance. It is most commonly encountered in the adults during 5th or 6th decade of life, but cases have also been reported in children.[3-5] PV is characterized by intraepithelial blister formation that results from breakdown of cellular adhesion between epithelial cells. The etiology of PV is uncertain as is with other autoimmune diseases.[6] Pemphigus is an autoimmune disease, characterized by the production of autoantibodies against the intercellular substances. The autoantibodies can be produced due to the presence of viral infections as well.[7] In some cases it may have a strong genetic basis and the other possible etiological factors are listed in Table 1.

Table 1: Possible etiological agents[8]

Diet	Members of Botanical family Allium Garlic Onion Leeks
Drugs	Penicillamine Captopril Phenol drugs Rifampicin Diclofenac ACE Inhibitors
Viruses	Herpes simplex Human herpes virus 8

	(HHV8)
Other factors	Possible contribution of high oestrogen levels (Pregnancy) Increased exposure to pesticides
Association with other disorders	Rheumatoid arthritis Lupus erythematosus Myasthenia gravis Pernicious anaemia

The underlying mechanism responsible for causing the intraepithelial lesions of PV is the binding of IgG autoantibodies to desmoglein 3 (Dsg 3), a transmembrane glycoprotein adhesion molecule present on desmosome. Recent studies suggests that the PV antibodies directly block the adhesion function of desmoglein (Dsg) rather than activating protease, resulting in the separation of the cells called acantholysis (Fig 3). This takes place in the lower layers of stratum spinosum, thus forming a suprabasilar blister. The blister gradually involves a larger area of epithelium, resulting in loss of large area of skin and mucosa.[9] The following flow chart explains the mechanism of acantholysis.

Flow chart showing intracellular mechanism of acantholysis[5]

Binding of PV IgG to Dsg3 of keratinocyte cell surface
↓
Activation of phospholipase C
↓
Increase in inositol 1,4,5-triphosphate (IP3) & diacyl glycerol (DAG)
↓ ↓
IP3 mediated release of intracellular stores — Activation of protein kinase C/Plasminogen
↓
Increase in intracellular calcium
↓
Phosphorylation of Dsg3 by kinase
↓
Dsg3 dissociates from plakoglobin
↓
Depletion of Dsg3 from desmosomes
↓
Loss of cell-cell adhesion
↓
Acantholysis

The proportion of Dsg1 and Dsg3 antibodies appear to be related to the clinical severity of PV. PV of skin is associated with the simultaneous presence of anti-Dsg3 and anti-Dsg1, while those with only Dsg3 antibodies have oral lesions predominantly. Thus depending on the type of antigen affected there are two phenotypes of PV, mucosal-dominant showing only Dsg3 antibodies and mucocutaneous with both Dsg1 and Dsg3 antibodies (Table 2). The levels of circulating antibody titre have traditionally been used to correlate the disease activity and as a guide to effectiveness of the therapy instituted. These antibodies are detected by indirect immunofluorescence. Specific enzyme linked immunosorbent assays (ELISA) are now available for detecting Dsg3 & Dsg1 autoantibodies. [10]

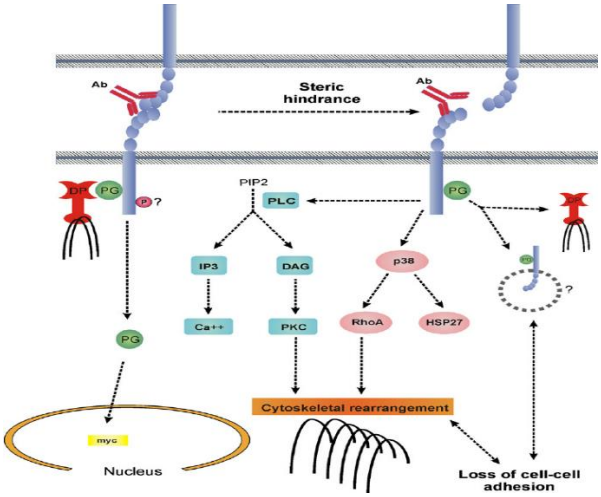

Fig 3: Adhesion signaling pathways affecting pemphigus acantholysis. Double-headed arrows indicate that signaling pathways may lead to loss of intercellular adhesion, or vice versa. P, phosphorylation; Ab, antibody; PG, plakoglobin; DP, desmoplakin; PIP2, phosphatidylinositol 4,5-bisphosphate; PLC, phospholipase C; IP3, inositol 1,4,5-triphosphate; DAG, diacylglycerol; PKC, protein kinase C.[14]

Table 2: Disease condition and antigen distribution[5]

DISEASE CONDITION	ANTIGENS
Mucosal predominant PV	High titers of Dsg3
Mucocutaneous type PV	Dsg3, Dsg1, possibly Dsg4
Pemphigus foliaceous	Dsg1
Paraneoplastic pemphigus	Dsg3, Dsg1, plakoglobin family

Oral lesions constitute an important feature of pemphigus, and for this reason it must always be considered in the differential diagnosis of blister-like eruptions of oral mucous membranes. Some difficulty may be experienced in differentiating

pemphigus from other bullous diseases such as dermatitis herpetiformis, erythema multiforme bullosum, bullous lichen planus, epidermolysis bullosa and other chronic bullous dermatoses such as bullous pemphigoid and cicatricial pemphigoid. Based on the clinical experience, aided by histopathology, usually helps to differentiate these disease entities.[3]

An important aspect of patient management is early diagnosis of the lesion ensuring administration of minimal dosage for a shorter duration to control the disease. Dentists must be well aware of the clinical manifestations of PV to warrant an early diagnosis and treatment for the better prognosis and outcome of the disease process. Institution of early treatment could prevent serious involvement of other mucosa and cutaneous sites and fatal complications. [9]

PV is generally managed with local and systemic corticosteroid therapy. Treatment is administered in 2 phases: a loading phase, to control the disease, and a maintenance phase, which includes consolidation and treatment tapering. Local treatment consists of a paste, an ointment or a mouthwash administered alone or in conjunction with systemic treatment.[11, 12] Before the advent of corticosteroid therapy in its management, pemphigus was considered life endangering disease, with a mortality rate of up to 75% in the first year. It is still a fatal disease of which 5% to 10% mortality rate is primarily due to the side effects of therapy.[13] Table 3 gives brief information about the different group of drugs employed in the treatment of pemphigus.

Table 3: Drugs used in treatment of Pemphigus Vulgaris [8]

CORTICOSTEROIDS	
LOCAL	
SYSTEMIC	Prednisolone Triamcinolone acetonide Betamethasone Dexamethasone
ADJUVANTS	
ANTI-INFLAMMATORY	Dapsone Tetracycline Minocycline
	Gold Salts (aurothiomalate) Retinoid
IMMUNOSUPPRESSORS	Cyclophosphomide Azathioprine Methotrexate Cyclosporin Chlorambucil
IMMUNOMODULATING THERAPY	Plasmapheresis Intravenous Gamma Globulins

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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