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Original

Pemphigus vulgaris: effects on periodontal health

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Abstract: Increasing evidence indicates that systemic conditions are risk factors of periodontitis. Pemphigus is a group of bullous diseases affecting the oral cavity. The aim of this study was to assess the periodontal status of pemphigus vulgaris (PV) patients. The periodontal status of 50 PV patients and 50 healthy subjects was assessed by a single examiner. PV patients were assessed based on the Clinical Severity Score (CSS). Periodontal clinical parameters such as plaque score, full mouth gingival bleeding score, probing depth (PD), clinical attachment level (CAL) and radiological bone loss were recorded. Effects of age, gender, daily tooth brushing habit, oral lesions and treatment duration on the periodontal status of PV patients were also determined. A statistically significant difference was found between the PV group and the healthy group with respect to the plaque score, PD and CAL ($P < 0.05$). Logistic regression analysis confirmed that age, gender, and treatment did not significantly influence clinical severity of the disease ($P > 0.05$). Increased PD and CAL were found with an increase in the CSS. The poor periodontal status in PV patients suggests that PV may be involved in the initiation or progression of periodontitis. (J Oral Sci 52, 449-454, 2010)

Keywords: pemphigus vulgaris; periodontitis; plaque.

Introduction

Pemphigus is a term derived from the Greek word *pemphix* meaning bubble or blister. It represents a group of potentially life threatening autoimmune mucocutaneous diseases characterized by epithelial blistering affecting cutaneous and/or mucosal surfaces (1,2). Pemphigus affects 0.1-0.5 per 100,000 individuals per year (3). It affects not only the skin and oral mucosa but also the mucosa of the nose, conjunctivae, genitals, oesophagus, pharynx and larynx, mainly in middle-aged and elderly patients (4), with intra-epithelial immune deposits, and loss of cell to cell contact (acantholysis), leading to intra-epithelial vesiculation. Pemphigus vulgaris (PV) is the most common form and it frequently affects the oral cavity (5).

PV has a fairly strong genetic background; certain ethnic groups, such as Ashkenazi Jews and those of Mediterranean and South Asian origin, are especially susceptible (6-8). It is characterized by circulating IgG antibodies directed against desmoglein 3 [cadherin-type epithelial cell adhesion molecules-(Dsg3)], with about half the patients also having Dsg1 autoantibodies (9). The proportion of Dsg1 and Dsg3 antibodies appears to be related to the clinical severity of PV and patients with only Dsg3 antibodies have predominant oral lesions (10,11).

PV typically runs a chronic course, almost invariably causing blisters, erosions and ulcers on the oral mucosa and skin. Before the introduction of corticosteroids, it was often fatal mainly due to dehydration or secondary systemic infections (12). A genetic predisposition for PV is recognized. HLA serologic studies have demonstrated a strong association between the presence of HLA-DR4 (Dw10) and HLA-DR6 (DQw1) haplotypes and PV (13,14). Recent molecular studies have shown that acantholysis can occur in the presence of antibodies against 9Éø nicotinic acetylcholine receptor (AChR). Cholinergic agonists can protect keratinocyte monolayers against anti-Dsg antibody-induced acantholysis and reverse acantholysis produced by PV IgGs (15).

Patients with PV may be on the long-term use of topical and systemic steroids or other immunosuppressive drugs,

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thereby suppressing the immune response to periodontal pathogens. Persistent painful oral lesions hinder effective tooth brushing, leading to plaque accumulation, which may in turn increase the risk of periodontal disease. Data on the correlation between PV and periodontal disease are few; hence, our study aimed to assess the periodontal status of PV patients, and compare them with healthy controls.

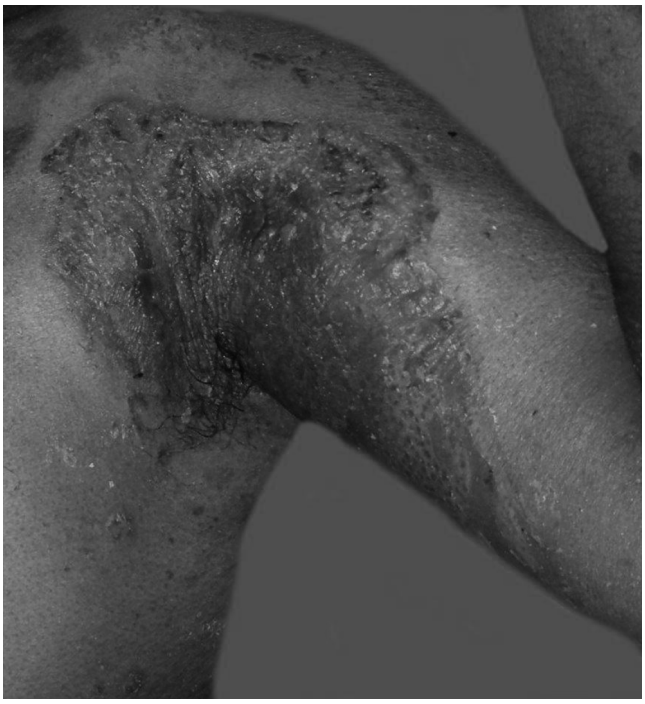

Fig. 1A Clinical picture showing irregular lesions over the left arm.

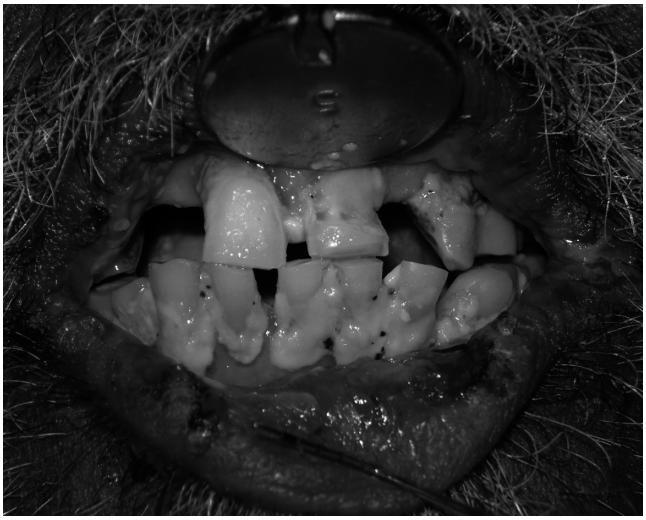

Fig. 1B Irregular oral lesions over the upper-lower lips.

Materials and Methods

A total of 100 subjects were enrolled in this study: 50 PV patients (mean age 35.2 ± 7.8 years) and 50 healthy subjects (mean age 37.0 ± 8.4 years). The PV patients were randomly selected from those attending the Department of Dermatology, Bangalore Medical College and Research Institute, Bangalore, India. The diagnosis of PV was based on the typical clinical features and confirmed by histo-pathological as well as direct immunofluorescence analysis (Figs. 1A, B and Figs. 2A, B). Patients who were under treatment for ≥2 years were included. In PV patients, Clinical Severity Score (CSS) of the disease was determined as described by Mahajan et al. (16). The patients were also interviewed for details of the treatment. The healthy control group was randomly selected from the outpatients attending

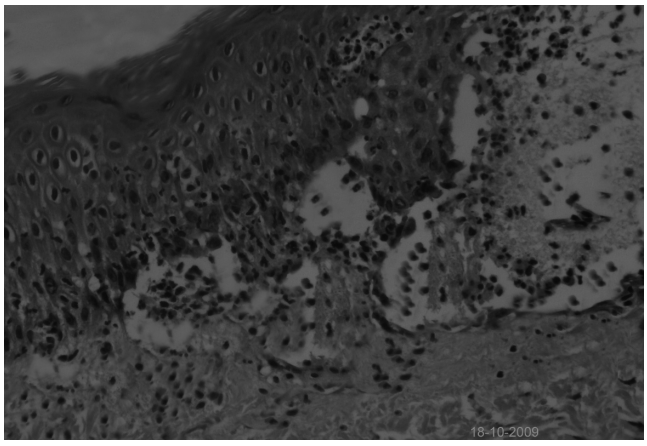

Fig. 2A Skin biopsy: scanning electron microscope showing 'suprabasilar split'.

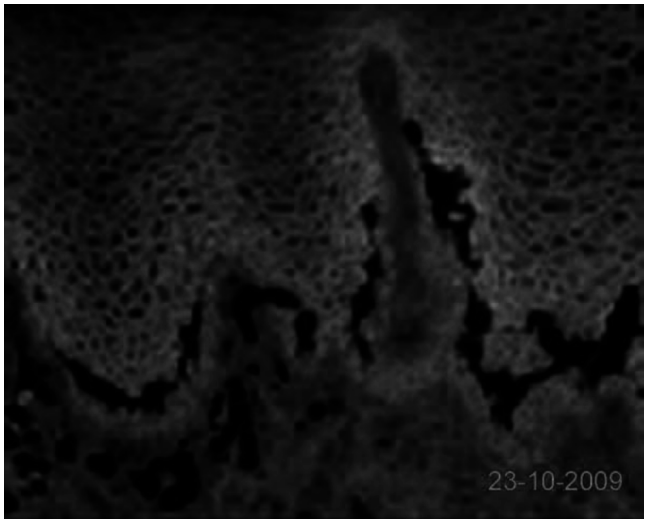

Fig. 2B Direct immunofluorescence: showing intercellular IgG deposition.

the Department of Periodontics, Government Dental College and Research Institute, Bangalore, India. They did not have any inflammatory disorders and were not under any systemic treatment. Patients who had received any periodontal therapy within the last 6 months were excluded. Patients with any systemic disease other than PV and smokers were also excluded. Written informed consent was obtained from patients, and ethical clearance for the study was received from the Ethical Committee, Government Dental College and Research Institute, Bangalore, Karnataka.

Disease severity score (DSS) (16)

Mild (1+):
10% Body suface area (BSA) involvement. Able to carry out daily routine without discomfort (or) localization to oral mucosa only.
Localized to buccal mucosa.
No difficulty in chewing or swallowing.

Moderate (2+):
10-25% BSA involvement along with oral mucosal involvement. Able to carry out daily routine but with discomfort.
Buccal and gingivolabial mucosal involvement.
Difficulty in solid food intake.

Severe (3+):
25-50% BSA involvement along with oral mucosal involvement. Unable to carry out daily routine.
Extensive oral mucosal involvement.
Difficulty in semisolid food intake.

Extensive (4+):
> 50% BSA involvement along with mucosal involvement. Bedridden or has complications.
Extensive oral mucosal lesions.
Involvement of other mucous membranes.
Difficulty in swallowing liquids also (unable to take anything orally).

The periodontal condition in both groups was assessed by the same examiner using the UNC-15 periodontal probe. Similar to the criteria used in the community periodontal index and treatment need (CPITN) (17), each sextant was examined to check whether there were >2 teeth present which were not indicated for extraction; the teeth examined were 17, 16, 11, 21, 26, 27, 47, 46, 41, 31, 36, and 37. Clinical parameters including plaque index (18), full mouth bleeding score, probing depth (PD), and clinical attachment level (CAL) were recorded. Bone loss was assessed dichotomously on a digital orthopantamogram (OPG). Both groups were interviewed by the same examiner to record the daily frequency of tooth brushing and other oral hygiene aids.

Statistical analysis

Analysis of variance (ANOVA) and chi square tests were carried out to compare the age, gender, plaque index, PD and CAL. Logistic regression analysis was used to determine the factors (age, gender, PD, CAL) affecting the CSS in PV patients.

Results

There was no significant difference between the PV group and healthy group with respect to age [PV; 35.2 ± 7.8, healthy group; 37.0 ± 8.4 (P > 0.05)] (Table 1). Significantly higher mean PD (4.51 ± 0.59) and CAL loss (3.16 ± 0.80) was noticed in the PV group compared to the healthy group (PD; 3.84 ± 0.79, CAL; 2.44 ± 1.23) (*P*

Table 1 Descriptive parameters of subjects in both groups

	Pemphigus vulgaris patients (*n* = 50)	**Healthy controls (*n* = 50)**	***P* value**
Age (years)	35.2 ± 7.8	37.0 ± 8.4	-
Gender:			
Female, *n* (%)	24 (48.0)	24 (48.0)	-
Male, *n* (%)	26 (52.0)	26 (52.0)	
Full mouth plaque index (PI)	41.6 ± 20.4	24.8 ±18.3	0.001*
Full mouth bleeding score	13 ± 6	13 ± 6	0.728
Daily tooth brushing, flossing, per day	Y 6 N 9	Y to all	-
Oral Lesions[£]:			
Present, *n* (%)	13 (86.67)		
Absent, *n* (%)	2 (13.33)	-	-

Y = Yes; N = No; [£]oral lesions present at the time of examination. *Statistically significant at $P < 0.05$

< 0.05) (Table 2). The plaque index in the PV group (41.6 ± 20.4) was significantly higher than that in the healthy group (24.8 ± 18.3) ($P < 0.001$).

When intra- and inter-arch (upper arch and lower arch) comparison was performed, it was found that, in the PV group, the upper arch showed greater PD (4.86 ± 0.74) and CAL (3.73 ± 0.95) values compared to the lower arch PD (4.16 ± 0.70) and CAL (2.60 ± 0.96), and again it was higher than that of the healthy control group. The CAL in the lower arch in both groups was statistically not significant ($P >$ 0.05) (Table 2).

Logistic regression analysis confirmed that age, gender, PD and CAL did not significantly influence the severity of PV ($P > 0.05$) (Tables 3, 4). It was found that PV patients (86.66%) had more bone loss than that in the healthy group (46.66%). Also, the treatment (drug therapy) did not affect the PD and CAL in the PV group. All patients with PV had oral lesions at the time of the periodontal examination with a mean clinical severity score of 2.0 ± 0.76.

Discussion

Periodontitis is a multifactorial disease having various etiological factors. Evidence indicates that systemic conditions can be risk factors for periodontitis (19). Pemphigus is a group of bullous diseases affecting the oral

Table 2 Comparison of PV and healthy groups with respect to PD and CAL scores

Variable	Group	Mean ± SD	*t* value	*P* value
Upper arch PD	**PV**	4.86 ± 0.74	2.2204	0.0347*
	Healthy	4.13 ± 1.03		
Lower arch PD	**PV**	4.16 ± 0.70	2.2824	0.0303*
	Healthy	3.56 ± 0.72		
Total	**PV**	4.51 ± 0.59	2.6030	0.0146*
	Healthy	3.84 ± 0.79		
Upper arch CAL	**PV**	3.73 ± 0.95	2.1609	0.0394*
	Healthy	2.70 ± 1.57		
Lower arch CAL	**PV**	2.60 ± 0.96	1.1754	0.2497
	Healthy	2.17 ± 1.02		
Total	**PV**	3.16 ± 0.80	1.9127	0.0661
	Healthy	2.44 ± 1.23		

*Statistically significant ($P < 0.05$)

Table 3 Logistic regression analysis for PPD >3 mm and clinical severity score (CSS) in PV

Variables	Coefficient	SE	*P* value	95% CI	
Age	-0.0666	0.1052	0.5270	-0.2728	0.1396
Sex	-0.7812	1.5252	0.6090	-3.7705	2.2082
PD	2.7702	1.8038	0.1250	-0.7653	6.3056
Treatment	2.49	0.41	0.078	0.76	190.70
Constant	-9.6854	8.3774	0.2480		

Table 4 Logistic regression analysis for severity of CAL and clinical severity score (CSS) in PV group

Variables	Coefficient	SE	*P* value	95% CI	
Age	-0.0520	0.1007	0.6050	-0.2494	0.1453
Sex	-0.6017	1.5949	0.7060	-3.7276	2.5243
CAL	1.5566	1.2463	0.2120	-0.8861	3.9993
Treatment	-0.60	1.17	0.60	0.05	5.43
Constant	-2.8463	5.4002	0.5980		

mucosa and skin, which leads to acantholysis and painful oral ulceration. The painful persistent oral lesions result in ineffective oral hygiene, allowing for accumulation of plaque, a causative factor for periodontitis. In the present study, there was a statistically significant difference in plaque index, PD and CAL ($P < 0.05$) between these two groups. The higher PD and CAL in PV patients compared to the healthy group could be explained by the role of plaque (high plaque score in PV) and various inflammatory cytokines in the development of periodontitis.

Mignogna et al. (20) observed that patients with PV showed generally extensive involvement of the oral mucosa and most of these were localized to the gingiva at the onset. Tricamo et al. (21) also showed that patients with mucous membrane pemphigoid exhibited more gingival inflammation (and higher plaque scores) than controls. The present data also showed that PV patients had impaired oral health compared to the control, probably because the presence of painful oral lesions hindered proper oral hygiene practice. It was documented that long-term immunosuppressive therapy alters the host defense, which in turn may negatively affect the oral health in these patients (22). The recent study by Akman et al. (1) using CPITN index revealed impaired oral health in PV patients. In the present study, we evaluated the periodontal status by taking into consideration periodontal clinical parameters like PD and CAL, which are the diagnostic and prognostic signs of periodontal disease. We also evaluated the influence of age, PD, CAL and treatment duration on the clinical severity score and found that there was no influence of these parameters on the severity of PV patients.

In this study, it was not feasible to assess the periodontal status by intraoral radiographs as most of the patients were hospitalized. Again, because of painful oral ulcers, it was difficult to take full mouth intraoral radiographs. Therefore, digital OPG, an extraoral radiographic technique, was employed to assess radiographic bone loss while assessing the periodontal status in these patients. In the present study, it was found that the PV patients had greater bone loss compared to that in healthy subjects. However, further studies with larger sample sizes have to be considered to confirm the above mentioned findings. To the best of our knowledge, the present study is the first to consider radiological bone loss assessment in these patients. However, we were only able to assess the periodontal status about 2 years after the onset of the disease. To confirm this, further molecular and large scale studies are required.

Because of hospitalization and difficulty in maintaining proper oral hygiene, it is important to consider the need for delivery of proper oral and periodontal care to PV patients. Patient education and motivation, additional dental care by regular recall visits, chlorhexidine mouthrinses, powered tooth brushes, and dental floss should be incorporated to maintain oral health. Furthermore, these patients should be educated by the dermatologist on the effects of the disease on periodontal health and measures to prevent it.

PV is the most common clinical subtype of this chronic and life-threatening autoimmune blistering disease. Tissue-specific autoimmunity could be the probable mechanism involved in the pathogenesis of the development of periodontitis as a sequel to PV. It is possible that information regarding the periodontal health status of patients with PV would lead to a more comprehensive understanding of the disease and facilitate development of a successful method of treatment. These patients should be informed of the risk of periodontitis and encouraged to attend long-term periodontal follow up by the dentist or dental hygienist so as to prevent periodontal disease progression.

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