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ORIGINAL ARTICLE

Periodontal status in patients with pemphigus vulgaris*

A Akman[1], H Kacaroglu[2], E Yilmaz[1], E Alpsoy[1]

Departments of [1]Dermatology and Venerology, and [2]Dentistry, Akdeniz University School of Medicine, Antalya, Turkey

OBJECTIVE: The aim of this study was to evaluate the periodontal status of pemphigus vulgaris (PV) patients and compare it with that of healthy controls. We also analysed the association between the periodontal condition and the clinical severity of the disease in PV patients.
STUDY DESIGN: Twenty patients (nine women, 11 men; mean ± s.d. age, 42.9±9.8 years) with PV and 22 healthy subjects (eight women, 14 men; mean ± s.d. age, 40.5 ± 12.1 years) were included in the study. The periodontal status of all subjects was evaluated according to the Community Periodontal Index of Treatment Needs (CPITN). PV patients were also assessed for Clinical Severity Score (CSS).
RESULTS: The mean CPITN values were observed to be higher in PV patients (2.8 ± 0.7) compared with those of healthy controls (1.0 ± 0.8) ($P < 0.001$). Nevertheless, there was no statistically significant difference in CPITN values according to the CSS ($P = 0.4$). The number of carious teeth was significantly higher in PV patients than that in healthy subjects.
CONCLUSIONS: Our results showed that periodontal status is worse in PV patients. Moreover, PV might contribute to the development and/or progression of periodontitis. PV patients should be encouraged for long-term periodontal follow up.
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Key words: pemphigus vulgaris; periodontal status; carious teeth; clinical findings; disease severity

Introduction

Pemphigus vulgaris (PV) is a rare, chronic, intraepithelial bullous disease with a potentially fatal outcome. Lesions are located mainly in the oral and pharyngeal mucosa, although conjunctiva, larynx, nasal mucosa, vulva, vagina, cervix, glans, anorectal and oesophagus mucosa may also be involved (Ahmed *et al*, 1980; Hale and Bystryn, 2001; Markopoulos *et al*, 2006). Although several immunological abnormalities have been demonstrated in patients with PV, the exact mechanism behind the inflammatory changes remains to be elucidated. The pathogenesis of this disease is manifested by IgG binding to desmoglein 3 in the intercellular spaces of the epithelium (Amagai *et al*, 1991). Two hypotheses make it easier to explain the pathomechanisms involved in blister formation in PV. One is that the binding of autoantibodies to their antigens can disrupt adhesion of the bound antigens through steric hindrance. The other hypothesis is that cell adhesion in the epithelium can be maintained if either Dsg1 or Dsg3 can function, which has been called the Dsg compensation theory (Amagai, 2003; Hashimoto, 2003).

Oral lesions are a hallmark of PV and occur in almost all cases, and represent the preliminary symptom in more than half of the patients (Ahmed *et al*, 1980; Mignogna *et al*, 2001). Clinically, oral lesions are characterized by blisters that rapidly rupture, resulting in painful erosions. Blisters may be localized or are more often diffuse, with little evidence of healing and a tendency to extension. The Nikolskiy sign is positive. While any area in the oral cavity can be involved, the soft palate, buccal mucosa and lips are predominantly affected. Gingival lesions are very common and, when solitary, often first recognized by periodontists (Mignogna *et al*, 2001). It seems logical to postulate that patients with PV may be affected by the long-term use of topical and systemic steroids or other immunosuppressive drugs and may have an impaired ability to perform efficient and effective oral hygiene practices. Furthermore, discomfort caused by lesions associated with PV may make individuals less liable to visit their dentists regularly for checkups and cleanings. Persistent lesions are painful, thereby limiting effective tooth brushing. This leads to lack of effective oral hygiene and plaque accumulation may increase the risk of long-term periodontal disease. No previous reports seem to have evaluated the correlation between PV and periodontal

Correspondence: Asst. Prof. Ayse Akman, MD, Department of Dermatology and Venerology, Akdeniz University School of Medicine, 07059 Antalya, Turkey. Tel: +90-242-2496708, Fax: +90-242-2274490, E-mail: aakman@akdeniz.edu.tr
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disease. Therefore, we aimed at investigating the periodontal status of PV patients, and compared them with healthy controls. In addition, we extended the study to determine the periodontal condition on the clinical severity of the disease in these patients.

Methods

Participants

Twenty patients (nine women, 11 men; mean ± s.d. age, 42.9 ± 9.8 years) with PV and 22 healthy subjects (eight women, 14 men; mean ± s.d. age, 40.5 ± 12.1 years) attending the Autoimmune Bullous Disease Unit of the Dermatology & Venerology Outpatient Clinic at the University of Akdeniz Hospital were enrolled in the study, in compliance with the principles of the Declaration of Helsinki. The study was approved by the local ethics committee (Akdeniz University School of Medicine Ethics Committee). For all patients enrolled, the diagnosis of PV was based on the typical clinical features of the disease, confirmed by histopathologic and direct immunofluorescence analysis. The mean ± s.d. duration of PV was 12.9 ± 11.6 months (range 1–36 months). The patients were treated with a modified protocol of Vien provided by Aberer *et al* (1987). The healthy control group did not have any inflammatory disorders or systemic treatments. In PV patients, the total Clinical Severity Score (CSS) was determined as described by Mahajan *et al* (2005). The mean CSS in the whole group was 1.6 ± 1.5. The patients were also evaluated for the treatment they were undergoing at the time of dental examination.

Dental examination

The same dentist (HK) examined the dental and periodontal status of the patients and controls. To assess the periodontal condition, he used the World Health Organization (WHO) Community Periodontal Index of Treatment Needs (CPITN) and the specially designed WHO periodontal probe with a sensing force of not >20 g (Tricamo *et al*, 2006). Briefly, the mouth of each patient was divided into sextants, each sextant only being examined if there were ≥2 teeth present and not indicated for extraction; the teeth examined were 17, 16, 11, 21, 26, 27, 47, 46, 41, 31, 36, 37; for each sextant we recorded the highest index found according to the following score: 0, periodontal health; 1, gingival bleeding; 2, calculus detected during probing; 3, pocket 4- to 5-mm depth; and 4, pocket ≥ 6-mm depth. The periodontal condition of every patient was reported as the worst sextant CPITN condition. The number of carious teeth was also recorded. The patients and healthy controls were questioned concerning the daily frequency of tooth brushing and the use of dental floss, by the dentist.

Statistical analysis

We used analysis of variance (ANOVA) and chi-squared analysis to compare the age, gender, CPITN, the number of carious teeth, the daily frequency of tooth brushing, the presence of oral ulcer and prosthesis of the cases and controls. Logistic regression analysis was used to determine the factors affecting severe CPITN score (CPITN > 2). Study groups, gender, the treatment used at the time of dental examination and the presence of prosthesis were considered as categorical variables, and age, the number of carious teeth and the daily frequency of tooth brushing were considered as numeric variables and were included in the logistic regression analysis. Logistic regression analysis was also used to determine the factors affecting higher CSS (CSS > 2) in PV, and gender, the treatment used at the time of dental examination and the presence of prosthesis were considered as categorical variables, and age, disease duration, the number of carious teeth, the daily frequency of tooth brushing and CPITN were considered as numeric variables.

Results

The mean CPITN score was observed to be statistically significantly higher in patients with PV (2.8 ± 0.7) compared with that in healthy controls (1.0 ± 0.8) ($P < 0.001$). The number of carious teeth was significantly higher in PV (6.5 ± 2.3) patients than that in healthy controls (4.2 ± 2.7) ($P = 0.007$). No statistically significant difference was observed according to age and gender among the groups. In addition, we found no difference with respect to the daily frequency of tooth brushing and the presence of prosthesis (Table 1). None of the patients or controls was using dental floss regularly. Twelve patients with PV (60%) had oral lesions at the time of the periodontal examination. However, no statistically significant difference was observed between the patients with oral lesions (2.8 ± 0.6) and those without oral lesions (2.8 ± 0.9) ($P = 0.801$) in the mean CPITN.

Logistic regression analysis revealed no significant difference. The results of logistic regression analysis of the factors affecting the severe CPITN are presented in Table 2, and the factors affecting the higher CSS in PV are presented in Table 3.

Discussion

Our results demonstrate that oral health is impaired in PV patients. Mignogna *et al* (2001) observed that patients with PV showed generally extensive involvement of the oral mucosa and in eight patients (45%) lesions were localized to gingiva at the onset. They suggested that the classic aspect of chronic desquamative gingivitis in PV is reached only at a later stage of the disease when extensive involvement of the oral mucosa is common. However, Tricamo *et al* (2006) showed that patients with mucous membrane pemphigoid exhibit more gingival inflammation than controls. In this study, patients currently under treatment had higher plaque indices than those in remission and not undergoing treatment. Furthermore, when comparing patients who were diagnosed as having mucous membrane pemphigoid for >5 years, with those who were diagnosed as having the disease for ≤5 years, statistically significant

Table 1 Main demographic and oral health characteristics and their distribution into the study population

	Pemphigus vulgaris (*n* = 20)	*Healthy controls* (*n* = 22)	*P-value*
Age (year)	42.9 ± 9.8	40.5 ± 12.1	0.481[a]
Gender			
Women, *n* (%)	9 (45)	8 (36)	0.754[b]
Men, *n* (%)	11 (55)	14 (64)	
CPITN[d]	2.8 ± 0.7	1.0 ± 0.8	**<0.001**[a]
The number of carious teeth	6.5 ± 2.3	4.2 ± 2.7	**0.007**[a]
The presence of prosthesis			
Present, *n* (%)	8 (40)	10 (45)	0.764[b]
Absent, *n* (%)	12 (60)	12 (55)	
The daily tooth brushing (no. per day)	1.1 ± 0.9	1.2 ± 1.0	0.252[a]
Oral lesion[c]			
Present, *n* (%)	12 (60)	–	–
Absent, *n* (%)	8 (40)	–	

[a]ANOVA; [b]chi-square; [c]at the time of periodontal examination; [d]Community Periodontal Index of Treatment Needs.

Table 2 Logistic regression analysis for severe CPITN[a] score (CPITN > 2)

	B	*S.E.*	*P-value*	*OR*	*95% CI for OR (lower to upper)*
Age	−0.024	0.072	0.733	0.976	0.8481–0.123
Gender	−2.0151	0.423	0.157	0.133	0.0082–0.170
Treatment	2.4881	0.410	0.078	12.033	0.759–190.693
Oral lesion	−2.660	1.547	0.086	0.070	0.003–1.452
Disease duration	0.062	0.068	0.366	1.064	0.930–1.216
Constant	1.803	3.838	0.639	6.068	

[a]Community Periodontal Index of Treatment Needs.

Table 3 Logistic regression analysis for higher CCS[a] (CCS > 2) in pemphigus vulgaris

	B	*S.E.*	*P-value*	*OR*	*95% CI*
Age	0.117	0.066	0.077	10.124	0.987–1.280
Gender	0.560	1.097	0.610	1.750	0.204–15.034
Treatment	−0.603	1.173	0.607	0.547	0.055–5.453
CPITN[b]	0.754	0.887	0.395	2.125	0.374–12.087
Constant	−6.719	3.845	0.081	0.001	

[a]Clinical Severity Score.
[b]Community Periodontal Index of Treatment Needs.

greater periodontal progression was measured. Chronic, painful oral lesions can limit tooth brushing. In addition, immunosuppressive treatments may alter host defences and affect oral health negatively (Mumcu *et al*, 2004). Furthermore, patients with severe organ involvement need immunosuppressive treatments with higher doses. However, in our study, CPITN was not higher in those patients treated with immunosuppressive agents compared with those not receiving any treatment at all. In addition, there was no relationship between disease duration, oral lesion at the time of periodontal examination and higher CPITN. Indeed, there is still a need for further longitudinal studies in a larger series to ascertain the cause of impaired oral health in those patients. It is clear that tooth brushing is insufficient to account for our findings. Other factors like genetic alteration and uncontrolled inflammatory response to various stimuli by the overreacting genes might play a role in higher CPITN in patients with PV compared with the control group. In addition, damaged oral mucosa in severe periodontitis might enhance presenting antigenic epitopes to stimulate the autoimmune response. Recently, investigators have hypothesized that periodontitis-induced elevations of inflammatory mediators and acute-phase proteins may play a major role in the development of a variety of systemic diseases and conditions such as Behcet's disease, diabetes mellitus and atherosclerosis (Grossi and Genco, 1998; Desvarieux *et al*, 2003; Akman *et al*, 2007). Therefore, we extended our research to analyse the periodontal findings of patients according to clinical severity. However, CPITN did not correlate with clinical severity of PV. Data were limited by the number of subjects and/or CSS. Different scoring systems that provide quantitative and qualitative parameters can be applicable to PV patients (Pfutze *et al*, 2007). In addition, our study had an important limitation because of its design. As PV and periodontitis were evaluated at the same time, it was not possible to determine which one started first. Therefore, we cannot conclude that periodontitis is a significant risk factor for the development of PV or vice versa, as we were only able to examine the periodontal status about 13 months after the onset of the disease.

Our previous study showed that the annual incidence rate was 0.24 cases per 100 000 for pemphigus and it is the most common autoimmune bullous disease in the

Mediterranean region of Turkey (Uzun *et al*, 2006). In addition, PV is the most common clinical subtype (83%). This observation indicates that PV is not a very rare disorder in our region. Furthermore, PV is a chronic and life-threatening autoimmune blistering disease, and the best way to treat the disease remains uncertain (Hale and Bystryn, 2001). If we determine the development of periodontitis as a sequel to PV, tissue-specific autoimmunity could be the probable mechanism involved in the pathogenesis (Lewkowicz *et al*, 2003). On the other hand, physicians should be encouraged to investigate the role of severe periodontitis in the development and/or progression of 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. Furthermore, alternative and preventative treatment methods may be developed in the future. This indicates a need to examine the long-term effects of PV on a patient's periodontal status. PV patients should be informed about the risk of periodontitis, and be encouraged to pursue long-term periodontal follow up by dental professionals to prevent their (PV and periodontal) disease progression.

Author contributions

Ayse Akman designed the study, analysed the data and drafted paper. She also performed the dermatologic examinations. Hasan Kacaroglu performed the dental examinations. Erkan Alpsoy and Ertan Yilmaz drafted the paper.

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