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Relationship between periodontal findings and Behçet's disease: a controlled study

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Abstract

Background: Behçet's disease (BD) is a chronic, relapsing, systemic vasculitis of unknown aetiology. The involvement of oral mucosal surfaces represents the onset feature of the disease in the majority of patients.

Objective: The aim of this study was to evaluate the periodontal status of BD patients and then compare with recurrent aphthous stomatitis (RAS) patients and healthy controls. We also determined the relationship between the periodontal condition and the clinical severity of the disease in BD patients.

Methods: Eighty-six patients with BD, 63 patients with RAS and 82 healthy subjects were included in the study. The periodontal status of all subjects was evaluated according to the community periodontal index of treatment needs (CPITN). BD patients were also assessed for clinical severity score (CSS) as described previously.

Results: The mean CPITN were observed to be higher in BD patients (1.79 ± 0.96) compared with RAS patients (1.22 ± 0.87) and healthy controls (1.18 ± 0.98) ($p < 0.001$). There was a positive association between CSS and CPITN ($p = 0.017$) in BD patients.

Conclusion: Our results showed that periodondal status is worse in BD patients and associated with disease severity. We can speculate that periodontitis may induce a systemic inflammatory process that may contribute to the development and/or progression of BD.

Key words: Behçet's disease; clinical findings; disease severity; periodontal status

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Behçet's disease (BD) is a chronic, relapsing, systemic vasculitis of unknown aetiology (Sakane et al. 1999, Verity et al. 2003). Although several immunological abnormalities have been demonstrated in patients with BD, the exact mechanism of the inflammatory changes occurring remains to be elucidated (Evereklioglu 2005). The most probable hypothesis is that of an immunologically driven inflammatory response set off by infectious agents such as herpes simplex virus 1 or streptococcus species in genetically predisposed individuals, and its major pathologic process is vasculitis (Sakane et al. 1997, Alpsoy et al. 1998). Current evidence suggests that the activated lymphocytes contribute to neutrophile and endothelial cell activation in these patients. Overexpression of proinflammatory cytokines from various cellular sources seems to be responsible for the enhanced inflammatory reaction in BD, and it may be associated with genetic susceptibility (Sakane et al. 1997, Gul 2001).

Oral microbial flora have long been implicated in the pathogenesis, as BD starts mostly from the oral mucosal surfaces (Lehner 1997, Mumcu et al. 2004). Several evidences indicate that oral microbial flora has a critical role in the pathogenesis of BD. Dental interventions or tonsillitis have been indicated to result in disease attacks such as oral ulcers as well as activation of other manifestations (Kaneko et al. 1997, Mizushima et al. 1998). Antimicrobial agents including antibiotics and antiseptic agents have been used to control disease activation (Alpsoy 2005, Mumcu et al. 2005). In a recent study, Mumcu et al. (2006) have shown that oral health-related quality-of-life assessments were impaired in patients with BD and associated with disease activity and treatment modalities. Previous studies demonstrated that periodontal scores were higher in patients with BD than healthy subjects (Nakae et al. 1981,

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Celenligil-Nazliel et al. 1999, Mumcu et al. 2004).

BD is particularly prevalent in ''Silk Route'' populations but has a global distribution. The highest prevalence of BD has been reported in Turkey. The prevalence of the disease in Turkey is found to be in approximately 1 in 250 of the population aged 12 or older (Azizlerli et al. 2003), whereas that in England is less than 1 in a 100,000 (Sakane et al. 1999). This marked geographic variation in BD can be explained by the genetic basis of the disease and/or environmental triggers. Considering the effect of genetic and environmental factors on the occurrence of BD, it could be important to determine periodontal scores of our population. Therefore, we aimed to investigate the periodontal status of BD patients, and compared them with recurrent aphthous stomatitis (RAS) patients and healthy controls. In addition, we extended the study to determine the effects of periodontal condition on the clinical findings and severity of the disease in patients with BD.

Materials and Methods

Eighty-six unrelated patients (43 women, 43 men; mean ± SD age, 34.9 ± 10.1 years) with BD fulfilled the classification criteria of the International Study Group for Behçet's Disease (1990); 63 patients with RAS (31 women, 32 men; mean ± SD age, 33.7 ± 13.3 years) and 82 healthy controls (50 women, 32 men; mean ± SD age, 33.9 ± 14.1 years) attending 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 mean ± SD durations of BD and RAS were 7.2 ± 6.1 years (range 1–25 years) and 7.6 ± 6.5 years (range 0.5–23 years), respectively. The RAS patients were evaluated for immunosuppresive or inflammatory disorders and systemic treatments. Only immunocompetent patients exhibiting idiopathic minor RAS were included in the study. The RAS patients and healthy control groups had neither a family history nor any other symptoms of BD. The clinical and laboratory findings till the beginning of the study in patients with BD are summarized in Table 1.

Table 1. Clinical and laboratory findings* of patients with Behçet's disease

	Patients ($n = 86$)	(%)
Clinical characteristics		
Oral ulcer	86	100.0
Genital ulcer	75	87.2
Papulopustular lesions	65	75.6
Articular involvement	60	69.8
Erythema nodosum	36	41.9
Ocular symptoms	25	29.1
Thrombophelibitis	8	9.3
Neurologic involvement	4	4.7
Gastrointestinal involvement	2	2.3
The skin pathergy test	43	50.0
HLA B_{51}	25	29.1

*Till the beginning of the study.

In BD patients, the total clinical severity score (CSS) was determined as described previously (Krause et al. 2001). This score was calculated as the sum of 1 point each for mild symptoms (oral ulcers, genital ulcers, arthralgia and typical skin lesions such as erythema nodosum-like lesions, papulopustular lesions and folliculitis), 2 points each for moderate symptoms (arthritis, deep vein thrombosis of the legs, anterior uveitis and gastrointestinal involvement) and 3 points each for severe disease manifestations (posterior/panuveitis, retinal vasculitis, arterial thrombosis, neuro-Behçet's and bowel perforation). The mean severity score in the whole group was 4.8 ± 1.7. Patients were categorized according to the disease CSS as follows: severe group, $\geqslant 7$ points ($n = 12$); moderate group, a score between 4 and 6 points ($n = 56$); and mild group, <4 points ($n = 18$). Patients were grouped according to the presence of active oral ulcers ($n = 22$). The patients were also evaluated for the choice of treatment such as colchicine, immunosuppressive treatment or no treatment at the time of dental examination. In addition, BD patients were recorded for the frequency and the healing time of oral ulcers during the previous 3 months.

Dental examination

The same dentist (H.K.) 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 a specially designed WHO periodontal probe with a sensing force of not >20 g (Ainamo et al. 1982). Briefly, the mouth of each patient was divided into sextants, each sextant only being examined if there were $\geqslant 2$ 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 4–5 mm depth; and 4, pocket $\geqslant 6$ mm depth. The periodontal condition of every patient was reported as the worst sextant CPITN condition. The number of carious teeth were 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 χ^2 analysis to compare the age, gender, CPITN, the number of carious teeth and the daily frequency of tooth brushing, the presence of oral ulcer and prosthesis of the cases and controls. ANOVA, χ^2 test and Kruskal–Wallis tests were used to compare the age, CSS, CPITN, the number of carious teeth, the daily frequency of tooth brushing, gender; the presence of active oral ulcer, the treatment used at the time of dental examination and the presence of prosthesis in each CSS group in patients with BD. The Mann–Whitney U test was used when the periodontal condition was analysed according to the clinical features of the BD patients. Forward conditional logistic regression analysis was used to determine the factors affecting severe CPITN score (CPITN $\geqslant 4$). Study groups, gender, the presence of prosthesis as categorical variables and age, the number of carious teeth and the daily frequency of tooth brushing as

Table 2. Main demographic and oral health characteristics and their distribution in the study population

	Behçet's disease ($n = 86$)	Recurrent aphthous stomatitis ($n = 63$)	Healthy controls ($n = 82$)	p
Age	34.98 ± 10.1	33.71 ± 13.3	33.94 ± 14.1	0.797*
Gender				
Women, *n* (%)	43 (50.0)	31 (49.2)	54 (65.1)	0.077†
Men, *n* (%)	43 (50.0)	29 (34.9)	32 (50.8)	
Community periodontal index of treatment needs	1.79 ± 0.9	1.22 ± 0.8	1.19 ± 0.9	<0.001*
Number of carious teeth	4.53 ± 2.9	5.19 ± 2.9	4.35 ± 3.1	0.232*
Presence of prosthesis				
Present, *n* (%)	39 (45.3)	25 (39.7)	30 (36.1)	0.470†
Absent, *n* (%)	47 (54.7)	38 (60.3)	53 (63.9)	
Daily tooth brushing (number/day)	1.23 ± 0.8	1.47 ± 0.9	1.41 ± 0.8	0.194*
Active oral ulcers‡				
Present, *n* (%)	22 (27.5)	11 (23.4)	—	0.611†
Absent, *n* (%)	58 (72.5)	36 (76.6)	—	

*Analysis of variance (ANOVA), *post hoc* test Scheffe were used.
†Chi-square were used.
‡At the time of periodontal examination.

numeric variables were included in the logistic regression analysis. The logistic regression analysis was used to determine the factors affecting BD and gender, the presence of prosthesis as categorical variables and age, the number of carious teeth, the daily frequency of tooth brushing and CPITN as numeric variables were included. The logistic regression analysis was also used to determine the factors affecting higher CSS (CSS ⩾ 4) in BD; gender, the presence of prosthesis and HLA-B51 as categorical variables and age, disease duration, the number of carious teeth, the daily frequency of tooth brushing and CPITN as numeric variables were included.

Table 3. Forward conditional logistic regression analysis for severe CPITN* score (CPITN ⩾ 4)

	B	SE	p	OR	95% C.I. for OR	
					lower	upper
Age	0.055	0.021	0.008	1.057	1.015	1.100
Tooth brushing (frequency/day)	−0.657	0.279	0.018	0.518	0.300	0.895
Behçet's disease	2.214	0.783	0.005	9.155	1.972	42.503
Constant	−4.741	1.150	0.000	0.009		

*The community periodontal index of treatment needs.

Results

Oral health in the study groups

The mean CPITN was observed to be higher in patients with BD (1.79 ± 0.96) compared with healthy controls (1.19 ± 0.98) ($p < 0.001$). Although the mean CPITN was higher in patients with RAS (1.22 ± 0.87) compared with healthy controls, the difference was not statistically significant.

No statistically significant difference was observed according to age and gender among the groups. The daily frequency of tooth brushing was lower in BD patients than in other groups but the difference was not statistically significant ($p = 0.19$). In addition, there was no significant difference among the groups when the patients were examined according to the number of carious teeth and having prosthesis. None of the patients or controls were using dental floss regularly (Table 2). Twenty-two patients with BD (27.5%) and 11 patients with RAS (23.4%) had active oral ulcers at the time of the periodontal examination. However, no statistically significant difference was observed between the patients with oral ulcers (1.59 ± 1.05) and patients without oral ulcers (1.90 ± 0.93) ($p = 0.210$) in the mean CPITN.

The results of forward conditional logistic regression analysis of the factors affecting the severe CPITN are presented in Table 3. Age ($p = 0.008$), having BD ($p = 0.005$) and frequency of tooth brushing ($p = 0.018$) were found to be significant risk factors for higher periodontal severity scores.

Oral health and clinical course in patients with Behçet's disease

There was an association between groups of CSS and periodontal disease severity ($p = 0.017$) in patients with BD. A correlation close to the statistical significance between the number of carious teeth and CSS (3.06 ± 3.02 in the mild group, 4.86 ± 2.88 in the moderate group, 5.25 ± 2.77 in the severe group) was observed ($p = 0.052$). However, the presence of prosthesis and the daily frequency of tooth brushing were not significantly different among groups of CSS. No statistically significant difference was observed in CSS according to age, gender and the disease duration (Table 4).

However, when the CPITN were analysed according to the clinical features, it was seen that the score was significantly higher in patients with central nervous system (CNS) involvement ($p = 0.015$). The CPITN was also higher in patients with eye involvement than those of patients without these findings but the difference was not statistically significant ($p = 0.084$). The number of carious was significantly higher in patients with arthritis ($p = 0.006$) (Table 5). The number of carious was also higher in patients with thrombophelibitis, but the difference was not statistically significant ($p = 0.089$).

At the time of dental examination, 12 of the patients with BD, mainly with

Table 4. Clinical severity scores according to the main demographic and oral health characteristics in patients with Behçet's disease

	Clinical severity score			*p*
	mild ($n = 18$)	moderate ($n = 56$)	severe ($n = 12$)	
Age	34.00 ± 14.2	34.73 ± 10.3	37.58 ± 7.0	0.609*
Disease duration	5.72 ± 5.6	7.52 ± 6.8	7.83 ± 6.8	0.579*
Sex				
Women, *n* (%)	6 (33.3)	32 (57.1)	5 (41.7)	0.176†
Men, *n* (%)	12 (66.7)	24 (42.9)	7 (58.3)	
Community periodontal index of treatment needs	1.56 ± 0.9	1.71 ± 0.9	2.50 ± 0.8	0.017*
Number of carious teeth	3.06 ± 3.0	4.86 ± 2.9	5.25 ± 2.8	0.052*
Presence of prosthesis				
Present, *n* (%)	9 (50.0)	25 (44.6)	5 (41.7)	0.639†
Absent, *n* (%)	9 (50.0)	31 (55.4)	7 (58.3)	
Daily tooth brushing (number/day)	1.32 ± 0.7	1.25 ± 0.8	1.03 ± 0.9	0.594*

*Analysis of variance (ANOVA), *post hoc* test Scheffe were used.
†Chi-square were used.

Table 5. Oral health characteristics in Behcet's disease patients with central nervous system involvement and without central nervous system involvement, and in patients with arthritis and without arthritis

	The CPITN†	*p**
Patients with central nervous system involvement (*n*:4)	3.00 ± 0.8	0.015
Patients without central nervous system involvement (*n*:82)	1.73 ± 0.9	
	The number of carious teeth	
Patients with arthritis (*n*:60)	5.07 ± 2.6	0.006
Patients without arthritis (*n*:26)	3.31 ± 3.4	

*Mann–Whitney *U* test were used.
†The community periodontal index of treatment needs.

active mucocutaneous involvement, were being treated by colchicine (1–2 mg/day). Nine patients with genital ulcer ($n = 3$), arthritis ($n = 2$), vascular ($n = 2$) and ocular ($n = 2$) involvement were taking immunosuppressive agents such as cyclosporine A, azathioprine and corticosteroids. In addition to an immunosuppressive agent, one patient was using colchicine. No statistically significant difference was observed in CPITN according to the choice of treatment (with colchicine, 1.55 ± 1.04; with immunosuppressive, 1.67 ± 1.22, no treatment; 1.85 ± 0.91, $p = 0.67$) (Table 6).

The results of the logistic regression analysis of the factors affecting BD are summarized in Table 7. The higher CPITN was found to be a significant risk factor for the development of BD ($p = 0.004$).

The results of the logistic regression analysis of the factors affecting higher CSS in BD are presented in Table 8. Male gender was found to be a significant risk factor for higher CSS in BD ($p = 0.039$).

Discussion

Our results demonstrated that oral health is impaired in BD and associated with disease severity. Nakae et al. (1981) observed that the presence of five or more decayed and extracted teeth were higher in BD compared with the healthy Japanese population. Celenligil-Nazliel et al. (1999) suggested that poor oral hygiene leads to rapid bacterial plaque accumulation. In our study, in addition to having BD, age and frequency of tooth brushing were found to be risk factors for severe periodontitis. Mumcu et al. (2004) have recently determined that oral health was impaired in patients with BD and RAS compared with healthy controls. Oral ulcers being painful, therefore, limiting effective tooth brushing was explained in this data. However, in our study, the difference was not statistically significant between patients with RAS and healthy controls. Moreover, there was no significant difference between BD and RAS patients with active oral ulcers and patients without oral ulcers at the time of periodontal examination. Subsequently, our results indicate that limitation of tooth brushing because of active oral ulcers is not sufficient to explain poor oral hygiene in these patient groups. The difference between the two studies could be explained by the numbers of patients enrolled in these studies. Our study group had more patients with RAS ($n = 63$) when compared with Mumcu's group ($n = 35$). However, memory factor could also have affected the knowledge about the frequency of brushing. The answer may vary according to persons who have or do not have periodontal disease. Thus, patients with periodontal disease may be more sensitive to recalling the frequency of brushing than healthy persons. Our findings support the notion that tissue-specific autoimmunity could be the probable mechanism in the pathogenesis of RAS (Lewkowicz et al. 2003). However, it seems likely that this immune response is not sufficient for the development of severe periodontitis in RAS patients. On the other hand, BD is a systemic inflammatory disease and not limited to oral mucosa.

Current data implicate that oral health might be an important factor in the pathogenesis of BD. In our study group, there was a relationship between severe periodontitis and BD according to the logistic regression analysis ($p = 0.004$, OR = 3.4). It can be speculated that BD might develop after the periodontitis. However, because of possible different variables in the development of the two conditions, the cause and effect relationship between periodontitis and BD might also be far from established. In addition, previous studies and our study have an important limitation because of their design. Because probable reason (periodontitis) and BD 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 BD as we were only able to examine the periodontal status about 7 years after the onset of the disease. Indeed, there is still a need for further longitudinally designed studies in a larger series to ascertain the cause of impaired oral health in these patients. It seems that in addition to insufficient tooth brushing, other factors like gene polymorphisms and uncontrolled inflammatory response to various stimuli by the overreacting genes might play a role in

Table 6. Use of the treatment at the time of dental examination in patients* with Behcet's disease

	Without treatment ($n = 66$)	With colchicine ($n = 11$)	With immunosuppressive‡ ($n = 9$)	p
CPITN†	1.85 ± 0.9	1.55 ± 1.0	1.67 ± 1.2	0.671

*Twelve of the patients with BD, mainly with active mucocutaneous involvement, were treated by colchicine (1–2 mg/day). Nine patients with genital ulcer ($n = 3$), arthritis ($n = 2$), vascular ($n = 2$) and ocular ($n = 2$) involvement were taking immunosuppressive agents.
†The community periodontal index of treatment needs.
‡In addition to the immunosuppressive agent, one patient was using colchicine.

Table 7. Logistic regression analysis for having Behçet's disease

	B	SE	p	OR	95% C.I. for OR	
					lower	upper
Male	− 0.139	0.295	0.639	0.871	0.488	1.553
Age	− 0.007	0.014	0.603	0.993	0.967	1.020
Number of carious teeth	− 0.025	0.047	0.601	0.976	0.890	1.070
Presence of prosthesis	0.382	0.339	0.259	1.465	0.755	2.845
Tooth brushing (frequency/day)	− 0.224	0.180	0.214	0.800	0.562	1.138
CPITN*	1.239	0.435	0.004	3.452	1.473	8.090
Constant	− 0.110	0.557	0.844	0.896		

*The community periodontal index of treatment needs.

Table 8. Logistic regression analysis for higher CCS* (CCS ⩾ 4) in Behçet's disease

	B	SE	p	OR	95% C.I. for OR	
					lower	upper
Male	1.551	0.751	0.039	4.716	1.081	20.567
Age	− 0.007	0.034	0.837	0.993	0.290	1.062
Number of carious teeth	0.194	0.109	0.073	1.215	0.982	1.503
Presence of prosthesis	− 0.439	0.662	0.508	0.645	0.176	2.361
Tooth brushing (frequency/day)	− 0.647	0.472	0.170	0.524	0.208	1.320
CPITN†	0.608	0.779	0.435	1.836	0.399	8.448
HLA-B51	0.665	0.784	0.396	1.945	0.418	9.043
Disease duration (year)	0.085	0.062	0.169	1.088	0.965	1.228
Constant	0.336	1.193	0.778	1.399		

*Clinical severity score.
†The community periodontal index of treatment needs.

higher CPITN in patients with BD compared with other groups. Genetic alterations such as IL-1 and TNF-α polymorphisms in BD (Coskun et al. 2005, Akman et al. 2006) could contribute to genetic susceptibility in the development of periodontitis via an enhanced inflammatory reaction. At least one variant allele in the TNF-α − 1031, − 831 or − 857 single-nucleotide polymorphisms has been reported to be associated with severe periodontitis in the Japanese population (Soga et al. 2003). Aito et al. (2004) suggest that systemic inflammatory response is higher in severe periodontitis patients carrying rare alleles for functional inflammatory gene polymorphisms.

Besides BD, several other inflammatory diseases have been reported to be associated with severe periodontal disease (Fowler et al. 2001, Angeli et al. 2003). Amar & Han (2003) suggested that the infection-related host inflammatory response, which may influence a variety of homeostatic mechanisms, could be an explanation for the periodontal–systemic disease association. Some studies have shown that the levels of IL-1 and TNF-α are sufficiently elevated in gingival crevicular fluid to be detectable systemically by a biological serum assay in advanced periodontitis (Slots & Kamma 2001, Teng et al. 2002). 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 (Iacopino & Cutler 2000, Slots & Kamma 2001). Aito et al. (2004) showed that IL-1, IL-6 and TNF-α gene polymorphisms are associated with higher levels of serum IL-6 and serum CRP. Amar et al. (2003) demonstrated endothelial vasomotor dysfunction in the brachial artery and elevated serum levels of high-sensitivity C-reactive protein in patients with severe periodontal disease. Desvarieux et al. (2003) showed that tooth loss is a marker of past periodontal disease and is related to subclinical atherosclerosis.

BD starts mostly from the oral mucosal surfaces. Interestingly, atypical streptococci species were observed in the oral flora of BD patients. *Streptococcus sanguis* KTH-1-specific T-cell lines secrete the proinflammatory mediators IL6, IL-8, TNF-α in patients with BD (Direskeneli 2001). Antistreptococcal HSP60 antibodies are raised in the serum of patients with BD. Antibody response to microorganisms in the bacterial plaque ecology and elevated inflammatory mediators in BD may also circulate in the blood stream and interact with endothelial tissue.

Different from the previously published data, we extended our research to analyse the CPITN of patients according to their clinical features. As an interesting finding, patients with CNS and eye involvement were found to have higher periodontal scores. In addition, the number of carious was significantly higher in patients with arthritis. Studies focused upon demographic features, and prognosis, showed that male gender and early age at onset were associated with more severe presentations of the disease (Al-Otaibi et al. 2005). The present data suggest that BD patients with higher CPITN scores, who are under chronic inflammatory status because of advanced periodontal disease, showed more severe organ involvement. Therefore, we can speculate that advanced periodontal disease may represent a risk factor for severe organ involvement. On the other hand, this relationship is not as strong in the male gender, according to the logistic regression analysis.

This result can also be explained by the more frequent use of immunosuppressive treatments in patients with severe organ involvement. As expected, these compounds alter host defences and may affect oral health negatively (Mumcu et al. 2004). However, CPITN was not higher

in those patients treated with immunosuppressive agents compared with other BD patients receiving treatments other than immunosuppressive drugs or not receiving any treatment at all. Nevertheless, more work needs to be carried out to analyse the periodontal effects of the immunosuppresive drugs.

Our results show that oral health is impaired in BD and associated with disease severity and severe organ involvement. It is possible that chronic infections of periodontal structures in genetically susceptible patients could accelerate BD by promoting a chronic systemic inflammatory status through the release of bacterial products, heat shock proteins, acute-phase reactants and any other inflammatory mediators (Direskeneli 2001, Angeli et al. 2003). Therefore, BD patients should be informed about the risk of periodontitis and long-term periodontal follow-up should be encouraged by dental professionals to prevent (BD and periodontal) disease progression.

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References

Ainamo, J., Barmes, D., Beagrie, G., Cutress, T., Martin, J. & Sardo-Infirri, J. (1982) Development of the World Health Organization (WHO) community periodontal index of treatment needs (CPITN). *International Dental Journal* **32**, 281–291.

Aito, F. D., Parkara, M., Bretta, P. M., Readyc, D. & Tonettia, M. S. (2004) Gene polymorphisms in pro-inflammatory cytokines are associated with systemic inflammation in patients with severe periodontal infections. *Cytokine* **28**, 29–34.

Akman, A., Sallakci, N., Coskun, M., Bacanli, A., Yavuzer, U., Alpsoy, E. & Yegin, O. (2006) TNF-a gene 1031 T/C polymorphism in Turkish patients with Behcet's disease. *British Journal of Dermatology* **155**, 350–356.

Al-Otaibi, L. M., Porter, S. R. & Poate, T. W. (2005) Behcet's disease: a review. *Journal of Dental Research* **84**, 209–222.

Alpsoy, E., Yilmaz, E., Coskun, M., Savas, A. & Yegin, O. (1998) HLA antigens and linkage disequilibrium patterns in Turkish Behçet's patients. *Journal of Dermatology* **25**, 158–162.

Alpsoy, E. (2005) Behcet's disease: treatment of mucocutaneous lesions. *Clinical and Experimental Rheumatology* **23**, 532–539.

Amar, S. & Han, X. (2003) The impact of periodontal infection on systemic diseases. *Medical Science Monitoring* **9**, 291–299.

Amar, S., Gokce, N., Morgan, S., Loukideli, M., Van Dyke, T. E. & Vita, J. A. (2003) Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation. *Arteriosclerosis Thrombosis and Vascular Biology* **23**, 1245–1249.

Angeli, F., Verdecchia, P., Pellegrino, C., Pellegrino, R. G., Pellegrino, G., Prosciutti, L., Giannoni, C., Cianetti, S. & Bentivoglio, M. (2003) Association between periodontal disease and left ventricle mass in essential hypertension. *Hypertension* **41**, 488–492.

Azizlerli, G., Kose, A. A. & Sarica, R. (2003) Prevalence of Behcet's disease in Istanbul, Turkey. *International Journal of Dermatology* **42**, 803–806.

Celenligil-Nazliel, H., Kansu, E. & Ebersole, J. (1999) Periodontal findings and systemic antibody responses to oral microorganisms in Behcet's disease. *Journal of Periodontology* **70**, 1449–1456.

Coskun, M., Bacanli, A., Sallakci, N., Alpsoy, E., Yavuzer, U. & Yegin, O. (2005) Specific interleukin-1 gene polymorphisms in Turkish patients with Behcet's disease. *Experimental Dermatology* **14**, 124–129.

Desvarieux, M., Demmer, R. T., Rundek, T., Boden-Albala, B., Jacobs, D. R., Papapanou, P. N. & Sacco, R. L. (2003) Relationship between periodontal disease, tooth loss, and carotid artery plaque. *Stroke* **34**, 2120–2125.

Direskeneli, H. (2001) Behçet's disease: infectious aetiology, new autoantigens, and HLA-B51. *Annals of Rheumatic Disease* **90**, 996–1002.

Evereklioglu, C. (2005) Current concepts in the etiology and treatment of Behçet disease. *Survival Ophthalmology* **50**, 297–350.

Fowler, E. B., Breault, L. G. & Cuenin, M. F. (2001) Periodontal disease and its association with systemic disease. *Mil Medicine* **166**, 85–89.

Gul, A. (2001) Behcet's disease: an update on the pathogenesis. *Clinical and Experimental Rheumatology* **19**, 6–12.

Iacopino, A. M. & Cutler, C. W. (2000) Pathophysiological relationships between periodontitis and systemic disease: recent concepts involving serum lipids. *Journal of Periodontology* **71**, 1375–1384.

International Study Group for Behçet's Disease. (1990) Criteria for diagnosis of Behçet's disease. *Lancet* **335**, 1078–1080.

Kaneko, F., Oyama, N. & Nishibu, A. (1997) Streptococcal infection in the pathogenesis of Behcet's disease and clinical effects of minocycline on the disease symptoms. *Yonsei Medical Journal* **38**, 444–454.

Krause, I., Mader, R., Sulkes, J., Paul, M., Uziel, Y., Adawi, M. & Weinberger, A. (2001) Behcet's disease in Israel: the influence of ethnic origin on disease expression and severity. *Journal of Rheumatology* **28**, 1033–1036.

Lehner, T. (1997) The role of heat shock protein, microbial and autoimmune agents in the aetiology of Behçet's disease. *International Review of Immunology* **14**, 21–32.

Lewkowicz, N., Lewkowicz, P., Kurnatowska, A., Banasik, M., Glowacka, E., Cedzyñski, M., Świerzko, A., Puchala, B. L. & Tchórzewski, H. (2003) Innate immune system is implicated in recurrent aphthous ulcer pathogenesis. *Journal of Oral Pathology and Medicine* **32**, 475–481.

Mizushima, Y., Matsuda, T., Hoshl, K. & Ohno, S. (1998) Induction of Behcet's disease symptoms after dental treatment and streptococcal antigen skin test. *Journal of Rheumatology* **15**, 1029–1030.

Mumcu, G., Ergun, T., Inanc, N., Fresko, I., Atalay, T., Hayran, O. & Direskeneli, H. (2004) Oral health is impaired in Behcet's disease and is associated with disease severity. *Rheumatology* **43**, 1028–1033.

Mumcu, G., Ergun, T., Elbir, Y., Eksioglu-Demiralp, E., Yavuz, S., Atalay, T. & Direskeneli, H. (2005) Clinical and immunological effects of azithromycin in Behcet's disease. *Journal of Oral Pathology and Medicine* **34**, 13–16.

Mumcu, G., Inanc, N., Ergun, T., Ikiz, K., Gunes, M., Islek, U., Yavuz, S., Sur, H., Atalay, T. & Direskeneli, H. (2006) Oral health related quality of life is affected by disease activity in Behcet's disease. *Oral Diseases* **12**, 145–151.

Nakae, K., Agata, T., Maeda, K., Masuda, K., Hashimoto, T. & Inaba, G. (1981) *Behcet's Disease, Pathogenic Mechanism and Clinical Future: Case Control Studies on Behcet's Disease*, 1st edition, pp. 41–49. Tokyo: University of Tokyo Press.

Sakane, T., Takeno, M., Suzuki, N. & Inaba, G. (1999) Behcet's disease. *New England Journal of Medicine* **341**, 1284–1291.

Sakane, T., Suzuki, N. & Nagafuchi, H. (1997) Etiopathology of Behcet disease: immunological aspects. *Yonsei Medical Journal* **38**, 350–358.

Slots, J. & Kamma, J. J. (2001) General health risk of periodontal disease. *International Dental Journal* **51**, 417–427.

Soga, Y., Nishimura, F., Ohyama, H., Maheda, H., Takashiba, S. & Murayama, Y. (2003) Tumor necrosis factor-alpha gene (TNF-alpha) -1031/-863, -857 single-nucleotide polymorphisms (SNPs) are associated with severe adult periodontitis in Japanese. *Journal of Clinical Periodontology* **30**, 524–531.

Teng, Y. T., Taylor, G. W., Scannapieco, F., Kinane, D. F., Curtis, M., Beck, J. D. & Kogon, S. F. (2002) Periodontal health and systemic disorders. *Journal of Canadian Dental Association* **68**, 188–192.

Verity, D. H., Wallace, G. R., Vaughan, R. W. & Stanford, M. R. (2003) Behçet's disease: from Hippocrates to the third millennium. *British Journal of Ophthalmology* **87**, 1175–1183.

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Clinical Relevance

Scientific rationale for the study: As the pathophysiologies of inflammatory diseases and periodontitis have similar features, we decided to investigate the relationship between BD and periodontal status.

Principal findings: A significant relationship was found to suggest that patients with BD exhibited higher community periodontal index of treatment needs (CPITN) scores than RAS patients and healthy control groups. In addition, the high CPITN score was associated with disease severity and severe organ involvement in patients with BD.

Practical implications: BD patients should be informed about the risk of periodontitis and long-term periodontal follow-up by dental professionals should be encouraged in order to prevent their (BD and periodontal) disease progression.