

Relationship between Generalized Aggressive Periodontitis and Rheumatoid Arthritis: A Case Control Study

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Abstract: Many recent studies have established the relationship between rheumatoid arthritis and chronic periodontitis. In this study we try to explore the relationship between rheumatoid arthritis and a more severe form of periodontitis, the generalized aggressive periodontitis. A total of 8 subjects who satisfied the criteria for generalized aggressive periodontitis were included in this study. Subjects having rheumatoid arthritis were found to be 3.33 times more likely to have generalized aggressive periodontitis than the healthy control group. Moreover the rheumatoid disease activity in subjects who had generalized aggressive periodontitis was found to be more severe than those without generalized aggressive periodontitis. The study shows a positive but not conclusive relationship between rheumatoid arthritis and generalized aggressive periodontitis.

Keywords: generalized aggressive periodontitis, rheumatoid arthritis, periomedicine

1. Introduction

Generalized aggressive Periodontitis is a relatively rare type of periodontitis characterized by early onset and rapid destruction of periodontal tissues. Like other types of periodontitis it serves as a reservoir for pathogenic organisms, toxic bacterial products and inflammatory mediators. Also ulceration of the sulcular epithelium seen in periodontitis allows entry of bacteria and bacterial products into the gingival tissues. Periodontal pathogens like Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans have been found to invade gingival tissues [1], and then enter systemic circulation [2]. These host-bacterial interactions adversely affect the various systems of the body [3]. These interactions include not only those produced by the oral organisms but also various chemical mediators produced by host like interleukin-1, interleukin-6 and tumor necrosis factor-alpha [4]. This periodontal-systemic disease interrelationship is believed to be mediated through systemic inflammatory reactants such as acute-phase proteins and immune effectors [3, 4]. Recent evidence suggests that periodontal infection may significantly enhance the risk for various systemic diseases including rheumatoid arthritis. Various studies have shown a positive association between rheumatoid arthritis and chronic periodontitis [5]. In this study we have tried to explore the relationship between a more severe form of periodontitis, the generalized aggressive periodontitis and rheumatoid arthritis.

2. Materials and Methods

6 Patients with rheumatoid arthritis who were diagnosed as having Generalized Aggressive Periodontitis formed the case group (RA group). Control group was formed by 2 patients without rheumatoid arthritis but having Generalized

Aggressive Periodontitis (NRA group). Written informed consent was obtained from all subjects.

Subjects fulfilling the American Rheumatism Association revised criteria for classification of RA were included in the study [5].

Subjects suffering from systemic diseases known to modify their periodontal status or alter systemic parameters like serum CRP and blood ESR levels were excluded. Also those subjects who had periodontal therapy in the past 6 months or had antibiotics intake in the past 3 months and smokers were excluded from the study.

Rheumatoid disease activity in the RA subjects was assessed using DAS-28 score system. The DAS score system involved four parameters: 28 tender joints (TJ28), 28 swollen joints (SJC28), ESR and patient general health (GH) based on a 100-mm visual analog scale. The 28 joints assessed included 10 metacarpophalangeal joint and 10 proximal interphalangeal joints of the hand, 2 wrists, 2 elbows, 2 shoulders and 2 knees. 100-mm visual analog scale was used to assess patient's GH with grade 0 corresponding to no disease activity and grade 100 corresponding to high disease activity. DAS score was calculated by using the formula:
$$\text{DAS-28} = 0.56 \cdot \text{SqRt}(\text{TJ28}) + 0.28 \cdot \text{SqRt}(\text{SJC28}) + 0.70 \cdot (\log \text{ESR}) + 0.014 \cdot \text{GH}.$$

Rheumatoid disease activity was defined as low, moderate and high according to the DAS-28 score. Low disease activity was confirmed if DAS-28 score was ≤ 3.2 , moderate if DAS-28 score was > 3.2 but ≤ 5.1 , and high if DAS-28 score was > 5.1 .

All patients demographic details were collected using a detailed questionnaire. Oral hygiene and gingival status were

assessed by using Greene and Vermillion Oral hygiene Index Simplified (OHI-S) and Loe & Silness Gingival Index (GI), respectively. The numbers of missing teeth were recorded. Probing pocket depth (PPD) and clinical attachment loss (CAL) were examined on six sites per tooth using a graduated periodontal probe with Williams's markings. Both cases and controls were graded into mild, moderate and severe periodontitis based on the clinical attachment level score. Systemic parameters of inflammation like erythrocyte sedimentation rate (ESR) and serum levels of C reactive protein (CRP) were assessed.

Subjects were diagnosed as having generalized aggressive periodontitis if they satisfied the following criteria: Generalized CAL involving at least 3 teeth other than the incisors and first molars, good or fair OHI-S score of < 3, periodontal destruction inconsistent with the amount of local deposits and early age of onset of < 30 years. All measurements were made by a single trained examiner.

All data were analyzed using a SPSS 17.0 statistical software package. The t test for independent samples was used to test the significance for quantitative data. The association of categorical variables was assessed by chi-square test. Statistical significance was declared if the P value was < 0.05.

3. Results

The mean age of cases with generalized aggressive periodontitis was 27.33 ± 5.04 years and of controls 20.5 ± 3.53 years. There were 5 females and 1 male having generalized aggressive periodontitis in the RA group, whereas in the NRA group, there were 1 female and 1 male (Table 1).

Table 1: Comparison of demographic details between cases and controls with generalized aggressive periodontitis

Parameters	Cases	Controls	p value
Age	27.33±5.04	20.5 ± 3.53	0.13
Gender	Male	1	
	Female	5	

The number of missing teeth, probing pocket depth, clinical attachment loss, blood ESR, serum CRP levels were found to higher in RA patients with generalized aggressive periodontitis than NRA patients with generalized aggressive periodontitis. The difference in serum CRP levels in RA patients with generalized aggressive periodontitis compared to that to NRA patients with generalized aggressive periodontitis was found to be statistically significant (Table2).

Table 2: Comparison of periodontal and systemic parameters in cases and controls with generalized aggressive periodontitis

Parameter	Groups	Mean ± SD	95% CI		P value
			Low.	Upp.	
Missing Teeth	Case	12.66 ± 4.36	9.17	16.16	0.02
	Control	2.5 ± 2.12	0.44	5.44	
Gingival Index	Case	1.01 ± 0.17	0.87	1.15	0.043
	Control	1.35±0.17	1.25	1.44	
Oral Hygiene	Case	1.53±0.33	1.26	1.8	0.803

Index-Simplified	Control	1.6± 0.14	1.4	1.79	
Probing Pocket Depth	Case	3.35 ± 0.35	3.06	3.63	0.303
	Control	3.05 ± 0.07	2.95	3.14	
Clinical Attach. Loss (mm)	Case	4.11 ± 0.24	3.91	4.31	0.056
	Control	3.65 ± 0.21	3.35	3.94	
ESR level	Case	63.33±17.51	49.32	77.34	0.104
	Control	37.50±10.60	22.8	52.2	
Serum CRP level	Case	4.01 ± 0.29	3.78	4.25	0.000
	Control	1±0	1	1	

The percentage of subjects in RA group having generalized aggressive periodontitis with moderate rheumatoid disease activity was 66.66% and severe rheumatoid disease activity was found to be 33.33%. (Table 3).

Table 3: Rheumatoid disease activity in patients having generalized aggressive periodontitis in RA group

Rheumatoid disease activity	No of cases	% of cases
Mild	0	0
Moderate	4	66.66
High	2	33.33

4. Discussion

Rheumatoid arthritis and periodontitis are chronic inflammatory diseases with remarkable pathological and clinical similarities. Common underlying pathological features and deregulations of the inflammatory mechanisms may predispose them to advanced, aggressive and severe form of either disease. [7]

It was found that 2 out 102 patients without rheumatoid arthritis examined had generalized aggressive periodontitis. This is consistent with the reported prevalence of 1.6% of the population. [8]

It was found that there was an increased occurrence of generalized aggressive periodontitis in RA subjects than in NRA subjects. It was found that rheumatoid arthritis patients are 3.33 times more likely to have generalized aggressive periodontitis than control subjects. Several recent studies have shown a positive relationship between rheumatoid arthritis and chronic periodontitis but no study has so far been done to find relationship between rheumatoid arthritis and the more severe form of the disease, specifically the generalized aggressive periodontitis.

The increased occurrence of generalized aggressive periodontitis in RA subjects than in NRA subjects may be due to the common features of an underlying and presently unknown deregulation of the inflammatory mechanism, which predisposes these individuals to either disease [7]. Another possible explanation is monocyte hyper secretory trait present in subjects with RA, which may have led to an overproduction of PGE2 in response to bacterial lipopolysaccharides and thus the severe periodontal destruction seen in generalized aggressive periodontitis [9]. Periodontitis has very similar cytokine profile to RA consisting of persistent high levels of proinflammatory cytokines, including IL-1beta, IL-6 and TNF-alpha, and low

levels of anti-inflammatory cytokines such as IL-10 and transforming growth factor-beta [7, 10]. These cytokines together with low levels of tissue inhibitor of metalloproteinases and high levels of matrix metalloproteinases and prostaglandin E2 are associated with active periods of tissue destruction in both rheumatoid arthritis and periodontitis [11, 12].

It was found that subjects having rheumatoid arthritis with generalized aggressive periodontitis were having more severe rheumatoid disease activity than rheumatoid arthritis subjects without generalized aggressive periodontitis. Ogrendik et al in 2005 had hypothesized that *P. gingivalis*, an organism associated with generalized aggressive periodontitis, is an environmental factor that impairs tolerance against autoantigens that contain citrulline in a genetically susceptible host [13]. When the immune system in patients having periodontal infection with *Porphyromonas gingivalis* is exposed to citrullinated antigens, autoantibodies are produced leading to rheumatoid arthritis [14]. Moreover, Presence of DNA of various periodontopathogens like *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythia*, and *Treponema denticola* have been detected from the synovial fluid of rheumatoid arthritis patients showing a more direct link between rheumatoid arthritis and periodontitis [15].

5. Conclusion

This study suggests a positive relationship between rheumatoid arthritis and generalized aggressive periodontitis. This relationship was however not found to be statistically significant most probably due to the low sample size involved. A study with a larger sample size will help in establishing the true relationship between rheumatoid arthritis and generalized aggressive periodontitis.

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