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Review Article

Current Evidence on The Association Between Periodontitis and Rheumatologic Diseases

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Introduction

Periodontitis, the most common cause of tooth loss, is a dysbiotic plaque biofilm-induced chronic inflammatory disease characterized by persistent gingival inflammation, alveolar bone resorption, and progressive attachment loss of the tooth-supporting structures [1]. According to the Global Burden of Disease 2010 study, periodontitis represents the sixth-most prevalent condition in the World [2]. Although the plaque biofilm that forms on the surfaces of teeth and in the periodontal pocket initiates the disease, the immune-inflammatory host response in a susceptible host determines the severity of periodontal tissue destruction [1].

Recent studies have confirmed the existence of a bidirectional association between periodontitis and rheumatologic diseases based on common etiopathogenic mechanisms [3-5]. Both periodontitis and rheumatologic diseases pathogenesis involve aberrant immune activation (increased infiltration of host cells, increased release of proinflammatory mediators, decreased levels of anti-inflammatory mediators), genetic background (gene polymorphisms) and environmental (smoking) interactions, and long-standing chronic inflammation. In addition, periodontitis and rheumatologic diseases also cause systemic inflammation, represented by elevated levels of the plasma C-reactive protein (CRP) [3, 5-9].

This mini review aimed to provide an overview of what is known so far in the relationship between periodontitis and the most common rheumatologic diseases including rheumatoid arthritis and ankylosing spondylitis.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial inflammation and hyperplasia that results in progressive disability, loss of function, and increased mortality [3]. The disease aetiology is still not fully understood but both innate and adaptive immune responses are involved in the pathophysiology of RA. RA patients present with chronic pain, swelling, stiffness and deformity in multiple joints. The diagnosis of RA includes both physical examination and laboratory features including morning stiffness, hand-joint arthritis, arthritis of three or more joint areas, symmetric involvement, rheumatoid nodules, presence of ACPA or RF antibodies, CRP and ESR, and changes in the radiography [3]. The treatment of RA consists of medications including non-steroidal anti-inflammatory drugs (NSAIDs), non-biologic disease-modifying antirheumatic drugs (DMARDs) and biological agents. These medications aim to reduce symptoms, achieve remission and slow the progression of joint damage.

Evidence from numerous studies indicates a strong bidirectional relationship between periodontal disease and RA mainly due to the remarkably parallel disease processes [5, 9-12]. Previous case-control and epidemiological studies demonstrated that patients with active RA show significantly increased frequency and severity of periodontitis, especially more calculus formation and gingival bleeding, and more tooth loss and increased alveolar bone destruction than non-RA patients [5, 8].

Recently, the role of the microbiome in the pathogenesis of RA has been investigated and suggested as a possible environmental risk factor for disease progression [3]. Moreover, elevated antibody levels against special periodontopathogens, P. Gingivalis and A. actinomycetemcomitans, have been determined in the plasma and synovial fluid of RA patients [9, 13]. These results suggest that periodontitis as a chronic low-grade inflammatory event may exacerbate RA disease activity.

Immunogenetic mutations, especially in the SE-encoding HLA-DRB1 gene (a shared epitope), have also been associated with both RA [14] and periodontitis [11]. This genetic locus has been related to bone erosion in RA and alveolar bone destruction in the course of periodontitis progression [14].

Non-surgical periodontal treatment mainly consists of mechanical debridement of the infected tooth surfaces and periodic disruption of recolonization of bacteria achieved by the patient's oral hygiene. This process significantly decreases the microbial load, reduces inflammation, eliminates disease progression, and also reduces the risk of tooth loss. Accordingly, studies have been conducted to determine the impact of non-surgical periodontal therapy on the course of RA. A recent systematic review assessed the possible effects of non-surgical periodontal treatment on the clinical activity and inflammatory markers of RA and reported a reduction in ESR and DAS28 scores after periodontal therapy [10]. Another systematic review with meta-analysis also assessed the effect of nonsurgical periodontal treatment on RA and gingival crevicular fluid (GCF) biomarkers and found that the periodontal therapy significantly reduced the GCF levels of PGE2, MMP-8, t-PA, and IL-6 in RA patients [15].

In addition, as both RA and periodontitis arise as a result of an imbalance between anti-inflammatory and proinflammatory cytokines, most studies have focused on agents that can target specific molecules in the inflammatory cascade, such as NSAIDs, DMARDs and biological disease-modifying antirheumatic drugs [3, 16]. The anti-TNF agents used for the treatment of patients with RA decrease periodontal disease activity as determined by clinical measurements and GCF biochemical markers of inflammation. In addition, a systematic review with meta-analysis also confirmed that RA patients treated with antirheumatic drugs have better periodontal status than untreated RA patients [12].

Ankylosing spondylitis

Ankylosing spondylitis (AS) is a chronic autoimmune disease characterized by inflammation of entheses, leading to new bone formation, syndesmophytes and ankylosis of joints [17]. The exact aetiology of AS is unknown, but strong genetic-environmental factors, especially the HLA-B27 phenotype, have been reported [17].

Although the association between RA and periodontitis is well known, studies on the relationship between AS with periodontitis are limited [4, 18-21]. A cross-sectional study conducted by Pischon et al. [18], documented an increased prevalence of periodontal disease in AS patients compared to non-diseased control subjects. In contrast, Sezer et al. [19] examined the clinical periodontal measurements and serum CRP, TNF-alfa and interleukin-6 levels in 48 AS patients and 48 systemically healthy control subjects and found no difference in periodontitis prevalence among the two groups. A recent review article, consisting of case-control studies evaluating the periodontal status in AS patients found an odds Ratio for periodontitis of 1.85 (95% CI 1.72, 1.98) [22].

Patients with AS suffer from reduced mobility, chronic back pain, and physical function, which affects their quality of life. Accordingly, Schmalz et al. [23], demonstrated a worse oral-health-related quality of life in AS patients than in healthy controls, regardless of the oral status. In another study, Kang et al. [21], reported a positive association between periodontitis, low toothbrush frequency, and impaired spinal mobility. Similarly, Ziebolz et al. [20], also documented that the Bath AS Metrology Index, which expresses the AS patients' movement ability, showed a significant association with the severity of periodontitis. Functional impairments in these patients can impair their ability to achieve proper oral hygiene, leading to an increased risk of developing periodontal disease.

To date, the molecular pathway, HLA-B27 phenotype, between AS and periodontitis has also been investigated but the result remains speculative [6]. Moreover, a microbiological relationship, especially the role of specific periodontal bacteria, has been evaluated [7, 24]. Although Bisanz et al. [7], did not show the existence of specific bacteria in AS, a current review article reported periodontal pathogens to be responsible for the development of AS in genetically susceptible individuals [24]. In addition, anti-TNF drugs and NSAIDs used for the treatment of AS have also been evaluated in AS patients with periodontitis and Fabri et al. [25], reported a significant reduction in periodontal disease activity as determined by clinical attachment loss in AS patients following the application of six-month anti-TNF treatment.

Conclusion

Current evidence suggests that an association may exist between rheumatologic diseases and periodontitis. However, future studies examining the complex cytokine network and its interactions with genetic and environmental factors may help to better understand the link between periodontal disease and rheumatic disease. Nevertheless, patients with rheumatologic diseases must be informed about the risks of periodontitis and receive preventive periodontal treatment to eliminate the risk of periodontitis progression.

Acknowledgment

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Conflicts of Interest

None.

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