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Original Research Paper

Periodontology

PERIODONTAL MANIFESTATIONS OF AUTOIMMUNE DISEASES BEYOND DIABETES: A COMPREHENSIVE REVIEW OF RHEUMATOID ARTHRITIS, SYSTEMIC LUPUS ERYTHEMATOSUS, SJÖGREN'S SYNDROME, AND HASHIMOTO'S THYROIDITIS

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ABSTRACT Periodontal disease is an inflammatory condition initiated by microbial biofilms but significantly modulated by host immune response and systemic health. While diabetes mellitus is the most established systemic risk factor, emerging evidence indicates that autoimmune disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), and Hashimoto's thyroiditis (HT) also enhance periodontal susceptibility and severity.[1–4] This review synthesizes current understanding of periodontal manifestations across these autoimmune diseases, highlights shared inflammatory pathways, and discusses clinical implications for interdisciplinary management. RA and SLE exhibit strong epidemiological associations with periodontitis, while SS influences periodontal health predominantly through salivary gland dysfunction. HT, though less extensively studied, appears to affect periodontal outcomes via immune dysregulation and altered bone metabolism. Understanding these interactions is crucial for early diagnosis, preventive strategies, and integrated care.

KEYWORDS : periodontitis, autoimmune disease, rheumatoid arthritis, lupus, Sjögren's syndrome, Hashimoto's thyroiditis, inflammation

INTRODUCTION

Periodontal disease results from a complex interaction between microbial biofilm and host inflammatory response, leading to connective-tissue breakdown and alveolar bone loss.[5] Although traditionally linked to diabetes mellitus, numerous autoimmune diseases also impact periodontal health through chronic systemic inflammation, immune dysregulation, and impaired tissue repair mechanisms.[6] Autoimmune disorders involve persistent activation of B cells, T cells, and autoantibody production, which can intensify local periodontal inflammation.[7]

Recent literature suggests that autoimmune diseases beyond diabetes-notably RA, SLE, SS, and HT-share overlapping pathophysiological pathways with periodontitis, including elevated pro-inflammatory cytokines, oxidative stress, and dysbiosis.[8–10] These shared characteristics justify the need for evaluating periodontal disease as a potential comorbidity and clinical marker in autoimmune patients.[11]

Rheumatoid Arthritis (RA)

Epidemiological Link

Multiple meta-analyses show a significantly higher prevalence and severity of periodontitis among RA patients compared with healthy controls. Patients often exhibit deeper periodontal pockets, more clinical attachment loss, and increased tooth mobility.[12]

Pathophysiological Link

RA and periodontitis share common inflammatory mediators including TNF-α, IL-1β, IL-6, and matrix metalloproteinases that drive joint and periodontal destruction.[13] A unique connection involves Porphyromonas gingivalis, which expresses peptidylarginine deiminase (PAD) capable of citrullinating host proteins. This promotes the formation of anti-citrullinated protein antibodies (ACPAs), a hallmark of RA. The citrullination process provides a potential biological bridge between periodontal infection and systemic autoimmunity.[14]

Systemic Lupus Erythematosus (SLE)

Epidemiology

SLE patients have approximately two to three times higher risk of periodontitis. Disease severity and duration correlate with worse periodontal outcomes.[15]

Pathophysiological Link

SLE is characterized by polyclonal B-cell activation, immune-complex deposition, and elevated cytokines such as IFN-γ, IL-6, and BAFF, which predispose to exaggerated inflammatory responses in periodontal tissues. SLE patients also exhibit altered subgingival microbiota, with increases in Prevotella, Fusobacterium, and other pathogenic taxa that amplify periodontal inflammation. This dual disruption of systemic immunity and microbial ecology explains accelerated periodontal destruction in SLE.[16]

Sjögren's Syndrome (SS)

Clinical Impact on Periodontium

SS predominantly affects the oral cavity through severe xerostomia due to autoimmune destruction of salivary glands. Reduced salivary flow impairs microbial clearance and increases plaque accumulation, resulting in higher risk of gingivitis and periodontitis.[17]

Pathophysiological Link

Saliva contains essential antimicrobial factors—IgA, lactoferrin, lysozyme—all of which are significantly diminished in SS. Without saliva's protective properties, biofilms mature faster, microbial diversity increases, and the host loses critical mucosal immunity. Furthermore, chronic mucosal inflammation induces epithelial atrophy and compromises periodontal barrier function.[18]

Hashimoto's Thyroiditis (HT)

Emerging Association

Although less studied, HT has been linked to worsened periodontal status and reduced response to periodontal therapy.[19]

Pathophysiological Link

HT features chronic lymphocytic infiltration and elevated anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin antibodies, producing systemic low-grade inflammation. In hypothyroid states commonly associated with HT, reduced bone turnover and altered mineral metabolism may predispose individuals to periodontal bone loss. Immune dysregulation may also impair tissue healing and increase periodontal susceptibility.[20]

Shared Mechanisms Across Autoimmune Diseases

Inflammatory Cytokine Overlap

IL-1β, IL-6, TNF-α, and MMPs are upregulated in both autoimmune diseases and periodontitis, contributing to connective-tissue destruction and bone resorption.[21]

Immune Dysregulation

Aberrant T-cell and B-cell signaling, autoantibody production, and impaired neutrophil function create a systemic hypersensitive state that amplifies periodontal inflammation.[22]

Microbial Dysbiosis

Autoimmune conditions often shift the subgingival microbiome toward pathogenic species, enhancing periodontal damage.[23]

Bidirectional Association

Periodontal inflammation produces systemic cytokines and bacterial endotoxins (e.g., LPS), which can worsen autoimmune disease activity, reinforcing a vicious inflammatory cycle.[24]

Porphyromonas gingivalis: The Keystone Pathogen Linking Periodontitis to Autoimmune Diseases

Porphyromonas gingivalis (P. gingivalis) is considered a keystone pathogen because—despite its low abundance-it can reshape the subgingival microbiome and trigger disproportionate inflammatory responses. This property enables it to initiate and sustain chronic periodontitis. P. gingivalis produces a wide range of virulence factors including gingipains, lipopolysaccharides (LPS), fimbriae, outer membrane vesicles (OMVs) and, uniquely, peptidylarginine deiminase (PPAD). These virulence molecules interfere with normal host immunity and promote destruction of periodontal tissues.[25]

PPAD-Mediated Citrullination: A Unique Mechanism Relevant to Autoimmune Disease

A defining feature of P. gingivalis is its expression of bacterial peptidylarginine deiminase (PPAD)-an enzyme that converts arginine residues in host proteins into citrulline. This is the same biochemical process involved in rheumatoid arthritis (RA) autoimmunity. The citrullinated proteins generated in periodontal tissues may:

- Trigger formation of anti-citrullinated protein antibodies (ACPAs)
- Break immune tolerance
- Enhance autoimmune inflammation in RA
- Circulate systemically and activate peripheral immune responses

This makes P. gingivalis the only known bacterium directly capable of promoting citrullination-linked autoimmunity.[14]

Gingipains: The Major Tissue-Destructive Proteases

P. gingivalis secretes arginine-specific (RgpA, RgpB) and lysine-specific (Kgp) gingipains, which are potent cysteine proteases. Gingipains:

- Degrade collagen, fibronectin, and extracellular matrix
- Cleave immunoglobulins, complement proteins, and cytokines
- Disrupt neutrophil and macrophage functions
- Promote bleeding and deep periodontal pocket formation

These processes accelerate tissue breakdown in periodontitis and amplify the systemic inflammatory burden relevant to RA, SLE, and Hashimoto's thyroiditis.[13]

Interaction Of P. gingivalis With Host Immune Responses

P. gingivalis manipulates host immunity by:

- Inhibiting IL-8 production ("chemokine paralysis"), blocking neutrophil recruitment
- Altering TLR2/TLR4 signaling
- Polarizing T-helper responses (favoring Th17 pathways)
- Suppressing phagocytosis through OMVs
- Triggering inflammasome activation

These immune-modulatory effects lead to chronic, dysregulated inflammation, characteristic of both periodontitis and autoimmune diseases.[22]

Microbiome Dysbiosis Induced By P. gingivalis

Even in low concentrations, P. gingivalis alters the subgingival microbial community by enabling the overgrowth of pathogenic species such as:

Tannerella forsythia
Treponema denticola (together forming the "Red Complex")
Fusobacterium nucleatum
Prevotella intermedia

This dysbiosis is a hallmark of chronic periodontitis and creates a persistent inflammatory stimulus affecting systemic autoimmune disease activity.[23]

Clinical Implications

- Early periodontal screening should be incorporated into the management of patients with RA, SLE, SS, and HT.
- Interdisciplinary care between dentists, rheumatologists, endocrinologists, and immunologists is essential.
- Periodontal therapy may reduce systemic inflammation, potentially improving autoimmune disease control.
- Customized treatment plans should account for xerostomia (in SS), reduced bone turnover (in HT), and immunosuppressive medications used in RA and SLE.[12]

CONCLUSION

Autoimmune diseases beyond diabetes significantly influence periodontal health through interconnected pathways involving immune dysregulation, chronic inflammation, altered microbial ecology, and impaired tissue repair. RA and SLE demonstrate strong pathophysiological and epidemiological associations with periodontitis, while SS primarily affects periodontal status via xerostomia. HT contributes through endocrine-mediated and immune-mediated alterations. Recognizing these associations is essential for early diagnosis and comprehensive management. Further longitudinal and pathophysiological studies are needed to deepen understanding and optimize care strategies.

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