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The Effect of the Autoimmune Conditions on Pulpal and Periapical Disease Progression: A Narrative Review

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Abstract

Systemic conditions known as autoimmune diseases are typified by an abnormal immune response against self-antigens, which frequently results in tissue damage to multiple organs and chronic inflammation. These systemic immune dysregulations have the potential to greatly impact the pathophysiology and healing results of the periapical tissues and dental pulp. Patients with autoimmune diseases like systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjögrens syndrome, and type 1 diabetes mellitus experience changes in their inflammatory response, which is essential in the onset and resolution of pulpal and periapical diseases. In addition to influencing the course of infection and inflammation, this compromised immunity also impacts the pulps and the periapical regions' ability to heal after endodontic treatment. Additionally, immunosuppressive therapies that are frequently recommended for autoimmune patients complicate dental care by postponing tissue repair and making patients more vulnerable to secondary infections. To better understand how autoimmune diseases affect the development course and resolution of pulpal and periapical pathologies, this narrative literature review will critically examine and summarize the existing data. Particular attention is paid to the biological processes, clinical signs and symptoms, treatment advances, and suggestions for customized dental care. Optimizing care and results for this particular patient population requires an understanding of the relationship between endodontic disease and systemic immune dysfunction.

Keywords: *Autoimmune Diseases, Pulpal Disease, Periapical Lesions, Endodontic Treatment, Immunosuppressive Therapies.*

Introduction

Maintaining tooth vitality and reacting to pathogenic insults like deep caries or trauma depend heavily on the dental pulp and periapical tissues(1). A complicated inflammatory cascade that can result in pulpitis and ultimately apical periodontitis is started when these tissues are subjected to bacterial invasion or damage(2). Usually, this immune response strikes a balance between protecting host tissue and getting rid of infections (Khattak et al., 2014). This equilibrium is frequently upset in autoimmune disease patients, though(3). The immune system's improper reaction against its cells and tissues is a hallmark of autoimmune diseases, which lead to systemic immune dysregulation, chronic inflammation, and poor healing(4). Rheumatoid arthritis (RA), Sjögrens syndrome, and systemic lupus erythematosus (SLE) are examples of immune-mediated diseases that can change the normal progression of pulpal and periapical disorders(5, 6).

For instance, the glandular dysfunction of Sjögrens syndrome or the pro-inflammatory environment of RA may affect oral cavity local immunity, increasing the risk of infections or causing poor healing after endodontic procedures(7).

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Furthermore, drugs used to treat autoimmune diseases, including biologics, corticosteroids, and disease-modifying anti-rheumatic drugs (DMARDs), can suppress immune responses, making it more difficult to diagnose and treat dental infections(8). Oral symptoms are becoming more widely acknowledged as early warning signs or secondary complications of autoimmune diseases, which frequently manifest as systemic symptoms(9, 10). Among autoimmune patients, xerostomia, mucosal ulceration, delayed healing, and recurrent infections are frequently reported oral symptoms(10). The dental pulp, a highly innervated and vascularized tissue, may also be especially susceptible to alterations in immune and vascular regulation brought on by autoimmune pathophysiology(11).

Because of this early diagnosis, individualized endodontic treatment is essential for those impacted. The growing prevalence of autoimmune diseases worldwide, where millions of people suffer from ailments like multiple sclerosis, autoimmune thyroiditis, and type 1 diabetes, is another factor to take into account when examining the relationship between dentistry and systemic disease(12, 13). Current dental protocols frequently fail to consider the altered immune environment in these patients, even though many of them need regular dental care. Atypical radiographic progression, increased abscess formation, or delayed periapical healing are a few consequences that could be missed or improperly treated as a result(14). In addition to assessing clinical data from case studies and trials, this review investigates the biological mechanisms by which autoimmune diseases impact the course of dental disease and offers a framework for patient-centered endodontic treatment in this demographic (Al-Taie & Khattak, 2024). We hope to shed light on the connections between systemic autoimmune diseases and endodontic pathology by conducting a thorough literature review and suggesting future lines of inquiry for clinical and translational studies.

Methods

To compile the body of knowledge regarding the connection between autoimmune diseases and the advancement of pulpal and periapical diseases, a narrative literature review was carried out. We used a combination of keywords such as “autoimmune diseases”, “pulpitis”, “apical periodontitis”, “endodontic outcomes” “oral immunity”, “Sjögrens syndrome”, “rheumatoid arthritis”, “systemic lupus erythematosus”, “diabetes” and “pulp inflammation” to search PubMed, Scopus, ProQuest and Google Scholar for Clinical trials in vivo and in vitro investigations and meta-analyses. Studies published in English between 2015 and 2024, both preclinical and clinical, were taken into account. Studies that examined the biological, immunological, or clinical impacts of autoimmune diseases on dental pulp or periapical tissues met the inclusion criteria. Only non-dental manifestations were the subject of the excluded articles. To find more sources, the reference lists of pertinent articles were also manually screened. Studies presenting clinical observations, histopathological information, and immunological insights into tissue responses in autoimmune patients were given special attention. A comprehensive understanding of the interaction between local dental pathology and systemic autoimmune dysfunction was created by thematically synthesizing the collected data.

Discussion

Pulpal inflammation and immune dysregulation

Encased in hard dentin, the dental pulp is a soft connective tissue particularly susceptible to inflammatory changes. When deep caries or trauma expose the pulp to microbial invasion, the pulp triggers a coordinated immune response that includes both innate and adaptive

mechanisms(15, 16). These reactions' normal functions include removing pathogens, controlling inflammation, and promoting tissue repair(17). However, these immune responses are persistently dysregulated in patients with autoimmune disorders, which can have a major impact on healing outcomes, inflammation resolution, and pulpal behavior(18). Changes in cytokine signaling and persistent immune activation are hallmarks of systemic autoimmune diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and type 1 diabetes mellitus (T1DM). Increased levels of cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) cause tissue damage and extensive inflammation in SLE. These pro-inflammatory mediators can impact the pulp's local microenvironment and spread throughout the body, intensifying the inflammatory response to even small stimuli(19). In such conditions, odontoblasts and pulp fibroblasts, the first line of defense in pulpitis, can become overactivated, releasing more cytokines that worsen tissue destruction(20). Neutrophil chemotaxis, phagocytosis, and oxidative burst are all known to be compromised in type 1 diabetes(21). These innate immune deficiencies make it more difficult for the host to eradicate bacterial infections early on, which permits the bacteria to colonize for a longer period and penetrate deeper into the dentinal tubules. According to research, diabetic pulp tissues have higher concentrations of matrix metalloproteinases (MMPs), specifically MMP-2 and MMP-9, which break down extracellular matrix and cause irreversible pulpitis(22, 23). Furthermore, diabetes-related microvascular alterations like capillary occlusion and thickening of the basement membrane reduce blood flow to the pulp, which lowers the delivery of nutrients and oxygen and hinders the recruitment of immune cells(24). Other autoimmune diseases like Sjögrens syndrome, typified by exocrine gland lymphocytic infiltration and extreme xerostomia, may not directly affect the pulp but produce an unfriendly oral environment(25). Early pulp exposure and inflammation are caused by reduced salivary flow, which also increases bacterial adhesion, reduces buffering capacity, and speeds up the development of dental caries(26). Because of the combined effects of a high bacterial load and a compromised host response, the resulting pulpitis in these patients may worsen more quickly. While the central nervous system is the primary target of multiple sclerosis (MS), peripheral neuropathies and changes in immune regulation are also noted. These alterations may have an impact on pulpal innervation, which could reduce the perception of pain and postpone the onset of pulpitis symptoms(27, 28). The prognosis becomes more complicated as a result of delayed diagnosis and treatment seeking at later stages of the disease. A pulpal environment that is more susceptible to chronic necrosis and a poor response to standard therapies is the result of the combined effects of systemic inflammation, compromised vascular function, and altered immune cell function in autoimmune diseases(3, 29).

Impact on the development and recovery of periapical diseases

When pulp infection spreads outside of the root canal, the periapical tissues act as a second line of defense. Periapical inflammation in health uses a localized immune response that includes neutrophils, macrophages, T-cells, and cytokines to try and stop the spread of microorganisms(30-32). The severity and resolution of this inflammatory response, however, are frequently aberrant in autoimmune patients.

In patients with RA and SLE, the balance is skewed toward bone resorption due to decreased osteoprotegerin (OPG) levels and increased expression of RANKL (Receptor Activator of Nuclear Factor Kappa-B Ligand)(33-35). To control bone loss and limit lesion size while promoting healing, this imbalance is especially important in the periapical setting. In RA, excessive osteoclastic activity may result in periapical lesions that are bigger and more

aggressive(36-38). Osteoblast suppression and impaired apoptosis are two factors that lead to poor regenerative outcomes and delayed lesion resolution in SLE(39).

Among patients undergoing biologic treatment (anti-tumor necrosis factor(anti-TNF) agents or interleukin-6 (IL-6) receptor blockers), Immune modulation may affect infection susceptibility and healing. Although these treatments have the potential to lower systemic inflammation, they may also impair the immune responses that are necessary for periapical containment(40, 41). Ironically, some reports indicate that patients receiving these therapies might heal better following endodontic procedures because they have fewer cytokine storms, although the results are still unclear. The development of granulomas or cysts is an additional crucial factor. Interleukin-10 (IL-10) and transforming growth factor beta (TGF-β), two cytokines that typically have anti-inflammatory functions, may be altered in autoimmune patients with persistent periapical inflammation(13, 42). A disturbance in their equilibrium could hinder the healing of lesions and encourage persistent granulomatous inflammation(43, 44).

Additionally, fibroblast dysfunction and impaired angiogenesis may compromise granulation tissue formation during healing. Sjögrens syndrome patients are especially vulnerable to the rapid progression of lesions because of the shift in oral microbiota brought on by xerostomia(3, 45). An increase in the colonization of acidogenic and proteolytic species, including Lactobacillus species and Streptococcus mutans, causes pulpal infections to worsen and speeds up demineralization. As a result, periapical lesions might appear sooner and be more challenging to clean using standard root canal techniques(46). Revascularization and collagen matrix deposition are also necessary for the healing of periapical lesions(47). These processes are postponed in autoimmune patients who have microangiopathy and defective fibroblast function. Radiographic persistence of lesions despite clinical resolution may be explained by histological analyses, which have revealed that healing in such cases frequently results in fibrotic scar tissue rather than normal bone regeneration. Finally, using immunosuppressants and corticosteroids may obscure periapical diseases' clinical and radiological manifestations(48). Corticosteroids may conceal an active infection by lowering inflammatory markers and inhibiting the formation of radiolucency(49). Therefore, to accurately evaluate treatment success, clinicians must rely on a combination of symptoms, microbiological findings, and extended follow-up(14).

Endodontic management and therapeutic considerations

In addition to technical proficiency, treating pulpal and periapical diseases in patients with autoimmune disorders necessitates knowledge of the systemic factors influencing local tissue responses(41). A complete medical history is essential and should include information on current medications, disease activity, immunosuppressive history, and bone metabolism. It is important to anticipate delays in healing. Bioactive materials with antimicrobial qualities and the ability to promote hard tissue formation may be beneficial for these patients(50-52). Because they can release calcium ions and create alkaline pH environments that are detrimental to bacterial survival, materials like calcium-enriched bio-ceramic sealers, mineral trioxide aggregate (MTA), and bio-dentine have shown improved healing in compromised hosts(53). In addition to guaranteeing sustained antimicrobial action, autoimmune patients may benefit from longer intracanal medication use, such as calcium hydroxide(54, 55). Regenerative endodontic procedures that depend on scaffold placement and stem cell recruitment may be less predictable in situations where chronic periapical lesions persist because of compromised cellular response(56, 57). Therefore, a cautious strategy that emphasizes thorough sealing and disinfection is frequently more realistic. Photodynamic therapy and laser-assisted irrigation

could be used as supplements to enhance canal disinfection, particularly in patients with weakened immune systems who are more likely to experience recurring infections(58, 59). Antimicrobial efficacy is provided by these modalities without exclusively depending on host immune activation. Prophylactic antibiotic use is usually not necessary for all autoimmune patients, but it might be necessary for those on high-dose immunosuppressants or for those whose disease is poorly managed, especially if they exhibit systemic infection symptoms(60, 61). Shorter follow-up times and long-term clinical and radiographic monitoring of healing are recommended. Care coordination frequently requires communication with the patient's rheumatologist, endocrinologist, or immunologist, especially when immunosuppressive medications need to be temporarily adjusted during acute dental infections. Therefore, depending solely on the symptoms reported by the patient may not be a reliable indicator of the state of the disease; additional diagnostic procedures like quantitative sensory testing or cone-beam computed tomography (CBCT) may be helpful.

Conclusion

The development course and resolution of pulpal and periapical diseases are significantly impacted by autoimmune conditions. Conventional endodontic care is complicated by alterations in immune responses, compromised vascular and cellular functions, and the systemic effects of immunosuppressive therapies. These patients are more likely to experience atypical healing, chronic inflammation, and treatment failure. When treating pulpal and periapical pathology in this population, dentists need to take a more knowledgeable and customized approach. Immunomodulatory treatments, regenerative methods, and improved diagnostic tools could all contribute to better results. Clearer clinical guidelines and a deeper comprehension of the cellular and molecular mechanisms underlying these intricate interactions should be the goals of future research. The future studies should focus on investigating the exact effect of each existing autoimmune disease and its treatment on the pulpal and periapical tissues.

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