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Potential relationship between periodontal diseases and eye diseases

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ABSTRACT

Periodontal diseases are inflammatory lesions initiated by oral bacteria and lead to the destruction of the supporting structures of the teeth (gingiva, periodontal ligament and alveolar bone) in susceptible patient. Via several biological mechanisms, periodontal diseases have been associated with multiple systemic diseases, such as rheumatoid arthritis, diabetes, cardiovascular diseases, Alzheimer's disease and adverse pregnancy outcomes. Similarly certain eye diseases have been associated with systemic diseases of the inflammatory pathway. We hypothesized that periodontal diseases are associated with eye diseases. Thus using literature data we find that several studies have reported that eye disorders are associated with the presence of periodontal diseases. But the mechanisms of this relationship are not clear. However the innate immune response involvement, the sharing of similar risk factors in pathogenesis and the changes of eye choroid thickness may be suggested as several hypotheses to explain this potential association.

Introduction

Periodontal diseases (PDs) are inflammatory lesions initiated by oral bacteria that lead to the destruction of the supporting structures of the teeth (gingiva, periodontal ligaments and alveolar bone) in susceptible patients [1,2]. Via several biological mechanisms, PDs are associated with multiple systemic diseases, such as rheumatoid arthritis, diabetes, cardiovascular diseases and Alzheimer's disease, and with adverse pregnancy outcomes [3–10]. Similarly, certain eye diseases (EDs) have been associated with systemic inflammatory diseases [11–15]. We thus hypothesized that PDs are associated with EDs. The objective of this article is to highlight this association.

Epidemiological evidence of an association between periodontal diseases and eye diseases

The possibility that dental infection induces eye problems has been demonstrated [16–22]. Sepic et al. reported that persons with dental inflammation had central retinitis [17]. Similarly, a significant correlation between uveitis and dental infections was reported [16]. However, the evidence of an association between PDs and EDs is fairly recent. A summary of relevant studies and their results is presented in Table 1. A case report indicated that gingival fibromatosis is associated with many eyes issues, such as bilateral congenital cataracts, esotropia, and high myopia [23]. Hujoel used US diabetic data (NHANES III, 1988–94) to show that persons with gingivitis had a 57% increased risk of retinal haemorrhage [24]. This finding suggests that gingivitis is associated with retinitis. Recently, we reported that the increasing data in this subject area suggest a link between PDs and age-related macular degeneration (AMD) [25,26], which is the most important cause of irreversible central visual loss in people older than 60 years [27,28]. Using the US NHANES III data (1988–94), the relationship between PDs and AMD was assessed among 5887 individuals [26]. After controlling for confounding factors, the authors reported that PDs are independently associated with AMD in those aged 60 years or younger, but not in older patients (odds ratio = 1.96, $p = 0.006$) [26]. Similarly, alveolar bone analysis of 1751 individuals in Finland showed that PDs were independently associated with AMD in males ($p < 0.05$). This relationship was not observed in women [25]. In this study, only participants who had more alveolar bone loss ($p < 0.001$) were found to have AMD [25]. Similar observations linking periodontal status and AMD have been reported [18]. In 56 patients with AMD, dental and periodontal check-ups were performed, including radiography [18]. The majority of patients showed inflammatory lesions in the oral cavity (235 lesions); most

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Table 1
Selected studies assessing the association between periodontal diseases, eyes diseases.

First author, date	Search focus	Study design	Observations
Sardella et al. (1998)	PD & corneal dystrophy	Case report	Generalized and severe periodontitis was associated with corneal dystrophy in DCCD
Guncu et al. (2011)	PD treatment & scleritis	Case report	PD therapy induce rapid resolution of scleritis and no recurrence
Hujoel et al. (2011)	Gingivitis & Retinitis	Cross-sectional study -Periodontal status -A1C concentrations	Gingivitis and Retinitis have mutual risk factor
Karesvuo et al. (2013)	ABL & AMD	Cross-sectional study 1751 individuals; ≥30 years Clinical and biological analysis	In Male, AMD et ABL: significative association In Female: AMD & ABL: no significative association
Tang et al. (2014)	Gingival fibromatosis & cataract	Case report	Bilateral congenital cataracts, esotropia, and high myopia were associated with gingival fibromatosis
Boillot et al. (2015)	PD & retinal microcirculation	Cross-sectional study -retinal diameter measured -periodontal evaluation	Significative association between severe periodontitis and larger retinal venular diameter in diabetic group ($p = 0.04$)
Wagley et al. (2015)	PD & AMD	Cross-sectional study 8208 individuals; ≥40 years	In patient ≤60 years, PD & AMD: significative association In patient >60 years: PD & AMD: no significative association

PD: periodontal disease; LRVD: larger retinal venular Diameter; Dermochondrocorneal dystrophy: DCCD; AMD: Age-related Macular degeneration; ABL: Alveolar bone.

lesions were in the periodontium (109 lesions), including teeth with deep pockets and high mobility [18]. Guncu et al. [29] reported that periodontal therapy was associated with the improvement of ED symptoms [29] in a 30-year-old female with persistent scleritis. In this patient, oral non-steroidal anti-inflammatory drugs and topical medications failed to alleviate her symptoms. Chronic periodontitis was detected, and after periodontal therapy, the scleritis showed rapid resolution, with no recurrence after 6 months [29]. The biological mechanism explaining these data remains unknown. These findings suggest that there is a relationship between PDs and EDs.

Plausibility of a potential relationship between periodontal diseases and eye diseases

The innate immunity involvment

Innate immunity has been suggested to play an important role in chronic inflammatory disease [30]. In periodontitis, pathogens induce a local inflammatory response and activate innate immunity through activation of Toll-like receptors (TLRs) [31]. This activation leads to the production of pro-inflammatory cytokines and the recruitment of phagocytes and lymphocytes into the inflammatory zone [32]. Meanwhile, in the retinal immune system, the retinal pigment epithelium (RPE) cells play a pivotal role in immune responses, and they express TLRs and are a rich source of cytokines, chemokines and growth factors [33,34]. The complement system is a pivotal actor in the innate immune system. Its activation through the classical, alternative, or lectin pathway produces several complement fragments (C3a, C5a, and C4a) that are frequently observed in the host response in ocular disorders [35–40] and periodontitis [41–43].

In the Chinese population, polymorphisms in the genes encoding the complement fragment C5 are associated with an increased risk of acute anterior uveitis [39]. Additionally, preclinical and clinical studies have demonstrated the role of the complement pathway in AMD pathophysiology [35].

Similar evidence has highlighted the implications of the complement pathway in PD pathogenesis [41,42,44–48]. The progression of induced gingivitis in four patients was correlated with an increased proportion of C3 complement cleavage in the gingival crevicular fluid [49]. Another study found that periodontal treatment led to a reduction of the C3 complement cleavage rate in human gingival crevicular fluid [46]. The beneficial effects of the use of complement inhibitors for the treatment of PDs have been recently demonstrated in a preclinical model [50–52]. Thus, complement dysfunction or alteration is considered to play an important role in PDs and EDs and could be a common pathway for these two diseases.

Many common risk factors for pathogenesis

The pathogenesis of PDs and certain EDs can be affected by many common risk factors, including age, cigarette smoking, higher body mass index (BMI), diabetes, and hypertension [53–56]. In addition, PDs and EDs occur in several pathologies [57]. In dermochondrocorneal dystrophy (DCCD), gingivitis and gingival hyperplasia are observed in addition to corneal dystrophy and xanthomatous nodules [58,59]. In a 42-year-old woman with classical DCCD symptoms (including reduction of visual acuity), both generalized periodontitis and severe periodontitis were reported [59]. In similar situations, severe periodontitis and retinal microcirculation alteration were observed together in patients with type 2 diabetes [60].

Evidence suggests that local or systemic inflammation plays a key role in specific EDs, such as AMD [61–63]. In PDs, the host response against periodontal pathogens induces persistent inflammation, which may extend to EDs [42,64]. In addition, increased levels of C-reactive protein (CRP) have been associated with an increased risk of developing AMD and PDs, suggesting that an inflammatory pathway is a plausible link between PDs and EDs [65–69].

Eye choroid thickness

The eye choroid is an important structure of the outer retina that plays a key role in eye physiopathology [70]. Thin eye choroids have been associated with various ocular disorders [71–74] and general diseases, including metabolic, cardiovascular and inflammatory diseases and other disorders [10,75–77]. Certain authors have proposed the use of eye choroid thickness as an indicator of systemic disease [78]. However, no study has compared the structure of the choroid between people with and without periodontitis.

Conclusion

Several studies have reported that EDs are associated with the presence of PDs [18,25,26]. The mechanisms of this relationship are not clear. Therefore, further epidemiological and interventional