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Exploring the Association between Atopic Dermatitis and Oral Health

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Abstract: ***This review explores the intriguing interconnection between atopic dermatitis (AD) and periodontitis by reviewing diverse studies. Studies examining cytokine and protease levels in gingival crevicular fluid have shown elevated IL-31, a key mediator in AD, potentially linking it to periodontal disease progression. Studies on oral symptoms highlight significant associations between AD and poor oral health. Animal studies have shown AD to exacerbate periodontitis and correlate with its severity. These findings illuminate potential pathophysiological links between AD and Periodontitis, urging further research into common mechanisms and offering prospects for novel personalized therapeutic interventions targeting this relationship.***

Keywords: atopic dermatitis, periodontitis, cytokines, oral health, therapeutic interventions

1. Introduction

Atopic Dermatitis (AD) is a chronic and relapsing inflammatory skin disorder that is characterized by pruritus, erythema, edema, and excoriation. It commonly presents in a biphasic manner with the highest prevalence in early childhood and late adulthood. AD has a multifactorial etiology which involves interplay of genetic susceptibility, immune dysregulation, skin barrier dysfunction, and environmental triggers [1].

Periodontitis is a chronic and inflammatory condition of the oral cavity that affects the supporting structures of the teeth namely, the gingiva, the periodontal ligament and the bony alveolar socket [1]. It also has a multifactorial etiology encompassing hereditary, immunological, infectious and inflammatory factors [1]. Over the years, the association between these two seemingly-unrelated entities, AD and periodontitis has been examined in literature but no consensus has been reached as of yet. This commentary aims to examine the existing literature on this topic in order to derive a possible relationship between the two diseases.

2. Review

Jimenez et al. [1] and Valenzuela et al. [2] both examined gingival crevicular fluid (GCF) of patients with moderate-to-severe atopic dermatitis and compared it with that of healthy controls. Jimenez et al. [1] found that GCF levels of interleukin (IL)-31 and thymic stromal lymphopoietin (TSLP) were significantly higher in patients with moderate-to-severe atopic dermatitis than those in the control group. IL-31 is a crucial cytokine involved in the clinical manifestations of AD. It is a member of the IL-6 cytokine family and exerts pro-inflammatory effects [3]. IL-31 is constitutively expressed in $CD4^+$ Th2 cells, monocytes/macrophages, dendritic cells, and certain non-immune cells [3]. Specifically, it plays an important role in the development of severe pruritus that is characteristic of this condition [1]. Recent studies have shown that increased levels of IL-31 in GCF can be a factor in the progression of periodontal disease. An in vitro study showed that the Porphyrormonas (P.) gingivalis increased the expression of IL-31 receptor (IL-31R) in human gingival epithelial cells [3]. The study demonstrated that IL-31 expression was not increased in mast cell deficienct WBB6F1-W/W^v mice, but was greatly increased in the wild type group [3]. P. gingivalis induces an increase in IL-31 in a mast cell dependent manner [3].

While Jimenez et al. [1] focused on cytokine levels in GCF, Valenzuela et al. [2] analyzed protease levels in GCF. They found significant decrease in the levels of zinc-binding ADAM8, ADAM9, MMP8, Neprilysin/CD10, aspartyl-binding Cathepsin E, serine-binding Protein convertase9, and Urokinase proteases in GCF in AD group as compared to controls [2]. Of these, ADAM9, MMP8, and Cathepsin E were of the highest sensitivity and specificity when it came to the detection of AD. Having tested a total of 35 proteases, they found no significant difference in the levels of the remaining 28 proteases [2]. While this study showed that low levels of MMP8 were significantly associated with AD, high levels of MMP8 in GCF have been associated with periodontitis [2][4].

Shim et al. [5] used survey data in order to investigate the association between AD and oral health in Korean adolescents. They found that AD was significantly associated with four symptoms of poor oral health namely bad breath, sensitive teeth, aching teeth, and gum bleeding. Wee et al. [6] conducted a similar study on a similar population as Shim et al. [5], however, they considered the symptoms of tongue or cheek pain and broken or chipped teeth in addition to the aforementioned four symptoms. The results were stratified into good, moderate and poor oral health based on the number of symptoms present. The association between AD and oral health was statistically significant across all the strata, with higher adjusted odds-ratios for the association between AD and poor oral health as compared to good oral health [6]. In contrast to Shim et al.[5] and Wee et al. [6], Silverberg et al.[7] found that severe AD was significantly associated with bleeding gums and toothache but not with tooth decay and broken teeth in a

population of children and adolescents from the United States.

Park et al. [8] also found that AD was significantly associated with decayed, missing, filled teeth (DMFT) in a population of Korean adults with the mean DMFT index being significantly higher for the AD group as compared to the non-AD group. Smirnova et al. [9] conducted a cross-sectional study on Swedish adults and found that AD was significantly associated with periodontitis, dental caries, tooth sensitivity, dry mouth and bleeding gums. Igawa et al. [10] found a 30% prevalence of odontogenic focal infections (OFI) in patients of AD who were resistant to conventional therapy, a statistic much higher than that of the general population. Their hypothesis that OFI could be involved in the exacerbation of atopic dermatitis was further validated when they found that patients with OFI showed better skin health on a three month dental care plan as compared to those without OFI on this plan [10].

Liu et al. [11] investigated the association between AD and periodontitis in mice. They first induced AD in mice followed by the induction of periodontitis. Specimens of the gingiva were examined for histopathological and cytological changes. Dynamic transcriptome changes were understood from RNA sequencing of the oral mucosal cells. To detect changes in the oral microbiota, 16S rRNA analysis was done. They found that mice with AD showed pro-allergic and inflammatory changes in the oral mucosa but not periodontitis while mice in the periodontitis group had elevated levels of IL-4. They also found that AD produced changes within the gut microbiome. Their study showed that AD worsened periodontitis when present and the severity of AD correlated with the severity of periodontitis [11].

3. Conclusion

The body of evidence examined, from cross-sectional to case-control to experimental studies, has shown a relationship between atopic dermatitis and poor oral health. Inflammatory and immune-mediated mechanisms have been suggested in the pathophysiology of periodontitis in patients of atopic dermatitis. The mechanistic understanding of both these diseases and the potential for therapeutic applications warrants further research in terms of experimental and clinical studies.

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