REVIEW

Periodontitis in oral pemphigus and pemphigoid: A systematic review of published studies

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Periodontitis and autoimmune bullous diseases, including pemphigus vulgaris and mucous membrane pemphigoid, are immunoinflammatory disorders leading to microbial plaque- and autoantibody-elicited tissue injury of the oral cavity, respectively. Evidence indicates that these autoimmune conditions may represent a risk factor for periodontitis, but no systematic evaluation exists to corroborate this assumption. A systematic literature review of periodontal status in pemphigus and pemphigoid was conducted. Electronic searches using PubMed from inception to July 2016 identified 10 studies meeting predetermined inclusion and exclusion criteria. Most reported some correlation between poor periodontal health and both oral pemphigus vulgaris and mucous membrane pemphigoid. Some demonstrated beneficial effects of oral hygiene procedures on periodontal parameters and clinical disease severity of the established blistering diseases. Inconsistent results were found between studies and within analyzed patient cohorts, likely because of methodological shortcomings. This review preliminarily suggests that patients with oral pemphigus vulgaris and mucous membrane pemphigoid appear somewhat more susceptible to periodontitis, which in turn may potentially trigger the bullous disorders. These patients should be encouraged by dermatologists to pursue collaborative professional periodontal follow-up with dentists. The true relationship and mutual interaction between both diseases needs to be more comprehensively addressed in well-designed prospective studies. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.10.028.)

Key words: autoimmune disease; mucous membrane; pemphigoid; pemphigus; periodontal status; periodontitis.

Pemphigus and pemphigoid diseases are rare and potentially fatal autoimmune disorders characterized by antidesmosomal and antihemidesmosomal autoantibody-induced intraepithelial and subepithelial split formation, respectively. Clinically, these diseases manifest as blisters and erosions on the skin and close-to-surface mucous membranes.[1,2]

Pemphigus vulgaris (PV) and mucous membrane pemphigoid (MMP) represent the major subtypes of autoimmune bullous diseases that most commonly and predominantly affect the oral mucosa; both usually require long-term immunosuppressive treatment.[1,2] Although any area in the oral cavity can be involved, gingival sloughing with erythema and erosive and/or vesiculobullous lesions is, especially in MMP, a common finding. This is referred to as desquamative gingivitis.[3] In PV, mucosal lesions are classically caused by autoantibodies to desmoglein 3. In MMP, the autoantibody response can be directed against different autoantigens of the basement membrane zone, of which type XVII and VII collagen along with laminin 332 are best characterized.[1,2]

Abbreviations used:

IL:	interleukin
MMP:	mucous membrane pemphigoid
PV:	pemphigus vulgaris

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Periodontitis is a chronic inflammatory disease that affects the tooth supporting structures. It can lead to progressive injury of the soft tissue, ligaments, and alveolar bone, resulting in potential loss of affected teeth. Periodontitis is multifactorial in nature being influenced by genetic and environmental risk factors, such as smoking, and associated with accumulation of microbial plaque.[4,5]

It has been discussed that oral lesions such as desquamative gingivitis could play a role in increasing the risk for periodontal tissue breakdown in patients with oral autoimmune bullous diseases.[6-15] This potential influence may possibly be indirectly based on plaque accumulation as a result of pain-related compromised oral hygiene practices and less frequent dentist visits for checkups and cleanings. Immunosuppressive treatment-associated reduced immune response to periodontal pathogens could represent another possibility. Direct effects related to possible shared pathogenic mechanisms between autoantibody-induced and bacterial-elicited inflammatory tissue damage may also be plausible.[2,5]

Because the potential link between autoimmune blistering disorders affecting the oral mucosa and periodontitis is not fully understood, a systematic review of published studies that addressed the periodontal status in these diseases has been conducted.

CAPSULE SUMMARY

- Co-occurrence of immunoinflammatory periodontitis and oral pemphigus/pemphigoid has been documented.
- Most studies have demonstrated a correlation between compromised periodontal status and pemphigus vulgaris or mucous membrane pemphigoid.
- Follow-up with dentists should be suggested for these patients.

METHODS

The literature for this review from inception to July 2016 was comprehensively searched using the US National Library of Medicine National Institutes of Health PubMed by 2 independent researchers and checked by a third researcher separately. The key words used in this search consisted of "*pemphigus*" or "*pemphigoid*" combined with "*periodontitis*" or "*periodontal*." The inclusion criteria were peer-reviewed full-length original articles related to the search terms and indexed in the above-mentioned database. Reviews, single case reports, and articles not related to both pemphigus/pemphigoid and periodontitis were excluded.

RESULTS

A total of 44 different citation hits related to the terms used in the electronic literature search were retrieved. After critical screening of titles, abstracts, and full text, 10 original articles were suitable in this review. These comprised case-control and pilot studies on periodontal disease, of which 4 were related to patients with PV (n = 94) and 6 to patients with MMP (n = 65).[6-15] These studies are summarized in Supplemental Table I (available at http://www.jaad.org).

Diagnosis of PV and MMP was based on characteristic clinical disease features confirmed by histopathologic and/or direct immunofluorescence microscopic analysis without performing immunoserologic tests in all but 1 study,[7-15] in which diagnostic criteria were not reported.[6] In the majority of articles (70%), the analyzed cohorts were mainly composed of women, which was particularly marked among MMP but not patients with PV (female:male ratio 4:1 and 0.88:1, respectively). The mean age ranges for patients with PV and MMP were 35 to 60 years and 54 to 76 years, respectively. In all, 3 articles reported subjects with a smoking history, 3 reported subjects without a smoking history,[8,10-13,15] and 4 did not mention smoking status.[6,7,9,14] Some studies established diabetes mellitus, cardiovascular disease, infectious disease, and/or any systemic disease other than the autoimmune bullous disorder as exclusion criteria,[8-11,13,14] whereas the others did not specifically address comorbidities.[6,7,12,15] PV and MMP lesions were reported to affect the oral/gingival mucosa in all but 1 study,[7-15] in which the precise location of PV lesions was not described.[6] Except for 1 study reporting an exclusive gingival localization of MMP,[13] information on the clinical status of other mucosal sites or concomitant cutaneous disease manifestation was generally lacking. In most articles (80%),[6,8-12,14,15] the duration of disease symptoms was not reported or specified. Considering the medication of patients, 4 articles reported no pharmacologic treatment,[12-15] and 1 study did not specify the drug therapy.[8] In the remainder of the studies, treatment included systemic/topical corticosteroids, azathioprine, and dapsone.[6,7,9-11]

Seven studies more or less broached the relationship of patients with oral PV along with MMP and periodontitis. These investigations indicated that worse periodontal disease parameters exist compared with control populations or unaffected gingival sites.[7,8,10-13,15] Inconsistent results were