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Cancer and periodontium : A review of the literature

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Abstract:
Objectives*: Periodontal disease has been linked to many systemic diseases and conditions. The purpose of this paper is to review the literature to explore the evidence to date of a relationship between periodontium, its diseases and cancer.*
Data/sources/study selection*: In this review, articles between the years 2000 and 2019 studying the relationship between periodontium and periodontal diseases with increased risk of several types of cancers, its clinical features and management were reviewed.*
Conclusions: *Studies to date indicate a positive correlation between several forms of cancer and periodontal disease. The molecular pathways underlying the roles of oral bacteria and periodontitis in Cancer pathogenesis require further research, since their current comprehension would preclude us from drawing conclusions about a causal relationship.*
Key Word*: human papilloma virus(HPV), head and neck cancer(HNC), human telomerase reverse transcription(hTERT) enzyme, osteoradionecrosis.*

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I. Introduction

Periodontal disease has been linked to many systemic conditions such as, cardiovascular disease, low-birth weight complications in pregnancy, diabetes, and, pulmonary disease[1]. More recently, a link between periodontal disease and cancer has been suggested through several studies looking both at specific types of cancers and at the overall total cancer rate and the relationship to periodontal disease[2].

Cancer is among the leading causes of global mortality and oral and pharyngeal cancers are its most common forms[3]. Several narrative reviews have reported an association between tooth loss, periodontal disease and cancer[4,5,6]. It has been suggested that patients with periodontal disease are at a greater risk of having various forms of cancer including pancreatic, skin, colon, breast, kidney, haematological cancers as compared to those without periodontal disease [7]. It is probable that dental biofilms and the resulting dysbiosis can lead to a variety of oral diseases, including cancer[8].

Javed et al in 2016 conducted a systematic review to assess any possible association between periodontal disease(PD) and oral cancer(OC) and to discuss the role of chronic inflammation of the periodontium as a link in the causation of cancer. The systematic review concludes that PD is associated with a small but significant increase in risk for OC and in several reported studies this association was attenuated following adjustment for tobacco and alcohol use[9]. The purpose of this article is to critically review the current literature reporting the association between periodontium and its disease with that of several types of cancer along with overall cancer risk, cancer therapy and considerations in managing cancer patients.

Periodontal considerations in diagnosis of cancer

Malignant diseases may present with gingival and periodontal involvement. Many cases have been reported of gingival squamous cell carcinoma presenting clinically similar to inflammatory periodontal or periodontal/endodontic lesions. Cases of other types of cancer mistaken for periodontal disease such as metastatic pancreatic cancer and osteogenic sarcoma have also been reported. Other malignancies, such as those of the hematopoietic system, may present with periodontal involvement prior to and following the diagnosis of the systemic disease.

Oral manifestations are important initial symptoms in the early detection of Leukemia. In approximately 25% of the patients with AML, dentists are involved in the diagnosis[10]. As gingival enlargement is one of the earlier signs of AML, early diagnosis and intervention can improve a patient's chances of remission[11].

Periodontal diseases and cancer

Epidemiologic studies have associated tooth loss and/ or periodontal disease with higher risk of cancer at several sites including the oral cavity, stomach, pancreas and lung. Periodontal diseases have also been implicated in the elevated risk of the occurrence and/or advancement of hematopoietic cancers. However, the exact mechanisms underlying these associations are far from being fully understood. Still, high expression of the human telomerase reverse transcription(hTERT) enzyme was demonstrated in patients with periodontitis[12], suggesting that both periodontitis and cancer share an important disease-oriented pathway linked to cellular differentiation and immortality.

Consistent increased risk was noted in studies of oral and esophageal cancers and periodontal disease. Gastric and pancreatic cancers had an association in most studies. Lung, prostate, hematologic and other cancers were less consistently associated or did not have sufficient studies to determine a predictable pattern5.

Periodontitis was demonstrated to increase the probability of having oral leukoplakia, a premalignant lesion, in a dose dependent manner[13]. Data obtained from NHANES III indicate that the severity of periodontitis was found to be markedly associated with both precancerous lesions and oral cancer[14]. Moreover, orodigestive cancer mortality was shown to be elevated according to the severity of periodontitis[15]. Likewise, periodontitis increased the risk of developing head and neck squamous cell carcinoma, particularly in the oral cavity, in a large clinical sample[16].

A history of alveolar bone loss due to chronic periodontitis was associated with the presence of the human papilloma virus(HPV) infection in tumors of head and neck cancer(HNC) patients, particularly with oropharyngeal cancer[17]. Although in some small studies, tobacco or alcohol use and socioeconomic confounders attenuated the association between periodontitis and OC, overall findings of a recent systematic review concluded that periodontitis is likely to be associated with increased HNC risk[18].

Cancer therapy and periodontium

Surgical resection, radio- and chemotherapy, either used singly or in combination, are the three most common modalities used in cancer treatment. Although these modalities are effective in eradicating the tumor, they also negatively impact the normal structures surrounding the tumor and other areas of body. Direct damage to soft and hard tissues of oral cavity can occur from radio- and chemotherapy, and indirect damage can arise from systemic toxicity.

Reported acute oral complications are mucositis, xerostomia, dysphagia, dysguisia, and opportunistic infections, and chronic complications includes trismus, irradiation caries, osteoradionecrosis, and changes in periodontal attachment. The long-term effects include alteration in vascularity of soft tissue and bone, salivary gland damage, reduction in cellularity of connective tissue, and risk of increased collagen synthesis which results in fibrosis[20].

Radiotherapy(RT) has cytotoxic effects on both normal cells and malignant cells, causing hypoxia, hypocellularity and hypovascularity. The peridontium is sensitive to the effect of radiation at high doses. Decreased vascularity and cellularity of the periodontal membrane with rupturing, thickening, and disorientation of Sharpey's fibers and widening of periodontal space have been reported[21].

The direct and indirect effect of high-dose RT on the periodontium possess increased risk of periodontal attachment loss and tooth loss. Blood vessels in the periodontium are affected leading to widening of periodontal ligament space and destruction of bony trabeculae. These changes may result in increased risk of periodontal disease and altered healing with impaired capacity for bone remodelling and repair.

Patients scheduled to undergo RT should receive a comprehensive dental assessment before starting therapy. Many of the oral complications associated with RT may cause discontinuity in the cancer treatment if not properly addressed. Maintenance of good oral hygiene in patients undergoing RT may reduce morbidity of the known oral and periodontal side effects.

Oral complications due to cancer treatment have an impact on quality of life, increase the cost of care, and prolong or compromise cancer treatment. It is recognized that oral care is an essential part of the overall care of cancer patients[19].

Periodontal treatment planning for cancer patients

Periodontal disease should be assessed and managed prior to medical treatment of cancer and for patients in whom neutropenia may develop during treatment. Pretreatment assessment and management, and maintenance of oral hygiene have been shown to be effective in preventing oral and systemic complications during treatment. A complete oral and periodontal examination should be done for all patients planned to receive head and neck radiation therapy and oral and periodontal care must continue following cancer therapy.

A prospective clinical study on patients undergoing radiotherapy to the head and neck region with or without chemotherapy, do not show aggravations of their clinical periodontal status for up to 6 months after cancer treatment if they also receive periodontal therapy and maintenance[21]. Evidence indicates that the failure

rate of dental implants is higher in irradiated patients. Therefore, clinicians should wait for a partial recovery of vascularization and the emergence of a new bone formation, which usually occurs within 3 to 6 months after radiotherapy, prior to implantion[22].

II. Conclusion

Cancer rises in frequency with age, and advanced age is no longer an exclusion criterion for intensive chemotherapy and radiotherapy. Since the prevalence of periodontitis also increases with age, it can be anticipated that more patients suffering from this condition will receive cancer therapy than in the past. Given the evidence to date, it would be beneficial to the dental provider to be aware of the real potential that periodontal disease may exist as a risk factor for many forms of malignancy. Additional studies are needed to explore these suggested associations.

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