

Relationship between Porphyromonas gingivalis and oral cancer: A short review

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Abstract:

The oral cavity is populated by various bacterial species. Some of them play a key role in causing oral disease. In recent years, interrelationships between oral microbiomas and systemic conditions such as head-and-neck cancer have become increasingly evident. Emerging evidences link oral cancer with key periodontal pathogenic bacteria's. This review analyse the existing evidences on the role of key periodontal pathogen Porphyromonas gingivalis in the pathogenesis of oral squamous cell carcinoma.

Key Words: oral cancer, Porphyromonas gingivalis, squamous cell carcinoma

Introduction:

Oral cancer includes malignant neoplasms, predominately oral squamous cell carcinoma (OSCC) which develops from the lip and mouth lining mucosa (oral cavity) including the anterior two thirds of the tongue as defined in the International classification of disease. ^[1]

The prevalence of oral cancer among men, the eighth most common cancer worldwide, is particularly high. Rates of incidence for oral cancer differ in many countries in men from 1 to 10 cases per 100000 populations. ^[2] It ranks among the three most common cancer forms cancer in South Central Asia. The age- standardized rate of incidence of oral cancer in India is 12.6 per 100000 populations. ^[3]

Smoking forms (e.g. cigarette smoking, cigars, beedies and pipes) and smokeless forms (e.g. betel quid (with or without tobacco), other forms of areca nut use) of tobacco use, is found to be the major risk factors for OSCC. ^[4, 5] Heavy alcohol, viral infections (e.g. human papilloma virus) and chronic inflammation are believed to play an adjuvant role in the development of OSCC. ^[6, 7, 8]

Periodontitis is a common oral cavity disease characterized by the progressive degradation of supporting teeth structures due to chronic inflammatory changes due to the host response to periodontal pathogens. ^[9] The red complex organisms which include Porphyromonas gingivalis, (P.gingivalis) Tannerella forsythia (T.forsythia) and Treponema denticola (T.denticola) are the key periodontal pathogens involved in the pathogenesis of chronic adult periodontitis. ^[10]

They are essentially opportunistic pathogens and can exist in commensal harmony with the host. Shift in the microbial ecological balance and dysregulated immune response result periodontal disease which is characterized by the chronic inflammation. ^[11]

Chronic or dysregulated inflammation has long been seen to lead to tumour growth, in part through tumor microenvironment modulation. ^[12, 13] Hence the analysis of the relationship between oral squamous cell carcinoma and proven periodontal pathogens is of recent interest to the researchers. The current review is updating the information available on the role of red complex microbes in OSCC.

P.gingivalis in OSCC:

P.gingivalis is one of the main pathogenic species responsible for chronic adult periodontitis and it belongs to the phylum Bacteroidetes. It was formerly named *Bacteroides gingivalis* until its reclassification into a separate genus as *Porphyromonas*.^[14]

It is an asaccharolytic, non-motile obligatory anaerobic, gram-negative bacteria and documented to be seen in 85.75% of subgingival plaque samples from chronic periodontitis patients.^[14]

It is known to produce a variety of virulence factors capable of penetrating periodontal tissue resulting in tissue destruction by induction of chronic inflammation in the susceptible host individuals.^[14]

The organism has a variety of virulence factors, including fimbriae, capsules, lipopolysaccharides (LPS), lipoteichoic acids, haemagglutinins, gingipains, outer membrane proteins, and outer membrane vesicles, which are responsible for effective host tissue colonization, contributing to chronic inflammation induction and retention.^[14]

Chronic inflammation, thought to play a crucial role in all stages of cancer including induction, growth, invasion and metastasis, was anticipated as one of the possible pathways by which bacteria contribute to oral cancer.^[12, 13]

There are few studies published in the past that relate the role that *P.gingivalis* plays in OSCC.

Nagy et al. in 1998^[15] cultivated the surface swab collected from oral cancer lesions and subsequently observed that the species of *Porphyromonas* in the OSCC tissue region were significantly higher than the adjacent normal mucosa of the same individuals

In 45 cases of OSCC and 229 normal controls, Mager et al. in 2005^[16] using checker board DNA-DNA hybridization analysed the salivary counts of 40 specific oral bacteria and they identified elevated levels of *P. gingivalis*, *Prevotella melaninogenica* and *Streptococcus mitis* species in OSCC cases compared to normal controls.

When these variations in the salivary counts of the aforementioned species were used as diagnostic criteria between OSCC cases and controls, it was possible to differentiate cases and controls with 80 percent sensitivity and 83 percent specificity.

Subsequently, Katz et al. in 2011^[17] analyzed the parts of gingival squamous cell carcinoma immunohistochemically and noticed the staining strength for P. Gingivalis is higher relative to the healthy gingival tissue, which suggests higher colonization in the cancer tissue.

Schmidt et al. in 2014^[18] using next generation sequence technology, studied the swabs from the OSCC lesion surface and contra lateral normal oral mucosa in 18 OSCC patients, eight pre-cases and nine normal controls. In OSCC cases both on the lesion surface and contralateral mucosa bacterial species (P.gingivalis) of phylum bacteroidetes were found to be present significantly in higher proportions compared to the precancer cases and normal controls.

Peters B.A et al. 2017^[19] in their nested case control study involving the 25 cases of oesophageal squamous cell carcinoma with 50 matched controls concluded that high presence of P.gingivalis correlated with high risk of oesophageal squamous cell carcinoma.

Conclusion:

In vitro analysis utilizing the OSCC cell lines suggest that P.gingivalis promotes the development of oral cancer at various stages including epithelial mesenchymal transformation, neoplastic proliferation, and invasion of malignant cells. Excluding the few mentioned above, clinical studies on the role of P.gingivalis in oral cancer are minimal.

Other red complex microbes T.forsythia and T.denticola although indicated as proven periodontal pathogens, studies on their role in OSCC pathogenesis are extremely limited except for few recent studies that suggest involvement of T.denticola chymotrypsin like proteinase in early oral cancer.^[20, 21]

Establishing the role of red complex microbes in the OSCC with further clinical studies would therefore strengthen the importance of better oral hygiene and early treatment of periodontitis, which will further restrict the development of oral cancer.

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