ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 04 | April - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

FIELD CANCERISATION IN ORAL CANCER AND THE CLINICAL IMPLICATIONS: CURRENT EVIDENCE

Dental Science

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ABSTRACT

Field cancerisation is a critical concept in understanding the multifocal and recurrent nature of oral squamous cell carcinoma (OSCC). First introduced in the 1950s, it recognizes that exposure to carcinogens produces widespread genetic alterations across the oral mucosal surface, forming a "field" of predisposed epithelium prone to neoplastic transformation. These alterations may be present in clinically normal tissue adjacent to tumors, contributing to second primary tumors and local recurrence even after complete resection. Molecular evidence, including mutations in TP53 and clonal expansions, supports this phenomenon. Advances in genomic sequencing and immunohistochemistry have further elucidated the mechanisms behind field formation, including roles for cancer stem cells and genetic instability. Recognizing field cancerisation has major implications for diagnosis, treatment, and surveillance in OSCC, highlighting the need for molecular-level assessments beyond routine histopathology. Improved understanding may drive better preventive and management strategies in high-risk populations.

KEYWORDS

Mouth Neoplasms, Field Cancerization, TP53 Protein, Oral Squamous Cell Carcinoma

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancies of the head and neck region, particularly in populations exposed to tobacco, alcohol, and areca nut. Despite advances in surgical and adjuvant therapies, OSCC continues to show high rates of local recurrence and second primary tumors. Traditional models of carcinogenesis viewed oral cancer as a localized disease arising from a single transformed cell. However, clinical observations of multicentric tumors and recurrences distant from the primary site challenged this notion.

The concept of field cancerisation was introduced to explain these phenomena and has since become central to understanding oral carcinogenesis.

Historical Background of Field Cancerisation

The term field cancerisation was first introduced by Slaughter et al. in 1953, based on their observations in oral cancer patients [1]. They noted that histologically altered epithelium extended beyond the visible tumor margins and that multiple independent carcinomas could arise within the same anatomical region. This led to the proposal that exposure to carcinogens produces a "field" of altered epithelium with increased malignant potential.

Subsequent studies expanded this concept beyond oral cancer to include malignancies of the upper aerodigestive tract, lung, and skin. The field cancerisation theory fundamentally shifted cancer biology from a single-cell origin model to a multifocal epithelial disease model, especially relevant in head and neck oncology.

Etiological Factors Contributing to Field Formation

Chronic exposure to carcinogens plays a crucial role in the development of field cancerisation. Tobacco smoke contains multiple mutagens capable of inducing DNA damage, while alcohol acts as a solvent enhancing mucosal penetration of carcinogens. Areca nut and betel quid chewing, prevalent in South Asian populations, contribute to oxidative stress and genetic instability in oral epithelial cells [2].

These agents do not act locally but affect wide mucosal surfaces, explaining why genetic alterations may be detected in clinically normal mucosa distant from the primary tumor site.

Molecular Basis of Field Cancerisation

Advances in molecular biology have provided substantial evidence supporting the field cancerisation concept. Early genetic events include mutations in tumor suppressor genes, particularly TP53, and loss of heterozygosity (LOH) at chromosomal regions such as 3p, 9p, and 17p [3].

These alterations can occur in histologically normal epithelium, indicating that genetic damage precedes morphological dysplasia. Accumulation of additional mutations leads to clonal expansion and progression toward malignancy.

Braakhuis and colleagues proposed a genetic model explaining field cancerisation, suggesting that a single genetically altered stem cell can clonally expand and spread laterally across the epithelium, creating a large precancerous field [4].

Clonal Expansion and Field Patterns

Field cancerisation can manifest through different patterns of genetic evolution. In the monoclonal theory, a single progenitor cell acquires initial genetic alterations and expands to form a field, from which multiple tumors may arise. In contrast, the polyclonal theory suggests that multiple independent cells undergo malignant transformation within the same field due to uniform carcinogen exposure [4].

Both mechanisms are supported by molecular studies, indicating that OSCC may arise through heterogeneous pathways even within the same patient.

Field Cancerisation and Oral Potentially Malignant Disorders

Oral potentially malignant disorders (OPMDs) such as leukoplakia, erythroplakia, and oral submucous fibrosis are often considered clinical manifestations of field cancerisation. These lesions frequently occur in multiple sites and show variable rates of malignant transformation [5].

Systematic reviews have demonstrated molecular similarities between OPMDs and adjacent carcinomas, reinforcing the concept that these lesions represent different stages within a genetically altered field rather than isolated pathological entities [5].

Role of Cancer Stem Cells

Recent research highlights the role of cancer stem cells (CSCs) in the initiation and maintenance of field cancerisation. CSCs possess self-renewal capacity and resistance to apoptosis, enabling them to survive carcinogenic insults and therapeutic interventions [6].

These cells may act as reservoirs of genetic instability, sustaining the premalignant field and contributing to tumor recurrence even after complete surgical excision. Studies have identified CSC markers in clinically normal mucosa surrounding OSCC, further validating their role in field formation [7].

Diagnostic and Biomarker Perspectives

Detecting field cancerisation remains a diagnostic challenge because altered fields often appear clinically and histologically normal. Immunohistochemical markers such as p53 and Ki-67 have been used to identify proliferative and genetically unstable fields [8].

Meta-analyses have shown that these markers are frequently expressed in normal-appearing mucosa adjacent to OSCC, supporting their utility in assessing field changes and recurrence risk [8]. Advances in next-generation sequencing have further enabled high-resolution mapping of clonal relationships between tumors and surrounding mucosa [9].

Clinical Implications

The presence of field cancerisation has significant implications for OSCC management. Histologically tumor-free surgical margins may still harbor genetically altered cells, explaining local recurrence despite adequate excision [10].

This understanding supports the need for wider surgical margins, long-term surveillance, and exploration of field-directed therapies. It also underscores the importance of eliminating etiological factors, as cessation of carcinogenic habits may reduce further genetic damage within the field.

Future Perspectives

Ongoing research aims to identify reliable molecular markers capable of predicting malignant transformation within fields. Integration of molecular diagnostics into routine clinical practice may enable personalized surveillance strategies and early intervention.

Understanding the genetic evolution of fields may also facilitate the development of chemopreventive agents targeting early carcinogenic events, potentially reducing OSCC incidence and recurrence.

CONCLUSION

Field cancerisation provides a comprehensive explanation for the multifocal nature of oral squamous cell carcinoma and its tendency for recurrence and second primary tumors. It emphasizes that oral cancer is not merely a localized lesion but a disease of widespread epithelial genetic alteration. Incorporating this concept into clinical decision-making is essential for improving long-term outcomes in oral cancer patients.

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