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Oral Cancer: Causes, Symptoms, Diagnosis, and Management

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Abstract

Oral cancer is a major public health concern, ranking among the most prevalent cancers globally. It encompasses malignancies affecting the lips, tongue, cheeks, floor of the mouth, hard and soft palate, sinuses, and pharynx. Despite advancements in diagnostic techniques and treatment modalities, oral cancer continues to have a high morbidity and mortality rate due to late diagnosis. This article provides a comprehensive overview of oral cancer, covering its epidemiology, risk factors, clinical presentation, diagnostic methods, treatment approaches, and preventive strategies. Oral cancer, a significant global health concern, encompasses malignancies that affect the lips, tongue, floor of the mouth, cheeks, hard and soft palate, sinuses, and throat. It is primarily classified as a subtype of head and neck cancers, with squamous cell carcinoma being the most prevalent histological type. The incidence of oral cancer continues to rise, particularly in developing countries, due to the widespread use of tobacco, alcohol, and betel quid, alongside emerging factors such as human papillomavirus (HPV) infections and genetic predisposition. Early symptoms are often subtle and easily overlooked, contributing to delayed diagnosis and poor prognosis. Clinical manifestations typically include persistent ulcers, difficulty swallowing, chronic sore throat, unexplained bleeding, and voice changes. The diagnostic process involves a combination of clinical examination, imaging modalities such as MRI and CT scans, and histopathological evaluation through biopsy. Adjunct techniques like toluidine blue staining, brush biopsies and salivary diagnostics have also shown promise in early detection. Effective management of oral cancer requires a multidisciplinary approach encompassing surgery, radiation therapy, chemotherapy, and targeted biological agents. Recent advancements in immunotherapy and molecular-targeted treatments have opened new avenues for improved survival outcomes.

Moreover, rehabilitation post-treatment is crucial in restoring speech, mastication, and overall quality of life. Public health strategies focusing on prevention, awareness, and early screening are essential to reduce the global burden of this disease. This review aims to provide a comprehensive overview of the etiology, clinical presentation, diagnostic tools, and therapeutic modalities associated with oral cancer, highlighting current trends and future directions in its management.

Keywords: Oral cancer, squamous cell carcinoma, tobacco use, HPV, diagnosis, biopsy, chemotherapy, radiotherapy, immunotherapy, early detection, head and neck cancers, oral lesions, cancer management, public health.

Introduction

Oral cancer is a subtype of head and neck cancers and accounts for approximately 3% of all cancers globally. According to the World Health Organization (WHO), oral cancer is the sixth most common cancer worldwide, with higher prevalence in Southeast Asia due to the widespread use of tobacco and betel quid chewing [1]. The disease is often diagnosed at an advanced stage, leading to poor prognosis and reduced survival rates. Oral cancer represents a growing public health challenge, particularly in low- and middle-income countries, where risk factors are widespread, and access to early detection and treatment is limited [2]. It ranks among the top ten most common cancers globally, with high morbidity and mortality rates, especially when diagnosed at advanced stages. Most cases of oral cancer are histologically classified as squamous cell carcinoma, arising from the mucosal lining of the oral cavity [3].

The etiology of oral cancer is multifactorial, with tobacco use (including smokeless tobacco), excessive alcohol consumption, and betel quid chewing being well-established causative agents [4]. The synergistic effect of tobacco and alcohol significantly elevates the risk [5]. Additionally, infection with high-risk strains of human papillomavirus (particularly HPV-16) has emerged as a key contributor, especially in younger individuals with no history of traditional risk behaviors. Genetic susceptibility, poor oral hygiene, chronic irritation, and exposure to ultraviolet radiation (in cases involving the lips) are also implicated [6]. The initial symptoms of oral cancer are often nonspecific and may mimic benign conditions, leading to misdiagnosis or delay in treatment. Common warning signs include non-healing oral ulcers, red or white patches (erythroplakia or leukoplakia), pain, bleeding, and difficulty with chewing or speaking [7]. Such subtle presentations underscore the importance of routine oral examinations and heightened awareness among both clinicians and the general public. Diagnosis relies heavily on clinical suspicion, supported by imaging techniques like computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), alongside confirmatory tissue biopsy. Recent advances in molecular diagnostics and salivary biomarkers are being explored for their potential in early, non-invasive detection [8].

Treatment of oral cancer is typically multimodal, tailored to the stage and location of the tumor. Surgical excision remains the cornerstone for resectable tumors, often followed by radiation or chemoradiation.

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In cases of advanced disease, systemic chemotherapy, immunotherapy, and targeted agents are employed to improve outcomes. Post-treatment rehabilitation, including speech and swallowing therapy, is essential to enhance quality of life.

This paper aims to explore the key causes, clinical features, diagnostic strategies, and management approaches of oral cancer, with a focus on recent innovations and the need for integrated prevention programs. Understanding these aspects is crucial to improving survival rates and reducing the global burden of oral malignancies.

Epidemiology

Global prevalence: Oral cancer incidence is highest in India, Pakistan, Bangladesh, and Sri Lanka, accounting for 30-40% of all malignancies in these regions.

Gender and age distribution, oral cancer is more common in men than women, with the average age of diagnosis being 50-60 years. However, younger populations are increasingly affected due to changing lifestyle habits.

Risk factors

Tobacco and alcohol consumption, smoking, chewing tobacco, and heavy alcohol consumption significantly increase the risk.

Human papillomavirus (HPV) infection, HPV-16 and HPV-18 are associated with oropharyngeal cancers.

Betel quid and areca nut chewing, common in South Asia, it is a major risk factor.

Poor oral hygiene, chronic irritation from ill-fitting dentures and poor dental care can increase cancer risk.

Genetic predisposition, individuals with a family history of oral cancer have a higher risk.

Pathophysiology and molecular mechanism

Oral cancer typically originates from the epithelial cells lining the oral cavity. The progression occurs in stages:

- Dysplasia, abnormal cellular changes with potential for malignancy.
- Carcinoma in situ (CIS), localized, non-invasive cancer.
- Invasive squamous cell carcinoma, the most common type, accounting for 90% of oral malignancies, characterized by uncontrolled proliferation and tissue invasion.
- Genetic mutations in TP53, CDKN2A, and PIK3CA genes promote malignant transformation.
- Overexpression of EGFR (epidermal growth factor receptor) is associated with aggressive tumor growth.

Oral cancer presents with a variety of symptoms, including:

- Non-healing ulcers or sores in the mouth.
- Red or white patches (erythroplakia or leukoplakia).
- Lump or thickening of oral tissues.
- Difficulty in chewing, swallowing, or speaking.
- Numbness or pain in the oral cavity.
- Loose teeth or ill-fitting dentures due to bone invasion.

A thorough oral examination involves visual inspection and palpation of suspicious lesions. Red and white patches, non-healing ulcers, and nodules should raise suspicion.

Orthopantomogram (OPG), a panoramic dental X-ray to detect bone involvement.

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), Used for tumor staging and evaluating soft tissue invasion.

Positron Emission Tomography (PET), Helps in detecting metastasis.

Incisional biopsy, involves removing a portion of the suspicious tissue for histopathological examination.

Fine Needle Aspiration Cytology (FNAC), Used for lymph node involvement evaluation.

P16 protein expression, used as a biomarker for HPV-associated oral cancers.

Ki-67 and p53, used to assess the proliferative activity of cancer cells.

Oral cancer is staged according to the TNM classification,

- T (Tumor), size and extent of the primary tumor.
- N (Node), lymph node involvement.
- M (Metastasis), distant spread of the cancer.

Grading is based on histological differentiation,

- Grade 1, well-differentiated (low-grade).
- Grade 2, moderately differentiated (intermediate-grade).
- Grade 3, poorly differentiated (high-grade).

Treatment modalities

Wide local excision, removal of the tumor with surrounding healthy tissue.

Neck dissection, performed for lymph node metastasis.

Reconstructive surgery, to restore oral function and aesthetics.

External beam radiation, commonly used in combination with surgery.

Brachytherapy, internal radiation therapy for smaller tumors.

Used in advanced stages or for recurrent cases.

Cisplatin, fluorouracil, and paclitaxel are commonly used agents.

EGFR inhibitors (e.g., cetuximab) for advanced oral cancer.

Checkpoint inhibitors (e.g., pembrolizumab, nivolumab) for metastatic cases.

Early-stage oral cancer has a 5-year survival rate of 70-90%.

Advanced-stage cases have a lower survival rate of 30-50%.

HPV-positive oral cancers have a better prognosis compared to HPV-negative cases.

Prevention strategies

Tobacco cessation programs, Crucial in reducing oral cancer incidence.

Regular dental check-ups, early detection of suspicious lesions.

HPV vaccination, Helps prevent HPV-associated oral cancers.

Public awareness campaigns, Educating about risk factors and symptoms.

Conclusion

Oral cancer remains a major global health burden. Early detection, proper diagnosis, and timely management significantly improve patient outcomes. Preventive measures, lifestyle modifications, and regular oral screenings are essential in reducing the incidence and mortality associated with oral cancer.

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