REVIEW ARTICLE

ORAL SQUAMOUS CELL CARCINOMA- AN UPDATE

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ABSTRACT:
Oral Squamous cell carcinoma is one of the most common malignant tumor of oral cavity. It accounts for 90% of all oral cancers. Tobacco, alcohol, diet and immunosuprression are the main etiological factors in oral cancers. It may affect any anatomical site in the mouth, but most commonly the tongue and the floor of the mouth. Squamous cell carcinoma is managed by surgery, radiation, and chemotherapy singularly or in combination.
Keywords: Oral Squamous Cell Carcinoma; malignant tumor; immunosuprression.

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INTRODUCTION

Squamous cell carcinoma is one of the most common malignant tumors of the oral cavity. It comprises 90-95 % of all oral malignancies. Oral squamous cell carcinoma (OSCC) is typically diagnosed in males in their fifth to seventh decade of life with long-term exposure to tobacco and alcohol. The incidence of oral cancer is high in many countries; furthermore the intraoral location differs in different population groups.[1]

The World Health Organization expects a worldwide rising oral squamous cell carcinomas (OSCC) incidence in the next decades. In the US, OSCC represents 2%-4% of the annually diagnosed malignancies, being responsible for 8,000 deaths every year.[2]

OSCC implies quite significant mortality and morbidity rates and in spite of the vast amount of research and the advances accomplished in the field of oncology and surgery, the mortality rates remain unchanged. This motivates the search of factors with prognostic relevance in order to better tailor the individual management of OSCC patients. The purpose of this article is to list and discuss some of these factors, focusing also on some of the most promising.[3]

EPIDEMIOLOGY OF ORAL SCC

Oral SCC more frequently affects men than women (M:F = 1.5:1) most probably because more men than women indulge in high-risk habits. The probability of developing oral SCC increases with the period of exposure to risk factors, and increasing age adds the further dimension of age-related mutagenic and epigenetic changes. In the USA the median age of diagnosis of oral SCC is 62 years. However, the incidence of oral SCC in persons under the age of 45 is increasing[4]. The reason for this is obscure.

A number of conditions have been associated with an elevated risk of developing oral SCC including Li Frau- meni syndrome, Plummer-Vinson syndrome, Fanconi anemia, chemotherapy induced immunosuppression of organ transplantation, dyskeratosis congenita, xeroderma pigmentosum and discoid lupus erythematosus.[5]

RISK FACTORS FOR ORAL CANCER

The risk factors include tobacco associated intra-oral carcinogens, which may play a synergistic role in oral tumorigenesis. The disproportionately higher incidence of carcinoma of the head-neck in relation to other malignancies in India, may be due to use of

tobacco in various forms, consumption of alcohol, low socioeconomic condition related to poor hygiene, poor diet and rampant viral infections.[6]

SEX AND AGE

Overall incidence and mortality attributed to oral squamous cell carcinoma (OSCC) is increasing, with current estimates of age-standardized incidence and mortality of 6.6/100,000 and 3.1/100,000 in men and 2.9/100,000 and 1.4/100,000 in women, respectively.[7] Recent studies confirm that oral cancer forms a large part of the cancer load in parts of India. The correlation of prognosis with age seems controversial, and some authors show no relationship between them, whereas others demonstrate worse prognosis in older patients.[8]

TOBACCO

Oral Cancer has been associated with chewing of tobacco with betel quid (BQ) in India and other Asian countries, whereas in western countries, cigarette smoking and heavy alcohol consumption are the main risk factors[9]. The international agency for research on cancer (IARC) confirmed that smoking of various forms of tobacco (e.g., bidis, pipes, cigars and cigarettes) is carcinogenic in humans.[10] Chewing of tobacco with BQ increases exposure to carcinogenic tobacco-specific nitrosamines (TSNA) and to nitrosamines derived from areca nut alkaloids. Tobacco smoke pro-carcinogens such as benzo-[α]- pyrene, are metabolized by oxidizing enzymes, particularly cytochrome p450, some resulting in the production of reactive carcinogenic intermediates. Betel quid chewing has been specifically correlated with poorer prognosis[11]. Smokers and alcohol drinkers seem to be at higher risk for the development of second primary oral cancer than nonsmokers and nondrinkers, thus facing more onerous outcomes. Some studies link that cytochrome P450 family 1, subfamily A (CYP1A1) and CYP2E1 genotype, shows susceptibility to oral cancer, but others have failed to confirm this association.[12,13]

ALCOHOL

Alcohol, acting both independently as well as synergistically with smoking, has been implicated in oral carcinogenesis[14]. Alcohol may act as a solvent and enhance the penetration of carcinogens into target tissues. Acetaldehyde, which is the alcohol metabolite, has been identified recently as a tumor promoter.[15,16] So alcohol is considered to be the one of the precipitating factor for development of Oral cancer.

VIRUSES

Human papillomavirus (HPV), which is also closely associated with benign and malignant oral lesions is one of the etiological factor for development of oral cancer. There are evidence of a causal association between HPV and OSCC[17,18] with several studies showing that HPV is associated with increased risk of oral cancer. This association is valid for high-risk HPV, which comprises subtypes 16, 18, 33, and 35. HPV-16 may be responsible for more than 80% of HPV-positive OSCC. This virus is detected in condylomas, focal epithelial hyperplasia, squamous cell papilloma and malignant oral lesions. HPV positivity is higher in tumors from the oral cavity (59%), pharynx (43%) and larynx (33%)[19]. Among those, only a small fraction of HPV-infected lesions rarely proceed to malignant transformation, especially those with HPV subtypes 16,18. Hence, these studies indicate that tumorigenic conversion requires the presence of other risk factors.[20]

DIET

The importance of diet and nutrition in oral neoplasia has been indicated in several epidemiological studies[21]. Fruits and vegetables (high in vitamins A and C) are described as protective in oral neoplasia, whereas meat and red chilli powder are thought to be risk factors. Although the individual micronutrients responsible have not been formally identified, vegetables and fruits that protect against oral cancer and precancer, are rich in b-carotene, vitamin C and vitamin E, with anti-oxidant properties. Iron deficiency, resulting in oral epithelial atrophy and the Plummer-Vinson (Patterson Brown Kelly) syndrome, is associated with cancer of upper air and food passages and dietary iron may play a protective role in maintaining the thickness of the epithelium.[22]

SOCIOECONOMIC CONDITIONS

Apparently, the outcome is somewhat worse for patients with lower socioeconomic status and education, most likely because of poorer oral hygiene and more difficult access to medical care.[23]

FAMILY HISTORY OF HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

Epidemiological evidence from case-control studies of HNSCC, indicates that a family history of head and neck cancer is a risk factor. The ability to repair

DNA damaged by tobacco carcinogens, such as benzo-[α]- pyrene diol epoxide, is defective in some patients with head and neck cancer. Head and neck cancer patients show an increased susceptibility to chromosome damage by mutagens[24]. Villaret et al used cDNA array and identified genes such as keratin 17 and 19, laminin-5, connexin-26 and VEGF as being differentially expressed in HNSCC tissues, with respect to normal tissue.[25]

IMMUNE DEFICIENCY

A defective immune response can be causative factor in cancer. In a human immunodeficiency virus (HIV)-infected individual the commonest oral malignancy is Kaposi's sarcoma and the Human Herpes virus type 8 (HHV-8) has been implicated as the aetiological agent[26]. Lymphoma, mostly non-Hodgkin B cell lymphoma in HIV-infected individuals, or other immunosuppressed states, is commonly associated with Epstein-Barr virus and may occur in the head and neck. Depressed host immune status seems to play an adverse role on survival of patients with oral cancer. Patients under immunosuppressive therapy following solid organ transplant who developed OSCC fare worse than individuals with a less depressed immune system. Oral squamous cell carcinomas of the lip are more common in transplant recipients receiving immunosuppressive therapy, but HIV infection does not predispose to intra-oral squamous cell carcinoma.[27]

CLINICAL FEATURES OF ORAL SCC

Oral SCC may take various clinical forms. It may resemble a leukoplakia, a verrucous leukoplakia, an erythroleukoplakia, or an erythroplakia, any of which may eventually develop into a necrotic looking ulcer with irregular, raised indurated borders, or into a broad based exophytic mass with a surface texture which may be verrucous, pebbled or relatively smooth. When traumatized, oral SCC bleeds readily and often becomes superficially secondarily infected. Oral SCC is usually painless unless it is-secondarily infected. Large lesions may interfere with nor- mal speech, mastication or swallowing.[28] About two-thirds of oral SCC are already of substantial size, and will have clinically detectable metastases to cervical lymph nodes at the time of diagnosis[29]. The affected lymph nodes are firm and non-tender to palpable. Squamous cell carcinoma of the lip, hard palate and maxillary gingiva infrequently metastasize to regional lymph nodes, usually run a relative indolent course and have a relatively favourable prognosis, while SCC of the tongue, of the floor of the mouth and of the mandibular gingiva- often metastasize to regional lymph nodes and are more aggressive with a less favourable prognosis. In general, SCCs of the posterior part of the oral cavity are much more likely to metastasize to regional lymph nodes than are comparable SCCs of the anterior part of the oral cavity.[30]

TREATMENT

The treatment of oral SCC generally requires the services of a multidisciplinary team, the primary aim of treatment always being to eradicate the cancer, to prevent recurrence, and insofar as is possible to restore the form and function of the affected parts. The selection of a specific treatment modality is dictated by the nature of the carcinoma and by the general condition of the patient. Salient factors related to the carcinoma include the specific site affected, the clinical size, the extent of local invasion, histopathological features, regional lymphnode involvement and distant metastasis. Patient factors include age, general health status, a history of previously treated oral SCC and high-risk habits.[25] A variety of modalities are available for the treatment of oral SCC. These include excision/resection, radio-therapy, systemic cytotoxic chemotherapy and blocking of epithelial growth factor receptor (EGF-R), or a combination of these, either concurrently or in an orderly sequence.[27,28]

Surgery is the preferred first line treatment of small, accessible oral SCCs. However, advanced-stage oral SCC is usually treated by a combined treatment program of surgery, chemotherapy, and radiotherapy.[30] In cases of recurrent oral SCC, EGF-R inhibitor coupled with chemoradiotherapy, is the first line of treatment. Surgical resection of oral carcinoma with tumour free margins of less than 5 mm may be followed by local recurrence and possibly by distant metastasis, and usually necessitates the administration of post-surgery chemo- radiotherapy. The importance of the presence of dysplastic epithelium in post-resection carcinoma-free margins is of debatable importance, but it is not usually considered to be a strong indication for further treatment.[30]

CONCLUSION

Oral Squamous cell carcinoma is one of the most common malignant tumor of oral cavity. Various etiological factors have been identified such as

tobacco, alcohol, diet and immunosuprression. Tongue and the floor of the mouth are the most common site for Oral Squamous cell carcinoma. It can be managed by surgery, radiation, and chemotherapy singularly or in combination.

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