Cancer of Oral Cavity: Pathology, diagnosis and management

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Introduction
Oral cancer is a subtype of head and neck cancer, the cancerous tissue growth located in the oral cavity. It may arise in any of the tissues of the mouth. It may arise as a primary lesion or as metastasis from a distant site of origin such as the nasal cavity. Worldwide, oral cancer is a prevalent malignancy, mainly associated with a variety of tobacco-related habits and forms, as well as poor diets with low intake of vegetables and fruits. It is the cause for significant morbidity, suffering, and death.

In USA, it is responsible for over 8,000 deaths each year, killing roughly 1 person per hour, 24 hours per day. Of those 36,000 newly diagnosed individuals, only slightly more than half will be alive in 5 years. This is a number which has not significantly improved in decades. The death rate for oral cancer is higher than that of cancers which we hear about routinely such as cervical cancer, Hodgkin's lymphoma, laryngeal cancer, cancer of the testes, and endocrine system cancers such as thyroid, or skin cancer (1).

Oral cancers may originate in any of the tissues of the mouth, and may be of varied histologic types such as teratoma, adenocarcinoma, lymphoma or melanoma, but around 90% are squamous cell carcinomas, originating in the tissues that line the mouth and lips. These are malignant and tend to spread rapidly (2).

Causes and risk factors
Cancer cells characterized by DNA damage that causes abnormal cell development and growth. They have two defining characteristics: first, they can no longer divide and differentiate normally and, second, they can invade surrounding tissues and travel to distant sites within the body.

The healthy body is well equipped to defend itself against cancer. Only when the immune system and other defenses fail does cancer prevail. Current evidence suggests that cancer develops from a complex interaction of exposure to carcinogens and accumulated mutations in several genes. Researchers have identified approximately 100 cancer genes, or oncogenes. Oncogenes provide growth-promoting signals, thereby causing one or more characteristics of cancer cells when overexpressed or mutated. These two types of oncogenes are called proto-oncogenes and tumor suppressor genes. Both types of oncogenes remain dormant unless they're transformed by genetic or acquired mutation. Common causes of acquired genetic damage are viruses, radiation, environmental and dietary carcinogens, and hormones. Other factors that interact to increase a person's likelihood of developing cancer are age, genetics, nutritional status, hormonal balance, and response to stress (3).

The demographics of those who develop this cancer have been consistent for some time. While historically the majority of people are over the age of 40 at the time of discovery, it is now occurring more frequently in those under this age. Exact causes for those affected at a younger age are now becoming clearer in peer reviewed research, revealing a
viral etiology (cause). There are also links to young men and women who use conventional "smokeless" chewing or spit tobacco. Promoted by some as a safer alternative to smoking, it has in actuality not proven to be any safer to those who use it when referring to oral cancers. It is also now confirmed that in a younger age group, including those who have never used any tobacco products, have a cause which is HPV16 viral based. The human papilloma virus, particularly version 16, has now been shown to be sexually transmitted between partners, and is conclusively implicated in the increasing incidence of young non-smoking oral cancer patients. This is the same virus that is the causative agent, along with other version of the virus, in more than 90% of all cervical cancers. It is the foundation's belief, based on recent revelations in peer reviewed published data in the last few years, that in people under the age of 50, HPV16 may even be replacing tobacco as the primary causative agent in the initiation of the disease process. From a gender perspective, for decades this has been a cancer which affected 6 men for every woman. That ratio has now become 2 men to each woman.

The accumulative damage from important risk factors, such as tobacco use, alcohol consumption, and persistent viral infections such as HPV, are the real culprits. It may take several decades of smoking for instance, to precipitate the development of a cancer. But, tobacco use in all its forms is number one on the list of risk factors. When you combine tobacco with heavy use of alcohol, your risk is significantly increased, as the two act synergistically. Those who both smoke and drink, have a 15 times greater risk of developing oral cancer than others. Biological factors include viruses and fungi, which have been found in association with oral cancers. The human papilloma virus, particularly HPV16, has been definitively implicated in oral cancers, particularly those that occur in the back of the mouth.

**Signs and Symptoms**

One of the real dangers of this cancer, is that in its early stages, it can go unnoticed. It can be presented as skin lesion, lump, or ulcer on the tongue, lip, or other mouth areas. Usually the lesion is small and most often pale colored, may be dark or discolored. Early sign may be a white patch (leukoplakia) or a red patch (erythroplakia) on the soft tissues of the mouth, usually painless initially. A burning sensation or pain might be develop when the tumor is advanced. Additional symptoms that may be associated with this disease including tongue problems, swallowing difficulty. Mouth sores that do not resolve in 14 days and pain and paraesthesia are late symptoms. Because there are so many benign tissue changes that occur normally in the mouth, and some things as simple as a bite on the inside of the cheek may mimic the look of a dangerous tissue change, it is important to have any sore or discolored area of the mouth, which does not heal within 14 days, looked at by a professional.

**Diagnosis**

An examination of the mouth by the health care provider or dentist shows a visible and/or palpable lesion of the lip, tongue, or other mouth area. As the tumor enlarges, it may become an ulcer and bleed. Speech/talking difficulties, chewing problems, or swallowing difficulties may develop. A feeding tube is often necessary to maintain adequate nutrition. This can sometimes become permanent as eating difficulties can include the inability to swallow even a sip of water.
There are a variety of screening devices that may assist dentists in detecting oral cancer, including the Velscope, Vizilite Plus and the identafi 3000. While a dentist, physician or other health professional may suspect a particular lesion is malignant, there is no way to tell by looking alone - since benign and malignant lesions may look identical to the eye. A non-invasive brush biopsy (BrushTest) can be performed to rule out the presence of dysplasia (pre-cancer) and cancer on areas of the mouth that exhibit an unexplained color variation or lesion. The only definitive method for determining if cancerous or precancerous cells are present is through excisional biopsy determines the tumor type. TNM classification system that is used by doctors to stage patients with tongue cancer into different groups by measuring the extent of spread of the cancer based on factors such as Size of the tumor(5), Lymph node involvement, and metastatic spread of the tumor to other sites in the body.

Management

After a definitive diagnosis has been made and the cancer has been staged, treatment may begin. In short, surgical excision (removal) of the tumor is usually recommended if the tumor is small enough, and if surgery is likely to result in a functionally satisfactory result. Radiation therapy with or without chemo is often used in conjunction with surgery, or as the definitive radical treatment, especially if the tumor is inoperable.

However, treatment of oral cancers is ideally a multidisciplinary approach involving the efforts of surgeons, radiation oncologists, chemotherapy oncologists, dental practitioners, and rehabilitation and restorative specialists. The actual curative treatment modalities are usually chemotherapy with concurrent radiation, sometimes combined with surgery. Chemotherapy while able to kill cancer cells itself is currently not used as a monotherapy for oral cancers. Added to decrease the possibility of metastasis, to sensitize the malignant cells to radiation, to reduce the size of any malignancy prior to surgery, or for those patients who have confirmed distant metastasis of the disease, it is a powerful component of treatment(6).

Whether a patient has surgery, radiation and surgery, or radiation, surgery, and chemotherapy, is dependent on the stage of development of the cancer. Each case is individual. Patients with cancers treated in their early stages, may have little in the way of post treatment disfigurement. For those whose cancer is caught at a later stage, the results of surgical removal of the disease may require reconstruction of portions of their oral cavity or facial features. There may be adjunctive therapy required to assist in speech, chewing and swallowing of foods, the problems associated with the lack of salivary function, as well as the fabrication of dental or facial prostheses. Viruses that only kill specific cancer cells, and techniques which would allow the replacement of a damaged p53 gene, are all being researched now. It is possible that in our lifetimes we will see cures for cancer develop from this ongoing research(7). Targeted therapies such as the use of monoclonal antibodies are now an FDA approved adjunctive treatment for combating head and neck cancers. In the long run prevention of cancer and reoccurrence are the ultimate goal.

References