lead story

Advances in Oral Cancer Detection and Diagnosis—How You Can Make a Difference and Save a Life!

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In 2008, more than 35,000 new cases of oral and pharyngeal cancer (OPC) will be diagnosed in the United States, with an estimated 7,590 people (5,210 men and 2,380 women) who will die.[1,2] This is the second consecutive year of an increase in incidence of a condition that occurs in men about two times more frequently than in women and is slightly more common in blacks than in whites.[2] OPC is a disease of aging, with more than 90 percent occurring in persons over 40. However, there is a current trend of OPC developing in younger patients, even those without any risk factors.

Types of Oral and Pharyngeal Lesions and Tumors

While OPC can occur in any mucosal site, the tongue is most common (25 percent), followed by the floor of the mouth (15 percent), and the lip (10 percent). The occurrence of cancer of the tonsil is increasing.[1] Many types of tumors can develop in the oral cavity and can be benign, precancerous or malignant. The benign oral and pharyngeal tumors may mimic malignant or premalignant conditions, and conversely, early malignant lesions may resemble benign ones. Therefore, a differential diagnosis is always in order, and all changes must be followed closely until a diagnosis is established or the lesion disappears.

Leukoplakia and erythroplakia are the two most common oral precancerous conditions, and they have varying degrees of risk for malignant transformation. Leukoplakia is a white patch or plaque that cannot be scraped off and can occur on any oral mucosal surface (figures 1 and 2). Erythroplakia is a well-circumscribed flat lesion that also can occur on any oral surface (figure 3). The risks depend upon the site, patient habits and histologic classification (primarily degrees of cellular dysplasia). At this time, cell markers do not possess the sensitivity and specificity to replace microscopic morphology in assessing and risks for malignant transformation.

More than 90 percent of OPCs are squamous cell carcinoma, which develops as abnormal cells in the stratified squamous epithelium lining the entire oral cavity. Salivary gland tumors may develop in the major salivary glands (mainly parotid) and minor salivary (mucous) glands of the mouth. There are several types of salivary gland cancers, which include adenoid cystic carcinoma, mucoepidermoid carcinoma and adenocarcinoma. These will often present as persistent lumps that may or may not be associated with pain. Any mass that persists for more than two to three weeks without a diagnosis being established must be evaluated or referred to rule out tumor. Figure 4 shows four lesions that were diagnosed as early squamous cell carcinomas at the University of California San Francisco, having been previously misidentified as indicated.

Pain and discomfort are usually the most frequent complaints, but in the early stages, OPC is often minimally symptomatic. Since 90 percent of OPCs develop in the lining stratified squamous epithelium as squamous cell carcinoma, early recognition can be enhanced through accessible signs and symptoms.

Risk Factors

While OPC, like all cancers, is basically a genetic disease, it is influenced by many other factors that play important roles in malignant transformations. There is no question that tobacco in any form and alcohol consumption significantly increase the risk. About eight out of 10 people with OPCs use or have used tobacco. The risk factors are related to the quantity and duration they smoked. Smokeless tobacco (spit, snuff, chewing) also incurs a risk, although not as great as combustible tobacco. That is why educating patients about tobacco cessation is an essential

Figure 1. Leukoplakia

Figure 2. Leukoplakia

Figure 3. Erythroplakia

Originally identified as an infection

Originally identified as an area of trauma

Originally identified as an infected traumatic area

Originally identified as an atypical aphthous ulcer

Figure 4

Signs and Symptoms of Oral and Pharyngeal Cancer

The possible signs and symptoms of OPC may include the following:[2,7]

- A pain in the mouth that doesn't go away
- A sore in the mouth that will not heal
- A persistent lump or thickening in the mouth
- A persistent white or red patch in the oral cavity
- A chronic sore throat
- Trouble chewing or swallowing
- Trouble moving the jaw or tongue
- Numbness of the tongue or other areas of the mouth
- Swelling of the mouth or jaws the may cause denture(s) to fit improperly or be uncomfortable
- Loosening of teeth that may be associated with pain
- Changes in voice
- A lump or mass in the neck
- Weight loss
- Persistent bad breath

point in practice. The American Dental Hygienists' Association launched a Smoking Cessation Initiative for dental hygienists to become involved in tobacco cessation and conducting educational programs with their patients in 2003. Many states (New York, California, Indiana and Iowa) have created initiatives in their states to help patients stop smoking. Visit ADHA's Web site www.adha.org or www.askadviserefer.com for more information.

Immunosuppression, whether disease- or drug-induced, increases the risk for carcinoma.[3] While nutrition has a less certain influence, in general, diets low in fruits, vegetables and fiber add to the numerous potential risk factors.[4] Some types of the human papilloma virus (HPV) are associated with the development for malignancy (mainly Type 16) in certain OPC sites, and current research is sorting out HPV influence.[5] HPV may be a possible explanation for the increase in tonsil cancers. HPV is also associated with squamous carcinomas of the base of tongue.[6] However, HPV is rarely associated with carcinomas of the mouth. HPV appears to be associated with younger patients and nonsmokers, and is possibly related to lifestyles.

Hence, it is important to observe the oropharynx when performing cancer screening examinations, as well as implications for an effective HPV vaccine in the future. Of critical significance is the need to understand and control precancerous lesions, primarily leukoplakia, which when treated may prevent some OPCs from occurring. See the box on this page for signs and symptoms of OPCs. These signs and symptoms should be assessed by a dental or medical professional to determine a cause and rule out neoplasia or cancer (see figures 5-7).

Proper Diagnosis and Treatment Outcomes

In spite of advancements in surgery, radiation and chemotherapy, the five-year survival rate is a disappointing 59 percent.[1] This poor control rate has not improved

Figure 5. Squamous cell carcinoma of the lip

Figure 6. Erythroleukoplakia that eventually developed into squamous cell carcinoma

Figure 7. Advanced squamous cell carcinoma of the tongue

significantly over the past five years. After analyzing the data, it is clear that the poor results are due to delays in diagnosis, leading to more advanced tumors and the need for aggressive treatments. This not only worsens the prognosis, but causes severe side effects, such as decrease in saliva (xerostomia), loss of functions (chewing, swallowing), altered taste, trismus, dental caries, pain/discomfort, oral infections, depression, more costs on the part of the patient diagnosed and an overall poor quality of life.

The solution becomes obvious: reduce risk factors and improve prevention and early detection. However, regarding detection, early OPCs can mimic a variety of benign diseases, often making early recognition difficult and permitting the patient a feeling of false security. Therefore, taking a biopsy, the gold standard for diagnosis, is often delayed because of low suspicion. Some techniques currently available have been helpful as intermediates in the diagnostic pathway and in accelerating biopsies.

The techniques or devices available for dental professionals used to accelerate and not replace the biopsy include cytodiagnosis (cytology), ViziLite (chemiluminescence), toluidine blue (surface cell stain) and the VELscope (fluorescence). These are all approved by the U.S. Food and Drug Administration (FDA) as devices and have code numbers; some insurance carriers will cover and reimburse their usage. There are no other breakthroughs in technology for predicting cell behavior that are practical and cost-effective, offer specificity or are readily available at present. Areas of investigation include a variety of protein cell markers, salivary proteins associated with neoplasia, and nanotechnology. Advances in these areas will benefit early identification as well as treatment.[8,9]

As a general rule, for any lesion that has been present for more than two to three weeks and for which a diagnosis has not been established, approaches for making a definitive diagnosis must be considered. This situation requires an office procedure, such as a biopsy or referral. However, there are many reasons on the part of patients and clinicians why this is not carried out and a delay is incurred. Therefore, the value of adjunctive techniques is evident.[10] Please note that these adjunctive techniques are not substitutes for biopsy, but are used to accelerate a biopsy or referral to a specialist.

Oral Cancer Detection Devices and Technology

As stated above, all of the techniques and tests have been classified and approved by (FDA).

Cytodiagnosis – Oral CDx is a computer-assisted brush biopsy that can determine if common oral white or red lesions or ulcerations contain potentially dangerous precancerous or malignant cells. This specially designed brush captures many thousands of cells with mild surface brush twisting at the suspicious area. The cells are transferred to a microscope slide, which is fixed, stained and microscopically scanned. The observed cell morphology is then reported as normal, atypical or positive. A positive report of findings has a high degree of accuracy for dysplastic and malignant cells. However, this method may not detect all cancers or dysplastic changes, and a biopsy is needed to establish the diagnosis if a lesion persists. It must be recalled that the brush biopsy is in order when for some reason the biopsy is delayed (usually due to a low degree of suspicion, medical reasons or inconvenience).

Incisional Biopsy – This procedure can be completed in the office under local anesthesia. When necessary, the patient can be referred for biopsy to a dental or medical professional with experience in oral diagnosis. In some cases, sedation may be in order.

ViziLite Plus with TBlue System – Zila Pharmaceuticals, Inc., developed the ViziLite System, which was approved by FDA in 2001, and introduced the ViziLite Plus with TBlue System in 2005. This device uses a specific low-energy blue-white light source that reflects off of abnormal cells following a 30-second acetic acid rinse. The light source is activated by bending the vial container. The practitioner then inserts the illuminated lightstick into a holder, dims ambient lights and conducts the examination of the oral cavity using the illumination from the ViziLite device, looking for acetowhite lesions (seen as a white glow on the epithelial surface). This system may enhance the clinical visualization of keratotic lesions that might not be definitively apparent with the normal chairside incandescent light. Such areas should be biopsied, followed for two weeks for confirmation, or referred.

TBlue is a patented toluidine blue-based (tolonium chloride) metachromatic dye that is a topically applied cell stain that binds to dysplastic and malignant epithelial cells with a very high degree of accuracy. This helps identify epithelial areas at high risk for dysplasia or malignancy, as well as indicating the most appropriate area to biopsy. Toluidine blue can be used in conjunction with ViziLite, which increases the detection accuracy of ViziLite illumination.

VELscope – LED Dental, Inc., developed VELscope, and FDA approved this oral mucosal examination device in 2006. This revolutionary handheld device provides an easy-to-use adjunctive mucosal system for early detection of abnormal tissue. The handpiece emits a safe blue light into the oral cavity that penetrates the stratified squamous epithelium, inducing fluorescence in normal cells. Dysplastic and malignant cells will interrupt and cause a loss of fluorescence, delineating a dark area of abnormality. This reaction assists both in clinical awareness and extent of the abnormality. More studies must be performed to evaluate the role of the VELscope in screening.

Microlux/DL – AdDent developed Microlux/DL, and FDA approved this product in 2007 for the examination of the oral mucosa. This device utilizes a battery-powered diffused blue-white LED light source to improve the visualization of oral lesions. The patient is instructed to rinse with the Microlux/DL rinse for 60 seconds and expectorate. With illumination from the Microlux/DL, the practitioner would look for acetowhite lesions. The utility of this system in screening has not yet been established.

Orascoptic DK – Orascoptic developed the Orascoptic DK, and FDA approved this product in 2007. It is a three-in-one dental device that employs a battery-powered handheld LED light source and three unique interchangeable diagnostic instruments. The role of Orascoptic DK in oral screening has yet to be determined.

A recent published study reported a systematic review of the literature for oral cancer devices and stated that there were published studies for toluidine blue, ViziLite, ViziLite Plus with TBlue, Oral CDx and VELscope. No similar studies were conducted for Microlux DL or Orascoptic DK.[11] The rigid review did not substantiate sufficient evidence that would warrant a specific endorsement. Further studies are planned to determine the predictive values of the tests and confirm their value in assessment of oral lesions.

Are Effective Oral Cancer Screening Examinations Being Conducted in Practice?

An American Dental Association (ADA) survey conducted in 2000 reported that only 15 percent of patients stated that an oral cancer screening examination was conducted during a routine dental appointment.[12] Other studies report that dental professionals are not as knowledgeable as they could be about oral cancer prevention and early detection.[13,14] A study conducted at the University of Maryland Dental School reported no statistically significant difference between second-, third- and fourth-year dental students in terms of knowledge of oral cancer. Results reported that third- and fourth-year dental students lacked confidence in conducting oral cancer screening examinations and lymph node palpation with their patients.[15]

Two other studies were conducted with dental hygiene students and licensed dental hygienists. The University of Maryland study reported that 91 percent of dental hygienists correctly conducted examinations of the tongue for oral cancer detection, while only 16 percent correctly identified leukoplakia and erythroplakia as conditions associated with oral cancer.[16] A study of licensed dental hygienists in California showed that 74 percent were adequately trained to provide oral cancer examinations, while only 27 percent were educated enough to provide tobacco cessation counseling.[17] Again, through ADHA's Smoking Cessation Initiative, dental hygienists are more informed to provide tobacco cessation counseling. See box on this page for the steps in the oral cancer examination process.

In Closing

Early detection is the most important step to improve oral cancer survival rates, prevent morbidity and enhance quality of life.

Careful oral cancer examinations are the first step in detection. Adjunctive techniques support early oral cancer detection and bring the importance of cancer awareness to the forefront. Positive findings should accelerate referral and biopsy. False negative results are controlled, since all lesions must be followed, and if the diagnosis has not been established, a biopsy should be performed.

Molecular markers are the focus of active research to improve early recognition of precancerous and malignant cells. However, at this point in time, neither their availability nor their specificity is sufficient for incorporation into practice.

Oral Cancer Examination Process[18]

1. Palpate the neck for any lumps.
2. Observe the lips with the patient's mouth closed.
3. Feel the lip for any abnormalities.
4. Retract the lips and observe all mucosal sites for any differences in appearance. This should be combined with palpation.
5. Ask the patient to stick their tongue out and check for any changes in size, color or lesions. Using a cotton square, gently move the tongue to the right and left sides to examine the lateral borders of the tongue.
6. Have the patient touch the roof of their mouth with their tongue and observe the floor of the mouth and the ventral portion of the tongue.
7. Have the patient say "ahhh" in order to observe any abnormalities of the oropharynx/tonsillar area.
8. All observations should be noted on the patient's chart or oral cancer screening form.
9. Obviously, knowing normal oral anatomy is basic to recognizing changes/deviations from normal.

Both dentists and dental hygienists play important roles in conducting and completing oral cancer screening tests to determine the health and well-being of their patients. Additional education in conducting effective oral cancer examinations and the use of adjunctive oral cancer detection devices in practice may help to detect early stages of oral cancer and prevent many patients from being diagnosed too late. As we move forward, oral cancer detection and awareness must be communicated to patients to continue to educate them about this devastating and debilitating disease. Future technologies like molecular markers and imaging methodologies may help to advance detection and diagnosis.

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