Importance of Early Detection of Squamous Cell Carcinoma

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INTRODUCTION

Oral cancer is one of many types of head and neck cancer. At the time of writing this article, it is expected that approximately 42,000 people in the United States will be diagnosed with oral cancer1 (in all regions of the oral tissues, including the oropharynx). In addition, 2013 should have marked the fifth year in a row of an increase in the rate of occurrence of oral cancers. Smoking/tobacco use and alcohol consumption have been historically blamed for oral cancer. However, viruses—especially exposure to human papilloma virus version 16 (HPV-16)—have also been associated with oral cancer, particularly squamous cell carcinoma (SCC).2 The remaining small percentage of oral cancers (fewer than 7%) are attributed to unknown causes; a genetic predisposition has been hypothesized (Oral Cancer Foundation1). There are other possible risk factors for oral cancer, but these may be harder for practitioners to assess. These include diet and nutrition, as a diet rich in antioxidants can help prevent cancers.3 About 100 new cases of oral cancer are diagnosed every day in the United States alone, and a person dies from oral cancer every hour of every day. Cancers that are detected early have an 80% to 90% survival rate. However, cancers diagnosed at a late stage have a high death rate of about 43% at 5 years from diagnosis.1 Therefore, dental professionals have the potential to play an important role in detecting oral cancers in an early stage.

A national strategic planning conference4 on the prevention of oral and pharyngeal cancer was convened in 1996, and the participants concluded, among other findings, that dental professionals must become more involved in oral cancer diagnosis. According to guidelines put forth by the Centers for Disease Control and Prevention,4 oral cancer screening should include a physical exam (visual inspection and palpation of the head, neck, oral, and oropharyngeal regions, including forceful protraction of the tongue with gauze to visualize fully the posterior lateral tongue and tongue base) and a careful review of the patient’s health history, including risk behaviors (eg, tobacco and alcohol use), a history of head and neck radiotherapy, a family history of head and neck cancer, and a personal history of cancer.

SCC is a malignant neoplasm of mucosal origin. It is the most common type of oral cancer, accounting for more than 90% of all malignant neoplasms of the oral cavity.5 Clinical signs of carcinoma, which can appear in any region of the oral cavity, are often absent until a lesion becomes large, indurated, or ulcerated. Early detection of SCC saves lives by preventing metastasis.

Tobacco use is well known as a risk factor for SCC, but
perhaps less familiar in the Western world is the use of paan, which is made of betel nut, betel leaf, and sometimes tobacco, and is used in many Asian cultures. (Editor’s note: Reportedly, paan is also being used in select areas of the United States.) It is either chewed or held in the mouth to serve as a breath freshener. Many studies have associated paan with oral malignancies.\(^6\)\(^{-12}\)

The following case report will serve as an example of the effects of paan on the oral cavity and, more importantly, as a reminder to all dental professionals of their importance in oral cancer prevention and treatment.

**CASE REPORT**

**Clinical Presentation**

A 57-year-old man, originally from India, presented at the clinic in Silver Spring, Md, with a 2.0-cm soft-tissue lesion, which was red and white and ulcerative, in the mandibular left posterior buccal vestibule (Figures 1a and 1b). It had been present for 6 months. Panoramic radiography and CBCT revealed only typical periodontal bone loss (Figures 1c and 1d). The patient had a history of smoking and intermittent use of paan for 2 years in the affected area. Surgical incisional biopsy of the lesion was performed.

The biopsy report disclosed SCC that was well to moderately differentiated, with perineural and perivascular invasion, and appeared infiltrative. It was diagnosed as a stage IV SCC lesion. The patient’s primary care physician was informed. The physician referred the patient to the head and neck surgery department of a local hospital; there, surgeons removed the part of the mandible associated with the mandibular left molars. The area was then reconstructed (a plate was placed).

The patient remains stable, thanks to thorough examination and proper diagnosis, documentation, and referral.

**Histologic Findings**

The histologic appearance of the excised lesion is shown in Figures 2a to 2d.

The lower-resolution images showed well to moderately differentiated material, with perineural and perivascular invasion, infiltrating the lamina propria (Figure 2a). A great deal of inflammation was evident (Figure 2b). Higher-power images (Figures 2c and 2d) showed microinvasion of the squamous carcinoma cells and cell nests with dyskeratosis dropping off from the overlying dysplastic epithelium into the superficial lamina propria, and heavy mixed inflammation.

**DISCUSSION**

Multiple factors are associated with the mutagenesis of oral cancer. As noted previously, smoking and other uses of tobacco have been implicated as risk factors in many studies,\(^7\)\(^{13}\)\(^{-16}\) along with HPV-16.\(^1\)\(^\text{2}\) Aging and exposure to a variety of biologic, chemical, and physical agents are also often blamed. Gustavsson et al\(^1\)\(^\text{7}\) observed an increased risk of oral SCC in persons with exposure to asbestos, welding fumes, and polycyclic aromatic hydrocarbons. Bacterial (eg, infection with *Treponema pallidum*) and fungal (*Candida albicans*) conditions may be responsible; nutritional deficiencies, oral neglect, chronic trauma, radiation, and immune system suppression are other etiological agents for SCC. In addition, recent studies by...
Jewett et al., Koontongkaew, and Pérez-Sayáns et al. have begun to elucidate the role of the so-called “oral microenvironment” in SCC. Koontongkaew described the interaction between tumor cells and cancer-associated fibroblasts and its contribution to increases in inflammation and angiogenesis in encouraging tumor growth. Pérez-Sayáns et al. reviewed the role of the protein p21 in furthering tumor development but reported mixed results.

Chewing of paan/betel products has been associated in many studies with a heightened oral cancer risk. Koontongkaew described the interaction between tumor cells and cancer-associated fibroblasts and its contribution to increases in inflammation and angiogenesis in encouraging tumor growth. Koontongkaew described the interaction between tumor cells and cancer-associated fibroblasts and its contribution to increases in inflammation and angiogenesis in encouraging tumor growth. Koontongkaew described the interaction between tumor cells and cancer-associated fibroblasts and its contribution to increases in inflammation and angiogenesis in encouraging tumor growth.

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Oral SCC is most common in the tongue, floor of the mouth, and retromolar region, although it can appear anywhere in the oral cavity. In an ongoing study by Mashberg and Meyers, 84.2% of asymptomatic SCCs were no larger than 2 cm, but of these, some 70% were invasive. They also recommended particular scrutiny in the “high-risk areas” of the floor of the mouth, the ventral and lateral tongue, and the soft palate complex, especially of any lesions present for 14 days or longer. Langlais and Miller noted that many oral SCCs were asymptomatic until they became large, indurated, and ulcerated, by which time they were likely advanced and had metastasized. Any red or white lesion should be investigated, regardless of whether the patient shows symptoms or is a current or past smoker, and especially if it has been present for more than 2 weeks.

Chimeno Zoth et al. noted that the histologic appearance of precancerous lesions in hamsters were remarkably similar to those seen in humans, ie, hyperplastic foci and silver-stained nucleolar organizer regions. Link et al. noted that SCC users of smokeless
tobacco typically featured well-differentiated tissues. Because smoking and the use of other tobacco-containing products have been heavily implicated in causing SCC, it is incumbent on all staff in the dental office to work with patients to encourage them to give up any tobacco-related habits. In a survey of dentists in Bhopal City, India, nearly all respondents indicated that dentists must inform patients about tobacco cessation, but only 58% strongly agreed that specific training and tools were necessary to equip clinicians in this role. Dentists in the study noted that lack of time, lack of training, and fear of patients not returning were among the factors leading them to minimize tobacco education. Johnson et al cited similar concerns among dentists, who were willing to assist with tobacco cessation protocols but felt underequipped to do so.

Several practical tools for dentists and hygienists to use with patients to quit paan/tobacco have been developed to increase the likelihood of success in quitting. In a 2-part series, Davis provided basic science information and evidence-based strategies for tobacco cessation for dentists and hygienists to use with patients in everyday patient care. Christen et al provided a structured approach to tobacco intervention that included nicotine replacement therapy. Antal et al recently presented their experiences with a video-based training program to train undergraduate dental students in this role. The program incorporated small interactive groups, simulations of real-life situations, and evaluations of students’ handling of the simulations; the students reported increased confidence in discussing tobacco-related issues with patients after undergoing the training. Binnie et al developed and tested a smoking cessation program designed for dental hygienists to use with patients. Hygienists treated 118 patients with either “usual care” (control group) or a structured advice protocol based on the “ask, advise, assess, assist, arrange follow-up care” method (the “5 As” approach) that included offers of free nicotine replacement therapy (test group). Although only a small proportion of patients were successful in quitting, more of the test group patients successfully quit nicotine (15%) than the “usual care” patients (9%) after 3 months, and this trend continued throughout the study’s one-year follow-up period. Also, significantly more test patients completed quit attempts of at least one week versus the control patients.

The reasons given for the failure, on the part of the general practitioners, to recognize oral cancers were discussed, in detail, by Dave; the author categorized delays as related to the patient, the doctor, or the system. Delay by the doctor is

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**Table. Clinical Recommendations**

1. Careful review of all patients’ health history is mandatory to detect risk factors. Dentists must carefully record any history of smoking (number of years and number of cigarettes per day) or any tobacco-containing products, whether smokeless tobacco or paan, qat, or other betel-and-tobacco products. In addition, age and any viral exposure, especially HPV-16, should be noted in patient records. Especially with expanded worldwide use of betel products and new trends in tobacco consumption (eg, waterpipes, as noted by Dave), oral cancers may be seen more frequently in Western dental practices.

2. Careful and deliberate examination of the oral cavity for any lesions that might signify squamous cell carcinoma (SCC) at any stage must be done. The duration of any lesions and disappearance/reappearance of any similar lesions should be noted in the charts, and any lesion or symptom that has not resolved within 2 weeks should be of particular concern. Dentists must remember that SCC lesions can often be smaller than 2.0 cm and most frequently appear on the tongue, floor of the mouth, and retromolar area, although they can appear anywhere in the oral tissues. Patient education material on oral cancer should also be available.

3. Dentists should recognize when a specialist is needed; to this end, developing relationships with cancer specialists with special skills in oral cancers is strongly advised.

4. Encouragement of smoking/tobacco cessation is essential. All dentists and hygienists should receive training in the facts about tobacco use and cancer, so that they can inform and remind patients of the risk of tobacco use, and should learn specific techniques to help them stop smoking. The aforementioned examples are just a few of the many possible approaches to tobacco cessation. Also, patient education pamphlets and booklets must be made available and reviewed with patients.
potentially modifiable and, therefore, an important aspect of care to address. Other factors included time constraints, a lack of compensation for the task, and insufficient training. Other authors also cited limited time to perform an oral cancer exam and a lack of adequate training in diagnosis of soft-tissue lesions, along with discomfort with inquiring about alcohol/tobacco use and the potential to generate patient anxiety. Small lesions will often go undiagnosed, as will lesions in areas that are difficult to see. Any initial misdiagnosis can lead to mismanagement through such means as analgesics, antibiotics, and mouthwash.

**CLOSING COMMENTS**

The patient reported on in this article was fortunate to receive a diagnosis early enough to avoid death, but he did undergo resection of a portion of the mandible. Had the lesion been noted any later, it is possible that more invasive treatment, including perhaps radiation and chemotherapy, would have been necessary due to metastasis. It is strongly recommended that every clinician gain a good understanding of the clinical and histologic appearance of cancerous and precancerous lesions of the oral tissues, since SCC is the most common of oral cancers. Excellent reviews of this topic have been provided by Dave, Hirshberg et al., Kerr and Cruz, and Langlais and Miller, and both the Oral Cancer Foundation and the National Cancer Institute provide helpful information on screening, risk factors, and the role that dentists should play as the “first line of defense in early detection of the disease.”

Dentists and hygienists are in a unique position to recognize the early signs of oral cancer in high-risk groups by paying close attention to health history, investigating all hard- and soft-tissue lesions (particularly red/white lesions), and giving appropriate referrals. Dental professionals should not rely on periapical or panoramic radiographs or even cone beam volumetric tomography to show cancer manifestations in the hard tissues if the goal is to detect cancer at an early stage, when the disease is most treatable. These actions reduce the overall prevalence of oral cancer and help to preserve both quality and length of life.

Our patient had most of the risk factors associated with oral cancer (smoking, alcohol consumption, paan chewing, aged older than 40 years, and a previous history of oral cancer) that were cited by Dave in his recommended checklist for dental professionals. It is the view of the authors that poor oral hygiene is an additional risk factor for oral cancer, especially when combined with the other risk factors present in our patient. Although our patient’s oral cancer was at stage IV at the time of diagnosis, his tumors apparently presented with low proliferative activity, and such cancers have been associated with a good prognosis, even with a long diagnostic delay such as that seen here.

**ACKNOWLEDGMENT**

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**REFERENCES**

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   a. True       b. False

2. However, viruses, especially exposure to human papilloma virus version 16 (HPV-16), have also been associated with oral cancer, particularly squamous cell carcinoma (SCC).
   a. True       b. False

3. Cancers that are detected early have an 40% to 50% survival rate.
   a. True       b. False

4. SSC is a malignant neoplasm of mucosal origin. It is the most common type of oral cancer, accounting for over 90% of all malignant neoplasms of the oral cavity.
   a. True       b. False

5. Perhaps less familiar in the Western world is the use of paan, which is made of hasish and sometimes tobacco, and is used in many Eastern cultures.
   a. True       b. False

6. Many studies have associated paan with oral malignancies. People using paan without tobacco were 9.9 times, those using paan with tobacco 8.4 times, more likely to develop oral cancer as compared with nonusers, after adjustment for other covariates.
   a. True       b. False

7. The average 5-year survival rate for SCC in most populations remains around 95%; however, survival is especially poor when the disease has progressed to stage III or IV.
   a. True       b. False

8. The reasons given for the failure, on the part of the general practitioners, to recognize oral cancers were discussed, in detail, by Dave; Dave categorized delays as related to the patient, the doctor, or the system.
   a. True       b. False
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