The keys to early cancer diagnosis: careful examination & timely biopsy

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The young man was just 19 when he came in to see his dentist after Halloween because of a sore on the side of his tongue. A non-smoker and non-drinker, he did not seem to be at risk for cancer, so his dentist decided to re-check the lesion before Christmas. By then the lesion was bigger. When he finally had a biopsy in January, it was an invasive squamous cell carcinoma.

Oropharyngeal cancer continues to claim the life of about one American every hour, accounting for 7,590 deaths in 2008, according to the American Cancer Society. Oral cancer takes a terrible toll if it is not caught early as it can rob its survivors of the ability to eat, speak and taste.

Dentists often fail to detect oral cancer until it has invaded deeply because it can mimic common traumatic, infectious or immune diseases. When oral cancer is detected early, however, it can be cured; recognized in its precursor stages, it can even sometimes be prevented.

The cancer screening examination includes looking at and palpating the neck, scalp and face as well as the mouth and oropharynx. About two-thirds of oral cancers arise in the lateral/ventral tongue and the floor of the mouth, but other common sites include the retromolar pad, the tonsillar pillars, the soft palate and the oropharynx. The dentist should thoroughly examine the lateral tongue by gently pulling it forward with gauze, examine the lateral tongue by gently pulling it forward with gauze, depress the tongue and examine the soft palate and oropharynx while the patient says “ah.” Even the act of gagging presents a momentary opportunity to glimpse the oropharynx and soft palate.

About 90 percent of oropharyngeal malignancies are squamous cell carcinoma of the surface mucosa. Precancerous mucosal lesions are often white and may appear slightly rough; unexplained white lesions are often called leukoplakia. Lesions such as that shown in Figure 1 look rough because the proliferating epithelium piles up on the surface, and the thickened epithelium hides the red color of the underlying blood vessels.

Malignancies of surface tissues, as seen in Figure 2, are often red and enlarged, and unexplained red lesions are often called erythroplakia. Unexplained red lesions are more likely than white lesions to be diagnosed as malignancies when they are biopsied because the expanding malignancy causes inflammation and secretes molecules that stimulate the formation of new blood vessels. However, both red and white lesions are capable of representing malignancy. Malignancies may also cause spontaneous pain or paraesthesia. The general rule of thumb is that unexplained red, white and/or ulcerated lesions that persist for more than 10 days should be biopsied.

Lichen planus, or lichenoid mucositis, has generated heated debate about its premalignant potential for years. It is now recognized that there are several conditions that can share the clinical appearance of lacy white lines on a red background and also the microscopic feature of a dense T-lymphocyte infiltrate along the basement membrane. Lichenoid conditions are probably not all equally likely to generate squamous cell carcinoma.

A lichenoid drug reaction, for example, is a reaction to a systemic medication that disappears when the medication is withdrawn. Lichenoid reactions also can result from contact with an allergenic material, such as a metal, in susceptible patients (Fig. 3), and for other reasons.

There are many reports in the literature of cancer arising in a patient previously diagnosed with lichen planus, but some retrospective analyses have confirmed that the original clinical or even microscopic diagnosis of lichen planus was incorrect. Apparent malignant transformation of oral lichen planus (OLP) may represent “red and white lesions that were dysplastic from their inception but that mimic OLP both clinically and histologically.” Figures 4 and 5 demonstrate this concept.

Warty-looking verrucous conditions also may confuse dentists. Many diseases in this group are caused by HPV. Benign members of this group include verucca vulgaris, the common wart (Fig. 6), which is self-limiting in most patients, and condylomata, genital warts (Fig. 7), which can be widespread in the immuno-suppressed patient.

There are also premalignancies and malignancies in this group. Proliferative verrucous leukoplakia (PVL) is a multifocal verrucous disease that eventually turns into carcinoma in a substantial proportion of cases. Figure 1 may represent a case of PVL. Verrucous carcinoma is a large warty malignancy that is slow to invade but can degenerate into squamous cell carcinoma.

A number of commercial chairside applications such as toluidine blue staining, tissue reflectance, fluorescence imaging and brush tests have appeared on the market in the past decade, and they are intended to help the dentist with early cancer detection. Despite their attractive marketing and their convenience, they have not been shown by rigorous Cochrane analysis to either help or hinder early cancer detection in the general population. Even visual screening programs have not been proven to help reduce oral cancer deaths, and more study is needed in this field. Table 1 summarizes the currently available adjunctive technologies.

This leaves the dentist with a very

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powerful tool: the biopsy, which is still the only technique that definitively diagnoses oral cancer. When coupled with a thoughtful patient history as well as a thorough head and neck examination, it can allow the dentist to diagnose oral lesions with as much confidence as possible.

Table 1: Commercial techniques intended to aid oral cancer detection.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Example of common brand name</th>
<th>How it works</th>
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<tbody>
<tr>
<td>Toluidine blue vital dye</td>
<td>Orascan</td>
<td>Dyes proliferating tissues blue</td>
</tr>
<tr>
<td>Tissue reflectance</td>
<td>Vizilite</td>
<td>Enhances the appearance of white areas</td>
</tr>
<tr>
<td>Tissue autofluorescence</td>
<td>Velscope</td>
<td>Abnormal tissue loses normal green autofluorescence, looks black</td>
</tr>
<tr>
<td>Brush test</td>
<td>Oral CDx</td>
<td>Superficial epithelial sample is classified as positive, negative or atypical</td>
</tr>
</tbody>
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Fig. 3: This lesion looks much like lichen planus, but it arose when the orthodontic brackets were placed and disappeared when they were removed. Lesions such as this are called lichenoid mucositis.

Fig. 4: This rough white lesion was initially thought to be lichen planus, but on biopsy it proved to be a microinvasive squamous cell carcinoma.

Fig. 5: This photomicrograph of squamous cell carcinoma demonstrates an area in which lymphocytes are attacking the overlying dysplastic epithelium, giving a microscopic appearance that is similar to lichen planus. Such an inflammatory reaction to dysplasia may explain why some cases are initially misdiagnosed as lichen planus and later prove to be squamous cell carcinoma.

Fig. 6: Verruca vulgaris, the common wart, is a benign discrete warty lesion that is usually self-limiting. It is caused by some types of HPV. It is more familiar on the skin, and may spread to the mouth by direct contact.

Fig. 7: Condylomata (genital warts) are also caused by HPV and may be florid in immunosuppressed patients such as this one. They are benign.

Fig. 8: Biopsy specimens should be of adequate size (3 mm or larger) and should be taken from a representative area of the lesion. The dentist should place them in formalin fixative immediately, and then transport them to the oral pathologist for microscopic diagnosis.
A biopsy is simply the removal of tissue from a living patient for the purposes of diagnosis. Whether the dentist uses a scalpel, surgical scissors or a surgical punch, the aim is to retrieve a piece of tissue that is representative of the entire lesion and preserve it en route to the oral pathology laboratory (Fig. 8). At the lab, the specimen is processed on a glass slide and diagnosed microscopically. Usually it takes a week or less for the oral pathologist to finalize the biopsy report.

The American Academy of Oral and Maxillofacial Pathology recommends that all tissue removed from the oral cavity be sent to an oral pathologist as a biopsy, unless it results from a routine procedure such as a gingivectomy for esthetic and functional reasons. Most oral pathologists’ services are covered by the patient’s medical insurance. General pathologists will also accept biopsies from dentists, but oral pathologists receive at least three years of specialty training after dental school and are truly specialists in oral disease.

By routinely examining every patient thoroughly for signs of head and neck cancer, and ensuring that any potentially suspicious lesion that persists for more than 10 days is appropriately biopsied and sent to an oral pathologist for diagnosis, dentists may indeed save lives.

**Literature**