The keys to early cancer diagnosis

Dr Sara Gordon
USA

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, the lesion proved to be 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 presents a momentary opportunity to glimpse the oropharynx and soft palate.

There has been a recent increase in Human Papillomavirus (HPV)-associated squamous cell carcinoma of the base of the tongue and tonsils in young patients, a change that is attributed to a rise in high-risk HPV infection in the oral cavities of sexually active young adults. Nevertheless, the most common risk factors for oral cancer remain tobacco and alcohol use.

About 90 per cent 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 termed leukoplakia. Lesions such as shown in Figure 1 look rough because the proliferating epithelium piles up on the surface and the thickened epithelium hides the red colour of the underlying blood vessels.

Fig. 1: This rough white lesion was diagnosed on biopsy as moderate epithelial dysplasia.—Fig. 2: This large red mass was a squamous cell carcinoma. The lateral tongue is the most common site for oral cancer.

Malignancies of surface tissues, as seen in Figure 2, are often red and enlarged; unexplained red lesions are often termed erythroplakia. Unexplained red lesions are more likely to be diagnosed as malignancies than white lesions 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. Malignant change may cause spontaneous pain or parasthesia. The general rule of thumb is that unexplained red, white and/or ulcerated lesions that persist for more than ten days should be biopsied.

Lichen planus, or lichenoid mucositis, has generated heated debate about its premalignant potential for years. It is now recognised 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 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 can also result from contact with an allergenic material, such as a metal, in susceptible patients (Fig. 5), 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
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be widespread in the immunogenital warts (Fig. 7), which can most patients, and condylomata, (Fig. 6), which is self-limiting in

tiary verruca 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 immunogenital warts (Fig. 7), which can arise in many different sites in the body, including the vulva, vagina, cervix, and anus. They are often painful and can cause bleeding, itching, and burning. There are also pre-malignancies and malignancies in this group. Proliferative verrucous leukoplakia (PVL) is a multifocal verrucaous disease that eventually turns into carcinoma in a substantial proportion of cases. Figure 1 may represent a case of PVL. Verrucae are a group of small, firm, rough, brown or black papules that are most common on the hands, feet, and face. They are caused by HPV. Renal members of this group include verruca plantaris, verruca plana, and verruca plantaris. Verrucae can be treated with several methods, including cryosurgery, electrocautery, laser therapy, and topical therapies such as salicylic acid or imiquimod. Verrucae can also be prevented by avoiding exposure to HPV and using protective gear when engaging in activities that increase the risk of exposure.

Figure 1 may represent a case of PVL. Verruca vulgaris (Fig. 6) is a common wart that is caused by human papillomavirus (HPV) and can be found on any part of the body where the skin is irritated or traumatized. Verrucae are contagious and can be spread by direct contact with an infected person or with objects that have been contaminated with the virus. Verrucae can be treated with several methods, including cryosurgery, electrocautery, laser therapy, and topical therapies such as salicylic acid or imiquimod. Verrucae can also be prevented by avoiding exposure to HPV and using protective gear when engaging in activities that increase the risk of exposure.

Several commercial side applications, such as toluidine blue staining, tissue reflectance, fluorescence imaging and brush tests, have appeared on the market in the past decade, which are intended to help the dentist with early cancer detection. Despite their attractive marketing and convenience, they have not been proven 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 summarises the currently available adjunctive technologies.

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

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 laboratory, the specimen is processed on a glass slide and diagnosed microscopically. Usually it takes a week or less for the oral pathologist to finalise the biopsy report.

The American Academy of Oral and Maxillofacial Pathology recommends that for aesthetic and functional reasons 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. Most oral pathologists’ services are covered by the patient’s medical insurance.

General pathologists will also accept biopsies from dentists; however, it should be considered that 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 persists for more than ten days, is not appropriately biopsied and sent to an oral pathologist for diagnosis, dentists may indeed save lives. 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 laboratory, the specimen is processed on a glass slide and diagnosed microscopically. Usually it takes a week or less for the oral pathologist to finalise the biopsy report.

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### 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>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue reflectance</td>
<td>Visite</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, appears black</td>
</tr>
<tr>
<td>Brush test</td>
<td>Oral CDx</td>
<td>Superficial epithelial sample is classified as positive, negative or atypical</td>
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</tbody>
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Authorities now recommend that instruments cannot be sterilised under review. This leaves the dentist with many different options for sterilisation and infection control.

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Dr. Bernard +61 446 1622 or email bernard@global2.co.za

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Dr. Yui Liu +86 20 81910812 or email plau@sciican.com

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2 Editorial note: A complete list of references is available from the publisher.