Changes in the Pattern of Oral Lesions Associated with HIV Infection: Implications for Dentists

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ABSTRACT

Broad access to better HIV treatment has resulted in a significant reduction in the prevalence of HIV-associated oral lesions in western industrialized countries. However, a possible increased prevalence of oral warts and a potential dissociation between CD4+ T-cell counts and oral manifestations of HIV require continued vigilance by oral health care providers. Head and neck and oral examination coupled with a careful consideration of the complications associated with hyposalivation remain essential components of a comprehensive oral health care program.

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HIV is a retrovirus carried by more than 40 million people worldwide.[1] HIV infection leads to gradual deterioration of the immune system and to the development of AIDS. As of June 2006, 61,423 people in Canada had been infected with HIV; 20,493 of them had been diagnosed with AIDS, and at least 13,326 people with AIDS had died.[2] Notwithstanding extraordinary progress in understanding and managing HIV pathogenesis, there is no cure for HIV-related disease and the treatment of choice is to target HIV viral replication with the expectation of delaying further immune suppression. With disease progression, the deleterious effect of HIV on the immune system results in an escalating incidence of widely recognized and extensively described opportunistic infections and diseases, among which are the oral manifestations of HIV (OMHs).[3–5] A summary of the most common OMHs and their recommended treatment is presented in **Table 1**.

Since the onset of the HIV pandemic, OMHs have been well documented as early markers of HIV infection[7] and as predictors of HIV disease progression.[8] Oral candidiasis (**Fig. 1**) and oral hairy leukoplakia (**Fig. 2**)[9] are lesions associated with fungal and viral pathogens, respectively, and are the most frequently occurring OMHs. Others, such as human papillomavirus (HPV) related warts (**Fig. 3**), aphthous-like ulcers and Kaposi's sarcoma have also been reported extensively. OMHs contribute to HIV-related morbidity and are believed to serve as important markers of HIV infection and disease progression even in those on modern HIV therapy.

The therapeutic breakthrough associated with the introduction of HIV-specific protease inhibitors more than 10 years ago has significantly improved the prognosis of HIV disease.[10,11] The use of HIV protease inhibitors combined with therapy targeting the HIV reverse transcriptase enzyme (highly active antiretroviral therapy or HAART) is associated with a sustained decrease in viral replication and stabilization or even an increase in the peripheral CD4+ T-helper cell count,[12] a subset of lymphocytes targeted by HIV. It is generally accepted that the risk of developing an OMH

Table 1 Most commonly observed oral manifestations of HIV and recommended treatment

Oral manifestations of HIV	Treatment	Comments
Oropharyngeal candidiasis	Clotrimazole: 10-mg troches, orally, 5 times a day for 7–14 days Fluconazole: 100 mg, orally, once daily for 7–14 days Refer when refractory to fluconazole[a]	• CDC guidelines do not recommend prophylaxis except for exceptional cases of severe or frequent recurrences. • Consider drug–drug interactions and liver status when choosing a systemic or topical treatment.
Oral hairy leukoplakia	In-office application of podophyllum resin (25%)	• There are insufficient data to support evidence-based treatment recommendations. Considering the inconsequential nature of the lesion, systemic antiviral medication may not be warranted.
Oral warts	Surgical excision and biopsy; refer for extensive/recurrent lesions[a]	• There are insufficient data to support evidence-based treatment recommendations other than surgical excision. • Consideration should be given to the possibility of spreading HPV to other surfaces during surgery, and potential cancer risk.
Oral herpes simplex	Acyclovir: 800 mg, 4 times a day for 7 days Valacyclovir: 500 mg twice daily for 7 days Refer those with severe, persisting or recurrent lesions[a]	• Topical antiviral medication should be considered for patients with CD4+ counts above 0.2×10^9/L and herpes labialis.
Recurrent aphthous-like ulcerations	High-potency topical steroids, such as fluocinonide and clobetasol Refer severe cases[a]; systemic steroids, thalidomide or immunosuppresives may be considered	• The use of topical steroids may result in increased incidence of oral pharyngeal candidiasis. • Systemic therapy should be limited to those experienced in the use of these medications.
Gingival and periodontal disease	Oral hygiene, prophylaxis, scaling/curettage, chlorhexidine rinse; may be combined with systemic antibiotics.	• Some studies report linear gingival erythema with a band-like pattern of erythema and increased intensity of bone and soft tissue loss
Malignant lesions: oral Kaposi's sarcoma, squamous cell carcinoma, lymphoma	Intralesional injection of vinblastine or sodium tetradecyl sulfate 3% and/or low-dose radiation therapy	• Patient with biopsy-confirmed disease should be referred to physician for evaluation of the involvement of other organs. • Intralesional treatment should be limited to those experienced in the use of these medications.
Hyposalivation	Stimulation of gland function: taste, chewing and sialogogues Prevention of oral complications (caries, candidiasis)	

Source: Reference 6
[a]Refer to an appropriate specialist
CDC = US Centers for Disease Control and Prevention; HPV = human papillomavirus.

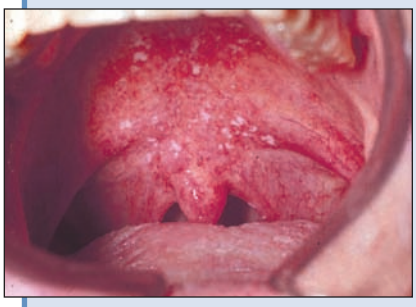

Figure 1: Pseudomembranous candidiasis on the hard and soft palate presents as white removable plaque.

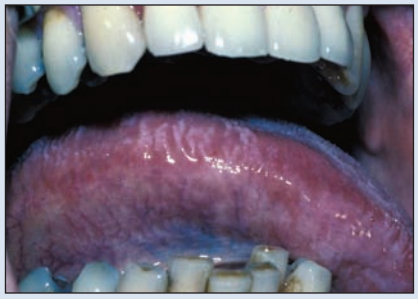

Figure 2: Hairy leukoplakia, a condition associated with Epstein-Barr virus, presents as a painless corrugated lesion on the right lateral tongue.

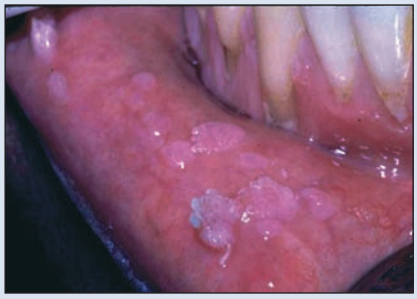

Figure 3: Multiple and recalcitrant oral warts presenting as sessile and pedunculated lumps on the lower lip.

increases with decreasing CD4 count and higher HIV load.[13,14] However, this observation may be less accurate in patient populations with long histories of HIV infection.[15] Because CD4+ counts are not a direct measure of immune function, opportunistic infections, such as OMHs, may be a more accurate reflection of HIV disease status. A disconnect between opportunistic infections and CD4+ counts could also be explained by a paradoxical transient deterioration of immune function during initial response to HIV medication, referred to as the immune reconstitution syndrome.[16]

Although the treatment of specific OMHs has been effective,[6] it is evident that the most successful treatment is to prevent or reverse the underlying primary immunodeficiency disease.[17] Accordingly, the introduction of HAART is associated with a significant decrease in the prevalence of opportunistic diseases including OMHs. For example, HAART is associated with a significant decrease in the prevalence of oral candidiasis and oral hairy leukoplakia coupled with an improved CD4 count.[18]

Seemingly in contradiction with those findings, an increased prevalence of oral warts has been noted by some investigators despite a marked improvement in CD4 cell count.[19] This observation may not reflect true increased prevalence in the population. However, because of the link between HPV and cancer, it suggests that, with increased life expectancy of HIV-infected patients, oral cancer may become a clinically significant long-term complication.

The prevalence of OMHs is declining in populations in industrialized countries with the introduction of better HIV therapies. However, an increase in salivary gland disease, xerostomia and oral warts has been seen.[20] This should be of utmost interest to the dental profession because saliva is an essential contributor to oral health. Xerostomia in HIV patients, either triggered by HIV disease directly or as a side effect of medications, represents an additional risk factor for caries and periodontal disease as well as OMHs, especially oral candidiasis, the most commonly diagnosed OMH.

Finally, in addition to poor response or adherence to HIV treatment, low CD4 counts or high HIV load, tobacco use is confirmed as a risk factor for OMHs.[21–23] Furthermore, the effect of tobacco use in addition to increased HPV disease may result in a dramatic increase in the incidence of oral cancer in HIV patients.

Taken together, the epidemiology of OMHs in the post-HAART era indicates that OMHs are less frequent, but new and poorly understood paradigms are emerging. Those paradigms include a possible upsurge in the prevalence of oral warts and the possibility that, with time, CD4+ T-cell counts and the prevalence of OMHs may not correlate. The practical significance of those 2 emerging paradigms is that oral health care providers have to continue to be vigilant in their examination and treatment of their HIV-infected patients. To deliver an optimal level of care, oral health clinicians should emphasize the early detection of oral cancer. They should remain vigilant in the diagnosis of OMHs traditionally associated with low CD4+ counts (i.e., Kaposi's sarcoma) even in patients with high CD4+ counts. In addition, clinicians must address the complications of hyposalivation and must offer an effective tobacco smoking cessation program either by referral or by the oral health care provider directly.

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