

Oral Manifestations of HIV and Their Management in A 41-Year-Old Male

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Abstract

Oral manifestations of HIV infection are an ongoing clinical burden in developing countries. The presence of HIV oral manifestations indicates a compromised immune status and are markers of disease progression. While the epidemic continues to grow in Eastern Europe, central Asia, Middle East, North Africa, and Latin America with a significant rise in new HIV infections, access of individuals living with HIV to dental professionals remains important to address the clinical burden and provide optimum clinical management. We present a case of a HIV-positive 41-year-old male presenting to the Oral Medicine Clinic with various oral manifestations. This case outlines multiple phases of the management plan and illustrates pre- and post-management clinical photographs.

Keywords: oral manifestations, HIV, candidiasis, oral warts, salivary gland disease

Introduction

Human Immunodeficiency Virus (HIV) disease increases the risk of opportunistic infections in affected individuals due to immunosuppression (Maartens G et al, 2014). HIV disease targets activated CD4+ T-lymphocytes via the interactions with CD4 and chemokine coreceptors (Maartens G et al, 2014). This mechanism constitutes the hallmark of HIV infection where progressive depletion of CD4+ T-lymphocytes results from reduced production and increased destruction (Maartens G et al, 2014). The failure of CD4+ T-lymphocytes homeostasis to the level necessary to prevent opportunistic infections lead to several comorbidities (Jung and Paauw, 1998). While HIV is known to be associated with several comorbidities

related to the virus, oral conditions are among the early indications. HIV-related oral manifestations (HIV-OM) occur in 30-80% of the affected patient population (DA Reznik, 2006) the presence of these oral manifestations indicates a compromised immune status and are markers of disease progression (AR Tappuni, 2020). A recent systematic review showed that the prevalence of HIV-OM continues to be significant in developing countries (El Howati and Tappuni, 2018) although oral manifestations are not diagnostic of HIV infection, they may suggest possible involvement for individuals with unknown HIV status. Clinicians are therefore expected to be aware and able to recognise HIV-OM infection for appropriate care and referral. The present case describes the management of HIV-

OM that were detected by a general dental practitioner. The patient was then subsequently referred to the Oral Medicine Clinic for evaluation and management.

Case Report

A 41-year-old male patient was referred to the Oral Medicine Clinic for evaluation and management of an exophytic papillomatous lesion involving the lingual gingiva of tooth 34. The lesion was asymptomatic and therefore the duration of its presence was unknown. Extra-oral examination revealed angular cheilitis (Figure 1a). Conventional intra-oral examination confirmed the presence of a 1 x 0.5cm pedunculated lesion with a papillomatous surface texture associated with the lingual gingiva of tooth 34 (Figure 2a). Clinical examination also confirmed the presence of salivary gland hypofunction as well as an objective complaint of dry mouth. His medical history was significant for HIV diagnosed in 1998, gastro-oesophageal reflux disease, hyperlipidaemia, epilepsy, asthma, osteoporosis, anxiety, and depression. The latest blood investigations showed undetectable viral load. A history of smoking 15 cigarettes a day for 5 years was noted, however the patient ceased smoking in 2005. The patient was informed about the possible relevance of the identified oral lesions to his HIV status as well as the management approaches including medical and surgical options. Additionally, the patient was informed on the possible persistence of angular cheilitis and recurrence of squamous papilloma which may be determined by the stability and/or progression of his HIV status. The management plan consisted of multiple phases. The first was the application of topical medicaments for the management of angular cheilitis and the use of local salivary stimulating factors for the management of his dry mouth. Hydrozole cream 1% to be applied to the corners of the mouth four times a day was advised

to manage angular cheilitis. The rationale behind the use of Hydrozole cream 1% is its combination of a broad-spectrum antifungal (clotrimazole 1%) with a glucocorticosteroid (hydrocortisone 1%) to relieve inflammation as well as eradicating the associated candidal infection. Several local salivary stimulating factors such as sugar free chewing gum were advised. Topical products were also utilised including frequent dry mouth oral gels and sprays. The second phase of the management plan involved surgical excision of the squamous papilloma involving the lingual gingiva of tooth 34. An additional supportive therapy phase included oral hygiene reinforcement to reduce the risk of dental caries and periodontal therapy which was coordinated with the patient's general dental practitioner.



Figure (1): a. Angular cheilitis on initial presentation, b. Angular cheilitis following one month review.

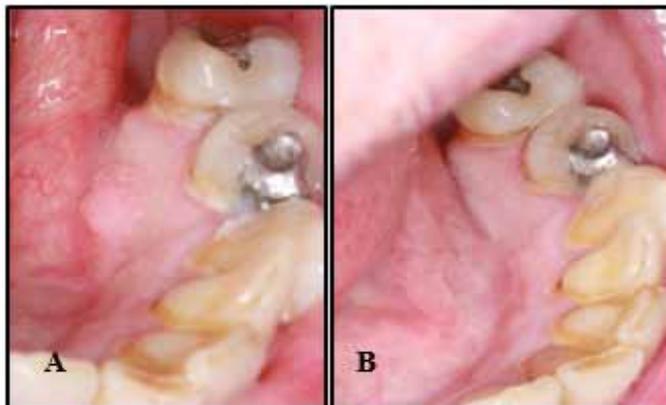


Figure (2): a. Squamous papilloma lingual gingiva of tooth 34; b. Biopsy site on review appointment.

Table (1): Based on the EC Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of HIV (1993).

Group 1. Lesions strongly associated with HIV infection
Candidiasis (Erythematous, Pseudomembranous)
Hairy leukoplakia
Kaposi's sarcoma
Non-Hodgkin's lymphoma
Periodontal disease (Linear gingival erythema, Necrotising (ulcerative) gingivitis, Necrotising (ulcerative) periodontitis)
Group 2. Lesions less commonly associated with HIV infection
Bacterial infections (Myobacterium avium-intracellulare, Myobacterium tuberculosis)
Melanotic hyperpigmentation
Necrotising (ulcerative) stomatitis
Salivary gland disease
Dry mouth due to decreased salivary flow rate
Unilateral or bilateral swelling of major salivary glands
Thrombocytopenic purpura
Ulceration NOS
Viral infections
Herpes simplex virus
Human papillomavirus (wart-like lesions)
Condyloma acuminatum
Focal epithelial hyperplasia
Verruca vulgaris
Varicella-zoster virus
Herpes zoster
Varicella

Group 3. Lesions seen in HIV infection
Bacterial infections (Actinomyces israelii, Escherichia coli, Klebsiella pneumoniae)
Cat-scratch disease
Drug reactions (ulcerative, erythema multiforme, lichenoid, toxic epidermolysis)
Epithelioid (bacillary) angiomatosis
Fungal infection other than candidiasis (Cryptococcus neoformans, Geotrichum candidum, Histoplasma capsulatum, Mucoraceae (mucormycosis/zygomycosis), Aspergillus flavus)
Neurologic disturbances (Facial palsy, Trigeminal neuralgia)
Recurrent aphthous stomatitis
Viral infections (Cytomegalovirus, Molluscum contagiosum)

Discussion

Oral manifestations of HIV infection are well reported in the literature. They can cause morbidity and affect patients' quality of life. A classification of the oral manifestations of HIV infection and their diagnostic criteria has reached consensus following the EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre meeting in 1993 (Classification and diagnostic criteria for oral lesions in HIV infection, 1993). The classification of oral lesions is divided into three groups; group 1 comprise lesions that are strongly associated with HIV infection, group 2 comprise lesions that are less commonly associated with HIV infection and group 3 comprise lesions that are seen in HIV infection (Table 1). This case has demonstrated oral manifestations that are strongly associated as well as conditions commonly associated with HIV infection, based on the diagnostic criteria of the ECC criteria. In the presented case, one of the oral manifestations is listed in group 1 of the classification criteria which is oral candidiasis (OC). It has been reported that OC is the most reported HIV-OM globally since the beginning of the endemic (AR Tappuni, 2020). In this case, OC is clinical-

ly seen as angular cheilitis with erythema and mild fissuring involving the corners of the mouth, with more involvement seen in the left corner on presentation (Figure 1a). The patient was instructed to apply Hydrozole cream 1% to the corners of the mouth four times a day. After one month, the patient was reviewed in the Oral Medicine Clinic and only mild improvement was clinically evident (Figure 1b). Upon investigating the patient's compliance with the frequency of medicament use, it was noted that the Hydrozole cream was only used twice a day for one month. Nonetheless, there were no symptoms associated with the clinical presentation of angular cheilitis at the review appointment. While OC is strongly associated with HIV infection, it is considered to be the most common oral disease in this group of patients (V Ramirez-Amador et al, 2003). The pathogen most commonly associated with OC is *Candida albicans* however; other candida species such as *C. krusei*, *C. glabrata* and *C. dublinensis* are also associated with OC in patients with HIV infection (O Lortholary, 2012). Other than the angular cheilitis form, OC can present as erythematous candidiasis and pseudomembranous candidiasis (M Nokta, 2008). The former has been found to be more prevalent among patients with HIV than in the general population (GR Thompson et al, 2010). Group 2 of the classification criteria listed both salivary gland disease which includes dry mouth due to decreased salivary flow rate and human papillomavirus-related oral lesions (HPVOL). Both oral manifestations were seen to be involved in this case. With regards to dry mouth, it has been found to be more frequent among men and is a major contributing factor to the development of dental caries and periodontal disease (M Nokta, 2008). Several theories that explain the cause of salivary gland hypofunction in patients with HIV are proposed. One is that elevated levels of HIV RNA may reside

in lymph nodes within the parotid glands during early development leading to salivary gland HIV infection (Palefsky J, 2009; LL Patton et al, 2000). A second theory is an indirect process where increased CD8+ lymphocytic infiltration into lymph nodes lead to salivary gland tissue hyperplasia manifesting as enlargement of the parotid region or salivary gland hypofunction (M Steinau et al, 2012), (AD Varnai et al, 2009). Another theory is the introduction of antiretroviral therapy in the mid-1990s where studies reported an increased prevalence of salivary gland disease including reduced salivary flow in patients with HIV (JE Cameron et al, 2005), (D Greenspan et al, 2001), (I Greenwood et al, 2002). A wart-like lesion involving the lingual mucosa of tooth 34 was surgically excised and histopathological assessment confirmed the diagnosis of squamous papilloma. The microscopic description of the biopsy specimen showed mature fibrous connective tissue covered by parakeratinised hyperplastic stratified squamous epithelium arranged as multiple exophytic blunt end projections, consistent with squamous papilloma. On the review appointment post-biopsy, successful healing of the biopsy site was confirmed clinically (Figure 2b). Although HPVOL are less commonly associated with HIV infection according to the classification, an increase in oral warts was noticed concurring with the introduction of highly active antiretroviral therapy (HAART) (G Anaya-Saavedra et al, 2013). This is further studied and was shown that patients with an undetectable viral load had a 6-fold risk of presenting HPVOL (G Anaya-Saavedra et al, 2013). Another study proposed that oral warts may represent a form of immune reconstitution inflammatory syndrome (IRIS) in response to cell-mediated immune function (MD King et al, 2002). Most HPVOL are benign and may be diagnosed as squamous cell papilloma, verruca vulgaris, condyloma acumi-

natum or multifocal epithelial hyperplasia. HPVOL are usually associated with low-risk human papillomavirus types, however, high-risk types were also identified (M Steinau et al, 2012; AD Varnai et al, 2009; Paparotto and Meeks, 2001). Moreover, the prevalence of HPVOL was found to be higher in HIV patients with oral candidiasis and oral leukoplakia compared with HIV patients without lesions (M Fatahza-deh et al, 2013). While diverse immunological abnormalities are thought to be the cause for the development of HPVOL, prolonged immunosuppression in HIV patients is also considered to prevent the reverse of lesions with therapy (JE Cameron et al, 2005). The overall management of the presented case focused on reinforcing oral hygiene measures to reduce the risk of dental caries and periodontal disease, encouragement to use local salivary stimulating factors to ameliorate the symptoms of dry mouth and the treatment of angular cheilitis. While there is no consensus on the treatment of HPVOL in HIV patients, the patient consented to surgical excisional biopsy of the squamous papilloma. Regular dental visits for long-term periodontal therapy were arranged with the patient's general dental practitioner. Symptoms of dry mouth were improved significantly following the use of topical measures only. Additionally, there also seem to be a mild improvement of angular cheilitis following the use of Hydrozole cream 1%, despite non-compliance with the frequency of use. Although the mentioned conditions were the only oral manifestations associated with HIV infection in this case, others (Table 1) are still quite prevalent.

Conclusion

This case has demonstrated the management of HIV-related oral manifestations. A management plan consisted of oral health-care measures such as oral hygiene regime and instructions for the management

of dry mouth were implemented. Minimal improvement in angular cheilitis might be attributed to poor compliance with frequency of medicament use. Understanding of the recognition and significance of the large spectrum of oral manifestations with HIV infection remain a significant clinical challenge in the developing world.

Conflicts of Interest

The author declares that there is no conflict of interest.

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