

Infected lesions of oral cavity in HIV patients: A Review

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Abstract: Oral lesions of patients infected with human immunodeficiency virus (HIV) are a leading cause of morbidity among afflicted patients. In this study we summarized the most prevalent oral infections among HIV patients and the appropriate treatments. The most common infection is candidiasis followed by viral infection. The oral lesions have direct association with CD4 lymphocyte count. Also, these conditions are seen less in populations with ART medications. HIV infected patients with oral lesion should be diagnosed and receive appropriate treatment.

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1. Introduction

In recent decades, concerns about human immunodeficiency virus (HIV) and its transmission has increased. Oral manifestations of HIV infection have special importance and occasionally reflect the immune suppression and progression e to AIDS (Glick, Muzyka et al. 1994, Haghghi, Alizadh et al. 2012). Oral lesions are presented as first manifestations in about 10% of HIV infected patients (Itin, Lautenschlager et al. 1993), and between 30-80% of these subjects show oral lesions during their lifelong (Mascarenhas and Smith 1999). The most prevalent lesions consist of fungal and viral infections (Feigal, Katz et al. 1991). These infections are known as opportunistic pathogens, and co-infections of these conditions are common among afflicted subjects (Patton, Phelan et al. 2002). Various risk factors have been described that prone HIV patients to develop oral lesions such as CD4 lymphocyte count below 200/ μ L, tobacco smoking and poor oral hygiene (Arendorf, Bredekamp et al. 1998).

Health care workers specifically dentists and dental specialists are believed to have an important role in spreading the HIV infection among the healthy population (Ghasemzadeh, Piraloo et al. 2013, Tabibzadeh, Yazdani et al. 2013, Yazdani, Tabibzade et al. 2013). Therefore, diagnosis and management of oral lesions is essential for clinicians (Ghasemzadeh, Piraloo et al. 2013). The aim of this paper was to present important clinical manifestations, predisposing

factors and treatment of oral infections among HIV infected patients.

2. Oral Candidiasis

Oropharyngeal candidiasis is the most common fungal infections among HIV infected patients (Anwar, Malik et al. 2012). It usually presents as an opportunistic infection in patients with CD4 lymphocyte counts less than 200 cell /mm³ (Glick, Muzyka et al. 1994, Anwar, Malik et al. 2012). The prevalence of oral candidiasis is estimated to be over 90% among untreated HIV patients and approximately 60% of them experience at least one episode of recurrence per year (Yang, Hung et al. 2010, Lin, Lin et al. 2012). Diagnosis of oral candidiasis is based on clinical characteristics. However, when the lesion doesn't response to common medication, a 10% potassium hydroxide (KOH) slide preparation may be necessary to confirm the diagnosis (Alborzi and Davarpanah 2010).

Four prevalent clinical presentations have been reported for oral manifestations of candidiasis among HIV infected patients. The most prevalent type is erythematous (atrophic) candidiasis (EC), followed by pseudomembranous candidiasis (PC) (thrush), angular chilitis (AC) and hyperplastic candidiasis (HC) (Patton, McKaig et al. 2000, Reznik 2004).

EC usually presents with red and flat patches on the mucosal surface of palates or dorsal surface of the tongue (Freeman, Liberali et al. 2012). EC is probable

to be misdiagnosed or underdiagnosed in HIV patients. Patients may complain of difficulty in eating, dryness of the tongue, burning of the mouth and even spontaneous gingival bleeding (Dupont and Drouhet 1988, Tosti, Piraccini et al. 1999, Nicolatou - Galitis, Velegraki et al. 2004). This type is also related to lower CD4 lymphocyte count and progression to AIDS. Patients with mild to moderate EC can be treated with topical treatments such as clotrimazole and nystatin suspensions (Robinson, Challacombe et al. 1997). It is demonstrated that clotrimazole troches are more safe than nystatin oral suspension because fructose which is used in the composition of clotrimazole oral treatments is less cariogenic than sucrose which is used in the formulation of nystatin oral suspension (Kasper, Richter et al. 2013). Patients with moderate to severe EC should be treated with systemic agents such as fluconazole, voriconazole and itraconazole (Patel, Erlandsen et al. 2012).

PC is typically characterized by a creamy white plaque that affects mostly tongue and other mucosal surface of oral cavity (Castro, Álvarez et al. 2013). It can also affect the esophagus and if the candida growths unusually in the mucosal surface give a white and swelling appearance to mucosa that called thrush (McManus, McGovern et al. 2011). If the plaque has obliterated with scraping, a red or pinkish surface with mild bleeding will be appeared (Hegde, Hegde et al. 2012). PC is also, correlated with lower CD4 count and progression to AIDS. The treatment strategy in PC is same as EC (Williams, Kuriyama et al. 2011).

Angular cheilitis presents with fissuring, erythema and ulceration of the corners of the lips. It can be associated with other conditions of candidiasis such as erythematous and pseudomembranous (Sharon and Fazel 2010). The untreated condition may continue for a long time. Treatment strategy consists of topical antifungal ointment (Verma, Balhara et al. 2012).

HC is a rare variant of oral candidiasis among HIV infected patients. This condition typically is a whitish plaque that appears in mucosa of the buccal area which is not removable by scraping and may be non-differentiable with EC (Pappas 2012).

All of the HIV associated candidiasis should be treated with topical or systemic antifungal medications at least for 2 weeks to decrease the risk of recurrent oral candidiasis. However, an important subject to prevent oropharyngeal candidiasis is the use of combination of potent antiretroviral treatment (ART) (Bensadoun, Patton et al. 2011, Scwingel, Barcessat et al. 2012).

In several studies fluconazole resistance has been reported to be between 5-56% in vivo. On the other hand, resistance to other azoles such as ketoconazole and itraconazole was less frequent and reported between 0-25% (Heinic, Stevens et al. 1993, Barchiesi, Colombo et al. 1994, He, Tiballi et al.

1994). In Patients with refractory oral candidiasis who are resistant to azoles, intravenous amphotericin B is recommended (Albouy and Naidoo 2002).

Several studies have been demonstrated that fluconazole can reduce the risk of oral candidiasis among patients with HIV infection. However, there was no significant associations between prophylactic use of antifungal medications and patients survival (Leen, Dunbar et al. 1990, Marriott, Jones et al. 1993). In additions some investigators showed that long term and frequent use of antifungal can result in refractory and even resistant infections. Accordingly, prophylactic consumption of antifungals is not recommended (Schuman, Capps et al. 1997).

3. Herpes simplex virus (HSV)

The most common viral infection among HIV infected patients is HSV. The condition has direct correlation with the progression of disease and lower CD4 lymphocyte count (Andrei, Lisco et al. 2011). HSV mainly manifests with vesiculoulcerative lesions on the lips and causes gingivostomatitis, however it can be seen throughout the oral cavity, which may be misdiagnosed with other infections (Lu, Celum et al. 2012). Clinical signs and symptoms among immunodeficient patients may be atypical and more severe. As well as, HSV can take for long period of time among the affected subjects. Evidence show that HSV outbreaks have been declined in the potent ART era. In addition, it should be treated with antiviral medication to prevent severe outbreak (Mark, Wald et al. 2008, El Hayderi, Delvenne et al. 2013). The suitable medication is acyclovir (400mg) that should be used three times per day. It is recommended to patients received antiviral medication within the first 72 hours after the clinical manifestations. Valacyclovir (500 mg) twice a day also, have equivalent effect with acyclovir but it is less administrated because of its expensiveness. Patients who suffer from odynophagia due to esophageal involvement may need to hospitalization and intravenous fluid to prevent dehydration. Also, intravenous antiviral therapy (acyclovir 5mg/day/dose three times a day) and pain relievers are recommended for patients who admitted in hospital. In addition, acyclovir and valacyclovir both can be used in secondary prophylaxis against HSV (Gallant, Moore et al. 1994, Aberg and Powderly 2010).

4. Oral Hairy Leukoplakia (OHL)

OHL is a HIV associated condition caused by viral replication of Epstein-Barr virus (EBV) on the lateral margin (unilateral or bilateral) of the tongue with thickened hair-like projections (Rushing, Hoschar et al. 2011). Although, it can be seen in other areas in the mouth such as buccal mucosa, soft palate, floor of the

mouth and even anterior surface of the tongue (González, Correnti et al. 2010). OHL is characterized by a painless, whitish, corrugated and non removable lesion that occasionally presents in early stage of HIV infection and shows the progression of disease to AIDS. It also, may present in HIV negative patients who receive immunosuppressive medications (Piperi, Omlie et al. 2010). The diagnosis of OHL should be confirmed by laboratory examinations, and clinical presentations of OHL are not sufficient for final diagnosis. DNA of EBV can be detected by immunohistochemistry or Nested PCR. There is no indication for treatment of OHL except due to cosmetic concerns. However, it is important to consider that this condition reveals the deterioration of immune system and decreases CD4 lymphocyte count and even failure to treatment. Other medical conditions which present with leukoplakia in the mouth and buccal mucosa such as lichen planus, candidiasis, squamous cell carcinoma and smokeless tobacco keratosis should be distinguished from OHL and biopsy should be considered for these patients, in special among them not responding to topical antifungal medications and corticosteroids (Rushing, Hoschar et al. 2011).

5. Kaposi's Sarcoma (KS)

KS is the most frequent oral malignancy attributed to HIV infection. It is almost caused by human herpes virus 8. It is estimated that up to 0.5 percent of HIV infected patients develop KS (Lodi, Guiguet et al. 2010). However, the incidence of KS among patients who received ART is reported to be lower than those without ART strategy (Maskew, MacPhail et al. 2011). Also, several studies demonstrated that KS has decreased after initiation of ART and consequently increasing of CD4 lymphocyte count (Maskew, Macphail et al. 2011, Maskew, MacPhail et al. 2011). KS, characterized with a purplish or brown-reddish maculae or papule in the oral cavity. In early stages it is flat and asymptomatic, as the lesion progresses, it becomes darker and protruded. The late lesions occasionally are susceptible for trauma and infection and can become symptomatic secondary to that. (Reznik 2005). The lesion may be misdiagnosed among patients with darker skin and for these subjects biopsy should be considered. The KS can be treated with localized intralesional injection of chemotherapeutic agents. Also, surgical removal can be considered for some subjects. Patients with coexisted extraoral lesions should be treated with systemic chemotherapy (Fernandes, Eloy et al. 2013, Maskew, Fox et al. 2013).

6. HPV

Although the incidence of HIV attributed infections have decreased since ART has been applied. In contrast, HPV has increased among HIV patients (Steinau, Reddy et al. 2012). The prevalence of HPV among HIV patients was reported between 2-6% in various studies (Chaturvedi, Madeleine et al. 2009, Syrjänen 2011). Oral HPV is defined as a risk factor for oropharyngeal cancer and has direct association with lower CD4 lymphocyte count. Also, the most prevalent HPV type among HIV positive patients is HPV 16 which is more frequently seen in patients with CD4 less than 200 (Beachler, Weber et al. 2012). This condition clinically presents with oral warts. Various shapes of wart may be seen in the oral cavity. Treatment strategies consist of cryotherapy, surgical method and laser surgery. However, recurrence is common and the treatment should be repeated (Denny, Bhatla et al. 2010).

7. Conclusion

Oral lesions in HIV patients show the potency of immune system, prognosis of the disease and treatment response to ART medications (Tami-Maury, Willig et al. 2013). Most of the oral lesions have been declined since ART was used. All of the patients with atypical oral lesions or lesions with long term duration should be referred to a specialist center for accurate diagnosis and initiation of appropriate treatment. Prophylaxis with ART medications are advised for HIV infected patients in order to decline HIV attributed oral lesions.

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