

Oral Manifestations in HIV Patients

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Abstract

The main characteristic of a patient with Acquired Immunodeficiency Syndrome (AIDS) is the ineffectiveness of the individual's immune system. The high degree of immunological weakness in which these patients are found has a high impact on their quality of life and can be seen clinically in the oral cavity. Because of this, the present study sought to evidence the most frequent oral manifestations of the AIDS disease. It has been demonstrated in this literature review that there is no specific oral manifestation of AIDS, but rather opportunistic lesions that are related to a deficient immune system. Such lesions may be of bacterial, viral, fungal origin, neoplastic processes and lesions of unknown etiology, as well as periodontal manifestations, which may be aggravated by the use of tobacco, alcohol, antidepressants and inadequate oral hygiene. It was also presented the ineffectiveness of saliva as a form of contagion and the importance of good oral hygiene for regression and control of some lesions. For this reason, it is important to note the importance of the dentist to correct the clinical diagnosis of such lesions so that it is possible to refer the patient to an infectologist in order to perform immunological tests that confirm their diagnosis and allow the correct follow-up and treatment. Only treatment with highly active antiretroviral therapy (HAART) does not provide full recovery of the epithelial cells of the oral cavity; therefore, the rapid initial implementation of antiretroviral therapy combined with constant patient visits to the dentist, for correct plaque control and adequate oral hygiene, avoids the appearance of certain lesions and helps in the regression of others.

Keywords: HIV Infections; AIDS; Mouth; Oral medicine; Saliva

Introduction

The first reports of AIDS (Acquired Immunodeficiency Syndrome) were reported in 1981 in the United States, is caused by HIV virus, which multiplies in the human body through body fluids and reach specific cells of the immune system, CD4+ T lymphocytes, making the patient immunosuppressed and vulnerable to opportunistic infections and diseases, from acute infection to death [1].

Carriers usually present the initial clinical signs of the disease in the oral cavity, thus giving the importance of the dental surgeon to the clinical assessment for a correct early diagnosis that is important for making fast decisions that will benefit the patient in relation to treatment results [1]. Saliva, however, is not a bodily fluid that facilitates the transmission of the virus, since, among other factors, saliva contains protease inhibitory proteins secreted by leukocytes, thus making it an ineffective vehicle of the virus [2]. According to data provided by UNAIDS (Joint United Nations Program on AIDS), in 2016 there were 48,000 new cases of HIV and by the end of the year 830,000 people in Brazil were living with the virus, and only 60% of those patients were undergoing active antiretroviral therapy (HAART) [3].

Oral manifestations associated with HIV are abundant, complex and interrelated, and because of this, deserve specialized attention, since the oral microflora is rich and suffers from the various metabolic, nutritional changes and immunosuppressed state of the patient. When

associated with the HIV virus, oral lesions may present as fungal, bacterial, viral, neoplastic processes and lesions of unknown nature. Factors such as tobacco use, poor oral hygiene, high viral load and regular consumption of alcoholic beverages are factors that contribute to the early development of such lesions. The HIV virus associated with immunosuppression increases the risk of specific types of carcinomas, such as Kaposi's Sarcoma and Non-Hodgkin's Lymphoma, which may appear alone or associated with Kaposi's Sarcoma [1].

Initially, a characteristic acute infection occurs, where oral alterations can be observed as focal ulcerations and mucosal erythema, but this acute viral syndrome disappears rapidly, giving rise to a long-term asymptomatic phase. Some of the oral manifestations most strongly associated with HIV are *Erythematous Candidiasis*, *Pseudomembranous Candidiasis*, *Angular Cheilitis* and *Leukoplakia Pilosa*. The most atypical periodontal problems seen in HIV-infected patients are Gingival Linear Erythema, GUN (Necrotizing Ulcerative Gingivitis) and PUN (Necrotizing Ulcerative Periodontitis). However, manifestations such as chronic periodontitis, progressive non-necrotizing periodontitis and conventional gingivitis are more easily encountered [4].

Early diagnosis increases the chances of an effective treatment to the patient, associated with the correct use of HAART. Patients living with HIV who started treatment earlier had a slower course of the disease, in the medium and long term, with a lower rate of complications, fewer opportunistic infections and longer life expectancy compared to patients who started treatment late [5].

	Group 1	Group 2	Group 3
Oral Manifestations Associated with HIV Infection (According to Neville, 2009)	<i>Candidiasis: Pseudomembranous, Erythematous, Angular cheilitis</i>	Bacterial Infections (Eg. <i>Ycrobacterium tuberculosis</i>)	Bacterial Infections (e.g. <i>Escherichia coli</i>)
	<i>Leucoplasia Pilosa</i>	Hyperpigmentation Melanica	Cat scratching disease
	<i>Sarcoma de Kaposi</i>	Necrotizing Ulcerative Stomatitis	<i>Angiomatose epitelioides</i>
	Non-Hodgkin's Lymphoma	Diseases related to the salivary gland	Drug Reactions
	Gingival Erythema Linear	Purple Thrombocytopaenic	Fungal Infections (Except <i>Candidiasis</i>)
	GUN	Non-specific ulcers	Neurological disturbances (Neuralgia Trigeminal)
	PUN	Viral infections	Foot-and-mouth disease recorrente
	-	-	Viral infections (<i>Cytomegalovirus, Molluscum contagiosum</i>)

Table 1: Oral manifestations associated with HIV infection.

The objective of this literature review is to help identify the lesions most strongly associated with AIDS infection, addressing the clinical characteristics of the lesions, treatment and prognosis.

Revision

The occurrence of oral manifestations caused by Human Immunodeficiency Virus infection is very wide and its occurrence depends on some factors such as the use of antiretrovirals, degree of immunological compromise, oral hygiene, alcohol consumption, tobacco among others, and can be determined by bacterial, fungal and viral infections, lesions of idiopathic cause and neoplastic processes [2]. The oral cavity epithelium, under normal health conditions, plays an important role against pathogens that cause certain types of infections [6]. However, in the case of patients with HIV/AIDS, the oral mucosa suffers from some molecular variations that considerably increase the patient's chances of developing certain infections [2].

There are no oral manifestations that are exclusively associated with HIV infection, as they can all be found in other diseases where immunosuppression occurs, therefore, they are lesions associated with the individual with the immunosuppressed system in general. Currently, AIDS patients have a considerable quality of life and good oral health when they undergo antiretroviral therapy [7].

The most accepted classification of oral manifestations was obtained by the Scientific Meeting and Consensus on Problems Related to HIV Infection and the World Health Organization Collaborating Center for Oral Manifestations of the Immunodeficiency Virus, which subdivided the manifestations into three groups. Group 1 includes lesions strongly associated with HIV infection; group 2 included less lesions associated with HIV infections; and group 3 includes some lesions seen in HIV infection, but not so relevant [8] (Table 1).

Although the appearance of some lymphomas has decreased considerably due to HAART, the presence of all HIV-related lymphomas does not present a significant change. Contrary to this, several studies have shown a higher prevalence of benign pathologies related to human papillomavirus (HPV) [9]. In relation to periodontal diseases, patients with HIV who have periodontal disease before

infection had more progressive periodontal deterioration and that smoking, lower nutrition, stress and anxiety are factors that aggravate the periodontal status of seropositive patients [8]. In addition to the manifestations developed by a deficient immune system, AIDS patients are depressed because of a nervous system invaded by the virus, the psychological impact of the discovery of the disease or the limitations imposed by the progression of the disease [10]. This, together with tricyclic antidepressants, causes a decrease in salivary flow, contributing to the patient being more inclined to the appearance of candidiasis in its various clinical forms and increased risk of caries [9].

According to the Brazilian Ministry of Health, oral *Candidiasis* is the most easily detected oral manifestation in HIV-infected patients. It is a lesion caused by fungi, and although it may be related to other species, *Candida Albicans* and most commonly seen [11]. It begins when the CD4 lymphocyte count is below 400 cells/mm³ in its erythematous form and 200 cells/mm³. Generally, the four clinical patterns are seen: *Pseudomembranous candidiasis*, *Erythematous candidiasis*, *Hyperplastic candidiasis* and *Angular cheilitis*, with the first two characterizing most cases. Studies have stated that the manifestation of *Candidiasis* is less linked to the decrease in CD4 lymphocytes and more linked to the patient's viral load [4,5,7]. The individual can present painful symptomatology and reduction of smell and taste, leading to food reduction and consequent weight loss. The diagnosis is basically clinical, but must be confirmed by cytologic smear examination or biopsy. The treatment for patients with AIDS is much more complex, since nystatin often is ineffective, requiring an association with topical clotrimazole to present an improved response similar to systemic medication, but these are rarely used because, despite their effectiveness, some patients resistance to the drug after frequent use. For better reduction of relapses, the patient should be encouraged to improve oral hygiene and to perform mouthwash with physiological saline or homemade salt and water preparation several times a day. Antifungal therapies as a prophylactic form are only recommended if the patient has severe and frequent recurrences [12].

It is an injury that can cause discomfort, symptomatology of burning when consuming acidic or salty foods. It may appear together with pseudomembranous manifestation. Characteristically in patients

with HIV, it can progress to the esophageal mucosa, leading to the evolution of invasive esophageal candidiasis, a characteristic pathology that defines AIDS [5].

Angular Cheilitis is a manifestation that presents with cracks in the labial commissure, with erythema and, moreover, whitish plaques are also occasionally seen and the treatment is similar to that used to treat *Candidiasis* [8]. The combination of terbinafine with fluconazole has been well accepted in patients who have resistance to fluconazole [10]. It is not a specific lesion of immunosuppressed patients, since it may also be associated with aging, diabetes mellitus, among others [1].

Hairy leukoplakia is a lesion of viral origin caused by the *Epstein-Barr* virus and its onset is related to immunosuppression [12]. It is a white plaque that does not give rise to scraping, which may range from thick, corrugated leucoplastic areas to thin white streaks, of keratotic and rough surface. Its location is usually on the lateral margin of the tongue, and in a few cases, it may extend across the lateral and dorsal surface of the tongue, as well as rarely involve jugal mucosa, soft palate, esophagus and pharynx [13].

The treatment used is usually done with anti-herpesvirus drugs, but in case of discontinuation of the treatment, the relapse is expected. In cases of patients taking antiretroviral therapy, there is a relative reduction in cases of Leukoplakia Pilosa due to decreased viral load and increased CD4 lymphocyte count. There are reports that the presence of *Leukoplakia Pilosa* in patients with AIDS is a sign of severe immunosuppression [8].

Kaposi's sarcoma (KS) is a multifocal malignant neoplasm, originating from vascular endothelial cells, prevalent in patients older than 60 years. However, since the beginning of the AIDS epidemic, a very large increase was observed in the number of patients with KS. Associated with herpes virus, KS, which is found inside the tumor and is believed to be responsible for the evolution of the neoplasia. It is clinically characterized as multiple lesions on oral mucosa and skin, although it may arise as a single lesion. The most frequent anatomic sites of these lesions are neck, arms, trunk and head, although 80% of patients with HIV who have KS develop also in the mouth [9]. Although any part of the oral mucosa can be involved by this lesion, the hard palate, tongue and gum are the most frequently affected sites, and when placed on the gum or palate, can affect bone and overall dental mobility. Initially, they appear as red-purple macules where pressure reading is negative and progress to plaques or nodules with painful symptoms, bleeding and necrosis [8]. Although it may be similar to bruises, the pressure reading is negative. They may appear purplish as they increase in volume, causing facial deformities, difficulties in chewing, swallowing and speaking, with painful symptoms and spontaneous hemorrhage in some cases. For the correct diagnosis, it is essential to perform the biopsy and histopathological examination [1].

Non-Hodgkin's lymphoma is the second malignant neoplasm seen most commonly in HIV-infected individuals, affecting approximately 3% to 5% of patients, about 60 times more than in the healthy population. Characteristically, non-Hodgkin's lymphoma in AIDS patients presents as an invasive and high-grade disease, which is commonly associated with widespread involvement and short survival time. This type of lymphoma, when related to AIDS patients, is located in the extranodal region, which means that it has spread beyond the outer margin of the lymph node. In the oral cavity, it was observed that lesions involving mainly the gingiva, tongue, palate, maxillary sinus or amygdala may also occur in skeletal structures, and may be

characterized by diffuse progressive periodontitis, loss of periodontal ligament and dental mobility [13]. In these cases, a clue to the diagnosis is the loss of the hard blade and thickening of the periodontal ligament [8]. The lesion is characterized clinically as a mass of soft tissues, and may or may not present ulcerations and tissue necrosis. When they appear as a tumor, they have firm and raised edges with painful symptoms, especially when the lesion reaches neurological structures. However, for a correct diagnosis, a biopsy and a histopathological study are very important [1].

There are three types of periodontal manifestations that may be associated with HIV infection, and they are Gingival Erythema, Necrotizing Ulcerative Gingivitis (GUN) and Necrotizing Ulcerative Periodontitis (PUN), where the latter two are characterized as the same type of disease, however, in different phases, differentiated only by the type of tissue involved [11]. GUN is a manifestation that presents ulcerations and necrosis of the interdental papillae without loss of insertion, with painful symptoms, bleeding and halitosis. PUN was evaluated as presenting gingival and necrotizing ulcerations with rapid and progressive loss of insertion, reaching up to 6 mm of loss, also with intensified pain symptomatology, spontaneous edema and bleeding. It was also found that patients with HIV respond differently to conventional treatment, so for this type of patient, GUN and PUN are treated with debridement, which must be repeated from 7 to 10 days for 2-3 sessions, antimicrobial treatment and prolonged follow-up with monthly consultations [13]. Removal of the devitalized tissue is necessary associated with irrigation with povidone-iodine. Although not necessary, the use of systemic antibiotics is used for extensive lesions and severe pain, and the drug that is most effective in immunosuppressed patients is metronidazole. Linear gingival erythema was associated with HIV-related gingivitis, as it was possible to observe a linear range of erythema involving the free marginal gingiva and extending from 2 mm to 3 mm, in addition to showing pontiform or diffuse erythema in a significant amount of patients, however, such a diagnosis should only be concluded for gingivitis who did not respond to rigid plaque control treatment with high *erythematous* presentations. The Gingival Erythema Linear itself is difficult to diagnose because it is easily confused with conventional marginal gingivitis. Treatment with systemic antifungal agents such as ketoconazole and fluconazole for this type of lesion has a good response even in patients with AIDS [8].

Materials and Methods

This study had as methodology the active search for information in the databases of the MEDLINE, LILACS and BBO, as well as the SciELO virtual library. It was sought to carry out the bibliographic research on the two central themes of this work: buccal manifestations HIV, HIV oral manifestations, mouth care in HIV patients, oral care HIV, oral health in HIV, aids oral care, aids oral manifestations, mouth care in AIDS patients, Selected articles were published in English between 1986 and 2016.

Discussion

The test for antibody detection to the HIV virus in the patient is the ELISA, where after having tested positive, some confirmatory tests, such as HIV-1 Indirect Immunofluorescence test or Western Blot test, should be performed. There are also rapid tests, where it is possible to detect HIV antibodies in approximately 30 minutes, and there is yet another less frequently used test where HIV viral load and genetic material can be detected [7,14].

Saliva, in addition to being an ineffective medium, also acts as an antibody, especially in the IgA (Immunoglobulin A) group [2,9]. Regarding the content on the immunological perspective, in the first days of infection the virus causes an acute phase, reported with enlarged lymph nodes, fever, body pain and occasionally erythema. After the acute phase, the chronic phase begins, where the virus multiplies rapidly throughout the time, from the time of infection. It is at this stage that the white blood cells are destroyed in an attempt to contain the virus in the blood. Over time, the body slowly depletes its defenses and is dominated by the virus. However, the faster the disease is detected, the earlier HAART can be implemented, thus making the system more likely to fight the virus [1,8,9].

Some authors, however, disagree when there is the claim that only HAART reduces the incidence of lesions in AIDS patients, since only the increase in CD4 + T cell counts does not provide a full recovery of oral cavity epithelial cells, and factors such as xerostomia, poor oral hygiene, alcohol consumption and smoking are important factors in the frequency of oral manifestations [1,2,8,9,14].

When we evaluate the oral manifestations, it is affirmed that they are commonly seen and may represent the first clinical signs of the disease. It is also confirmed the agreement of several authors when affirming that the lesions may be of fungal, bacterial, and viral origin, besides neoplastic processes and lesions of idiopathic causes. The most frequent manifestations are *Candidiasis* in its various forms, such as Erythematous Candidiasis, *Pseudomembranous*, *Angular Cheilitis* followed by *Leukoplakia Pilosa*, *Kaposi's Sarcoma*, Non-Hodking Lymphoma and presentations of diseases periodontal diseases such as Gingival *Erythema*, Necrotizing Ulcerative Gingivitis and Necrotizing Ulcerative Periodontitis [1,8,9,13,15].

The importance of a correct dental diagnosis is evidenced by the fact that, at the appearance of some lesions, the dental surgeon must refer his patient to an infectologist for evaluation and examinations, so that he can have a correct diagnosis and treatment [8,16]. Regarding periodontal diseases, it was evidenced that in addition to a correct treatment with HAART, the follow-up of the dental professional, acting effectively on plaque control and improvement in the oral hygiene technique, has great influence for a significant reduction of appearance of these lesions [1,11,12,16,17].

Conclusion

The present study showed that there are no specific oral manifestations of a patient in AIDS. All of these occur because of a deficient immune system. Because of this, we note the importance of the dental surgeon in the clinical diagnosis of such lesions, referring the patient to an infectologist in order to perform immunological tests that confirm his diagnosis and allow the correct treatment. The rapid

early implementation of antiretroviral therapy, coupled with constant patient visits to the dentist for optimal plaque control and proper oral hygiene, prevents the development of certain lesions and aids in the regression of others.

References

1. Focaccia R, Veronesi R (2005) Treaty of Infectology (5th edn.) Publisher Atheneu, Sao Paulo.
2. McNeely TB, Dealy M, Dripps DJ, Orenstein JM, Eisenberg SPE, et al. (1995) Secretory leukocyte protease inhibitor: A human saliva protein exhibiting anti-human immunodeficiency virus 1 activity in vitro. J Clin Invest 96: 456-464.
3. <http://unaids.org.br/estatisticas/>
4. Ramphoma KJ, Naidoo S (2014) Knowledge, attitudes and practices of oral health care workers in Lesotho regarding the management of patients with oral manifestations of HIV/AIDS. SADJ 69: 448-453.
5. Scully C, Cawson RA, Porter SR (1986) Acquired immune deficiency syndrome: review. Br Dent J 161: 53-60.
6. Neville BW, Damm DD, Allen CM, Bouquet JE (2009) Patologia oral maxilofacial (3rd edn.). Elsevier, Rio de Janeiro.
7. Robbins MR (2017) Recent recommendations for management of human immunodeficiency virus-positive patients. Dent Clin North Am 61: 365-387.
8. Patton LL (2013) Oral lesions associated with human immunodeficiency virus disease. Dental Clinics of North America 57: 673-698.
9. Hirata CHW (2015) Oral manifestations in AIDS. Braz J Otorhinolaryngol 81: 120-123.
10. Yagiela JA, Neidle EA, Dowd FJ, Mariotti A (2000) Pharmacology and Therapeutics for Dentists (6th edn.). Editora Elsevier, Rio de Janeiro.
11. Ministry of Health, Secretariat of Health Policies, National Coordination of STD and AIDS (2000) Infection control and dental practice in times of aids: manual of conduits.
12. Donoso-Hofer F (2016) Oral lesions associated with human immunodeficiency virus disease in adult patients, a clinical perspective. Rev Chil Infectol 33: 27-35.
13. Lemos SS, Oliveira FA e Vencio EF (2010) Periodontal disease and oral hygiene benefits in HIV seropositive and AIDS patients. Med Oral Patol Oral Cir Bucal 15: 4417-4421.
14. Fox PC (1992) Salivary gland involvement in HIV-1 infection. Oral Surgery, Oral Medicine, Oral Pathology 73: 168 -170.
15. <http://aids.sc.gov.br/diagnostico.html>
16. Gasparin AB, Ferreira FV, Danesi CC, Mendoza-Sassi RA, Silveira J, et al. (2009) Prevalence and factors associated with oral manifestations in HIV-positive patients seen in a Brazilian city. Cad Saude Publica 25: 1307-1315.
17. Peacock ME, Arce RM, Cutler CW (2017) Periodontal and other oral manifestations of immunodeficiency diseases. Oral Dis 23: 866-888.