International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319 – 6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 9; September 2017; Page No. 6256-6263
DOI: http://dx.doi.org/10.24327/ijcar.2017.6263.0905

Research Article

ORAL MANIFESTATIONS OF HIVINFECTION AND AIDS: AN UPDATE ONCLINICAL DIAGNOSIS AND MANAGEMENT

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A R T I C L E I N F O

Article History:

Received 12th June, 2017
Received in revised form 3rd July, 2017 Accepted 24th August, 2017
Published online 28th September, 2017

Key words:

AIDS, Diagnosis, HAART, HIV, Management, Oral manifestations

A B S T R A C T

Acquired Immune Deficiency Syndrome (AIDS) has been a great challenge for dental and medical health care professionals. Dentists are in daily contact with HIV positive patients.In most populations, HIV-infected patients suffer from racism and discrimination and often avoid reporting their medical history. But in many cases, patients are unaware of being infected, and such situations would definitely increase the risk of cross-infection in dental surgeries. Multiple periodontal and oral lesions are strongly associated with HIV infection and AIDS, but with the advent of highly active antiretroviral therapy (HAART) therapy, patients are now sustaining long and fulfilling lives. Hospital dentists, oral pathologists, and oral surgeons have a major role in early detection of HIV/AIDS -related oral lesions. These periodontal and oral manifestations are markers of immune suppression and their early recognition can reduce patients' morbidity and improve their welfare.Dental knowledge and expertise are mandatory for an appropriate management of these oral manifestations. The purpose of this paper is to provide dental professionals with baseline knowledge on oral manifestations of HIV infection and AIDS, help them identify and diagnose such pathologies, and assist HIV positive individuals in getting timely treatment.

INTRODUCTION

Each year, medical professionals are discovering new immunodeficiency diseases: novel disorders are discovered, classified, and reclassified. Secondary immunodeficiencies – SIDs-patients still exceed those with primary immunodeficiencies-PIDs. Nowadays, the main causes of SIDs are HIV infection (that includes AIDS) and nutritional insufficiencies. AIDS was first recognized in 1981 by the USCenters for Disease Control and Prevention (CDC), and its cause(HIV infection) was identified in the early part of the decade.[14] HIV consists of two copies of single stranded RNA that code for the virus's nine genes enclosed within a protein capsid.[12] HIV infects vital cells in the human immune system such as helper T cells (specifically CD4+ T cells), macrophages, and dendritic cells.[9] This will eventually leads to low levels of CD4+ T cells rendering loss of mediated immunity: consequently, the body becomes significantly prone to opportunistic infections. Once entry into the host cell, the reverse transcription enzymecatalyzes reverse transcription of the RNA into double-stranded DNA and become integral part of the host's DNA. Two types of HIV exist: HIV-1 and HIV-2. HIV-1 is more virulent, more infective,[16] and is the cause of the majority of HIV infections globally. HIV-2 is largely confined to West Africa.[34] In 2014, about 36.9 million people were living with HIV and it resulted in 1.2 million deaths, and most of those infected live in sub-Saharan Africa.[18] HIV is transmitted by both homosexual and heterosexual contact; by blood and blood products; and by infected mothers to infants either intrapartum, perinatally, or via breast milk. After more than 20 years of scrutiny, there is no evidence that HIV is transmitted by casual contact or that the virus can be spread by insects, such as by a mosquito bite.[13] Following infection, a person may not notice any symptom or may experience a brief period of influenza-like illness termed Acute HIV Syndrome. [18] Clinical symptoms occur in at least 50% of cases, typically as a mononucleosis syndrome.[25] The host reaction against HIV, through neutralizing antibodies and particularly through strong cellular immune responses, can keep the virus suppressed for many years before the condition progresses to the asymptomatic stage (Clinical latency).[22]

AIDS represents the terminal stage of HIV infection.The risk of developing opportunistic infections and malignancies typical of AIDS increases progressively as CD4 counts fall below 200 cells/ mm3.[25] Every organ is a potential target for opportunistic infections.[8] Viral induced cancers, include

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Kaposi's sarcoma, lymphoma, and cervical cancer.[39] The natural course of HIV infection has changed notoriously as a result of the introduction of highly active anti-retroviral therapy (HAART), which was first administered in Spain, in 1997.[6] In 2013, the World Health Organization (WHO) has recommended a combination of antiretroviral drugs for treating and prevention of HIV infection: consolidated guidelines included the use of: TDF(tenofovir), EFV(efavirenz), and either 3TC(lamivudine) or FTC(emtricitabine). Such treatment has led to a drastic reduction in the morbidity and mortality associated with the acquired immunodeficiency.

Patients recently infected with HIV usually experience "flu-like" illness that may include severe fatigue, fever, lymphadenopathies, non-itchy rash, muscular pain, night sweats, sore throat, and oral ulcerations. Acute HIV infection is termed "Acute Retroviral Syndrome" –ARS- or primary HIV infection, and it may last from few days to few weeks. And after the acute stage, the HIV becomes less active in the body for as long as 10 years or more: during this period of clinical latency, patients might have no symptoms at all. The purpose of this review paper is to describe the various oral manifestations of AIDS and emphasize the role of dentist in the diagnosisand management of oral manifestations of HIV and AIDS.

Oral Lesions in AIDS Patients

Oral manifestations of HIV infection and AIDS are highly predictive markers of severe immunodeficiency and disease progression in these patients (Nayak *et al*., 2016). Oral tumors and manifestations of opportunistic infections are associated with HIV-related immunosuppression (D. Greenspan and JS. Greenspan, 1987). There are about 40 known oral manifestations of AIDS according to the classification of the European Economic Community.[31, 1] Oral manifestations of HIV infections are sometimes the first sign of the infection and often indicate its progression to AIDS.[37] HIV infected patients often experience a variety of opportunistic infections because of diminished cellular immune activity, leading to oral manifestations such ascandidiasis, reactivation of Herpes SimplexVirus(HSV), and cytomegalovirus (CMV)-related ulcerations.[10] More than 75% of AIDS patients sustain orofacial manifestations. Tongue has been involved in 75% of patients dying from AIDS.[7] An early study- conducted by Berberi and co-workers-involved 50 HIV infected patients and showed that the most common AIDS-related oral lesion identified was pseudomembranous candidiasis, accounting for 76% (38/50), followed by periodontal disease 34% (17/50), herpetic lesions and hairy leukoplakia- 10% for each (5/50), gingivitis 8% (4/50), Kaposi's sarcoma 6% (3/50), and non-Hodgkin lymphoma 2% (1/50).Apart from their diagnostic importance, oral manifestations may be of prognostic importance for the subsequent possible development of AIDS.[3]

Xerostomia

Approximately 30 to 40% of HIV-infected patients may experience moderate to severe xerostomia. Xerostomia or dry mouth is a medical condition associated with a change in the composition of saliva or reduction of salivary flow: In HIV infection and AIDS, it is believed that xerostomia results from the effect of medications (Didanosine) or the proliferation of CD8+ cells in major salivary glands (parotids, submandibular , and subligual). These changes in quality and quantity of saliva often lead to rapidly advancing dental decays and periodontal disease (DA Reznik, 2005, 2006). Xerostomia is usually managed by systemic sialogogues, such as pilocarpine and cevimeline, both approved by the US FDA. Pilocarpine is the most widely used drug and it is administered at a dose of 5mg, 3 times a day for at least 3 months (A Villa, CL Connell, and S Abati, 2015), and intraoral topical agents can help patients as well, and they include chewing gums, saliva stimulants, saliva substitutes, and oral sprays.

Oral Candidiasis

Oropharyngeal Candidiasis (OPC) is described as the most frequent opportunistic infection among HIV-positive patients, and it has been estimated that more than 90% of HIV-positive patients will develop this infection at some time during the progression of their disease.[27, 29] Candida albicans is the main etiological microbiological agent, however other elements such as Aspergillus may cause a solitary oral ulceration. Candidiasis reflects severe depression of the immune system: it has variable aspects. Studies published by Berberi *et al*. (2015), Li *et al*. (2013), Lin *et al*. (2013), and Arribas *et al*. (2000) showed that pseudomembranous candidiasis was the most common variety of oropharyngeal candidiasis.[3, 4-2] A clear medical history must be collected to distinguish HIV related thrush from other etiologies such as prolonged intake of antibiotics for management of serious infections or corticosteroids to control autoimmune and immune mediated diseases.

The presence of erythematous candidiasis revealed by extensive palatal red patch is another form of fungal infection: frequently, diagnosis may be confused with denture stomatitis; however the absence of denture is a strong motivation to rule out systemic immunodeficiency. OPC caused by C.albicans is generally managed by judicious use of fluconazole, [27, 29, 23, 38] a strong antifungal agent prescribed for Candida infections of vagina, mouth, throat, esophagus, and bloodstream. An epidemiologic shift of Candida species could significantly impact the usefulness of fluconazole as empiric treatment for candidiasis in patients with HIV/AIDS.[28]

Erythematous candidiasis is undoubtedly the most misdiagnosed and underdiagnosed oral manifestation of HIV infection (DA Reznik, 2005, 2006) if this condition presents on the tongue, palate should be examined for a matching lesion, and vice versa. Most frequently, infected patients will complain of oral burning sensation, especially while eating spicy or salty foods or drinking acidic beverages. Clinical diagnosisis also based on appearance (red, flat subtle lesion either on dorsal tongue or hard or soft palate) and confirmation of presence of fungal hyphae, or, more likely, blastospores.

Angular cheilitis (AC) is another manifestation of HIV-infection. However it is not pathognomonic sign. AC is a relatively common oral condition presenting as a persistent fungal infection of the corners of the lips. Healthy patients with moist lips can commonly present with AC, especially during cold winter months.AC is easily treated by antifungals such as Nystatin cream. Clinically, it appears as a triangle of erythema, edema, fissuring, and breakdown of skin at the corners of the mouth, sometimes involving solely the oral mucosa and in other conditions it extends past the vermilion

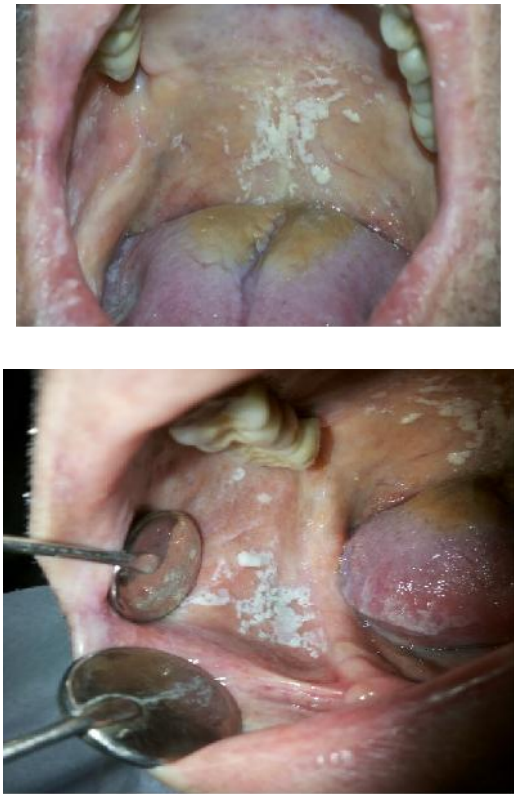

Fig.1 Oropharyngealand buccal thrush in HIV-positive patients.

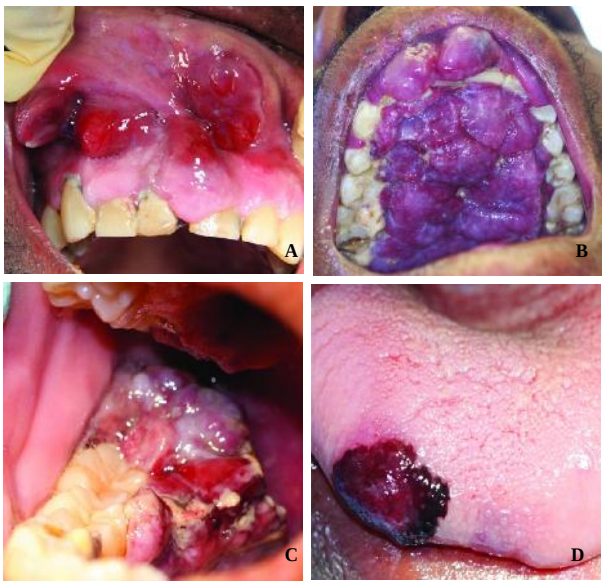

Fig. 2 Oral Kaposi Sarcomas-KS- in HIV-positive patients.
A: Exophytic oral HIV-KS lesions on the alveolar and labial mucosa in a 54-year-old male with a CD4+ T cell count of 258 cells/mm3. The patient died 15 weeks after his oral HIV-KS diagnosis.
B: Exophytic confluent oral HIV-KS lesion on the hard palate in a 31-year-old male patient with a CD4+ T-cell count of 5 cells/mm3.
C:Exophytic oral HIV-KS lesion on the lower right retromolar area extending into the oropharynx in a 29-year-old female patient with a CD4+ T-cell count of 49 cells/mm3. The patient died six weeks after her oral HIV-KS diagnosis.
D:Macular/nodular lesion on the dorsum of the tongue in a 44-year-old female patient with a CD4+ T-cell count of 13 cells/mm3. The patient died five weeks after the diagnosis of her oral HIV-KS.
(Reproduced from Razia A. G. Khammissa *et al*.AIDS Research and Treatment. 2012.
doi:10.1155/2012/873171)

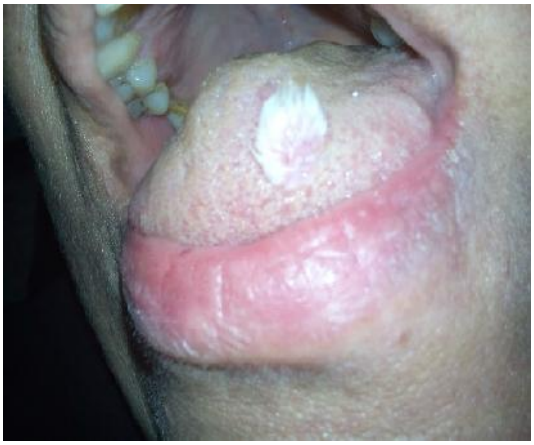

Fig. 3 Dorsal tongue condyloma acuminatum caused by HPV in an HIV-positive patient.

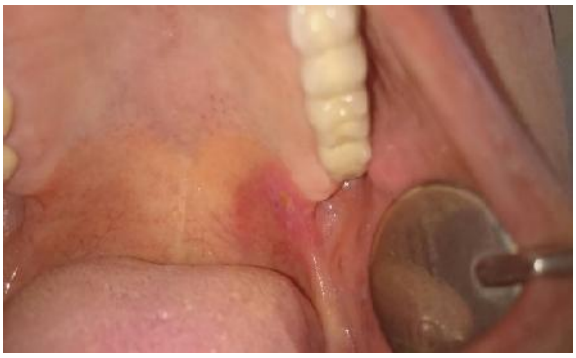

Fig. 4 Oral aphthous ulceration on left maxillary tuberosity in an HIV-positive patient

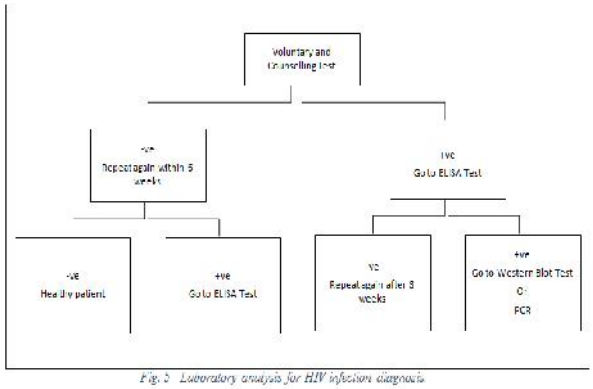

Fig. 5 Laboratory analysis for HIV infection diagnosis

border of the lips in order to affect facial skin. It may be unilateral or bilateral. AC is caused byCandida albicans and bacterial species such as staphylococcus aureus and β-hemolytic streptococci. Local predisposing agents include: edentulism, poorly constructed dentures, and elastic tissue damage due to smoking. All these predisposing factors may lead to loss of facial support and extenuate the skin folds at the angle of the mouth. Saliva is continuously pooled into the latter rendering it constantly wet, which favors the development of yeast infection. Lip licking, dry mouth, and sun exposure are other predisposing factors. AC may reflect allergic reaction to chemicals present in toothpastes, makeup, or even food. Nutritional deficiencies (Iron, folic acid, vitamin B12...) can also predispose to AC by deteriorating the immune system's functions to a certain extent. In such clinical situations, glossitis and recurrent aphthous stomatitis can occur,as well. HIV-infection can favor the oral flora to be

pathogenic following severe depression of immune system. Management of AC includes complete exclusion of local and systemic predisposing factors and application of a topical antifungal cream (Daktarin®) directly to affected areas, 4 times a day, for 2 weeks.Blood tests are mandatory to detect the level of nutritional components if anemia is suspected. Reconstruction of a new denture is a must if the patient is present with poorly constructed one. Application of barrier cream is beneficial in case of dry mouth and cold weather. AC manifested during HIV infection or AIDS will usually present as a whitish, ulcerated, severe variety, and this specific clinical presentation is more indicative of either HIV infection or AIDS.

Pseudomembranous candidiasis (known as "thrush") is another fungal manifestation in the oral cavity of HIV-infected patients: it presents as whitish, creamy, curdlike plaque on buccal mucosa, tongue, or other oral localizations (Fig. 1). These plaques can be easily wiped away with a wood tongue depressor, typically leaving a red or bleeding underlying surface. Candida albicans and non-albicans species may be involved and diagnosis is mainly based on appearance. Treatment is mainly based on topical anti-fungal agents for mild to moderate cases (Nystatin pastilles, or Clotrimazole troches). Severe cases are treated by fluconazole, or voriconazole in case of fluconazole resistance.

Oral viral mucosal lesions (Warts, herpes simplex, herpes zoster, hairy leukoplakia, and Kaposi's sarcoma-KS) Virally mediated mucosal lesions are not uncommon in AIDS patients. Oral Hairy Leukoplakia (OHL) is one of the most common oral signs associated with HIV and/or AIDS.It is associated with Epstein - Barr virus (EBV) (that causes Mononucleosis) and appears as painless white soft plaque, corrugated or hairy coating, mainly appearing on lateral border of the tongue . OHL was first described in 1984 as mostly occurring in HIV patients, both immunocompromised and immunocompetent patients.[21, 26] First OHL case in an HIV-negative patient was reported in 1999 in a 56-year -old patient with acute lymphocytic leukemia, and later, many cases were reported in transplant patients (kidney, heart, bone marrow,etc...,) and patients with hematological cancers.[36, 17]OHL can be eliminated by drugs such as acyclovir (Zovirax®), Famciclovir (Famvir®), or Valacyclovir(Valtrex®). Kaposi's sarcoma (KS)is an AIDS-defining cancer and was one of the first recognized HIV-related manifestations.[19] KS may manifest in any part of human body, at the same time,and it appears as visible purplish-black patches, or lesions, on skin, mucous membranes including oral ones, or internal organs. KS is observed at all stages of HIV infection, but it is usually serious when CD4 cell count falls below 250(Fig. 2). Patients with lower CD4 counts will more likely develop KS of internal organs, such as lungs and lymph nodes, with possible life-threatening sequelae. KS is caused by Human Herpes Virus 8 (HHV-8), known also as KS associated Herpes Virus (KSHV). This virus is known to be mainly sexually transmitted, especially within homosexual community. AIDS-related oral KS can be nodular, macular, raised, or ulcerated: its color ranges from red to purple but early lesions usually present as red, asymptomatic, and flat, whereas older ones feature a darker color. Palate is the most involved site in oral KS (56%, with 42% for hard palate and 14% for soft palate), but oral KS is also observed on gingiva (22%, with 15% for maxilla and 7% for mandible) and maxillary tuberosity (6%) (Flaitz *et al.* , 1995). Oral KS manifests as purplish macules or nodules that need to be distinguished from other pigmented lesions by histopathological examination. Management of oral KS ranges from localized injections of chemo-therapeutic agents (vinblastine), to surgical removal.

Oral KS has been conventionally treated with intralesional injections with vinblastine sulfate (a chemotherapy drug most often used for bladder cancer-Velbe®) (Flaitz *et al.* , 1995): Vinblastine belongs to a group of drugs called vinca alkaloids (or microtubules inhibitors). In 1996, SU McCormick reported the intralesional vinblastine injections for the treatment of oral KS with a 2-year follow-up: 18 patients were treated with up to 3 intralesional injections of 0.1 mg/cc vinblastine sulfate, all lesions responded to local injections, 40% required 1 injection, 31%, 2 injections, and 29%, 3 injections. Large exophytic lesions required multiple injections. All patients tolerated the protocol well and only 10 patients (out of 18) were followed for 24 months. Eight died of their general disease during this period, 4 patients developed new intraoral lesions (which were treated with) and responded favorably to the 3-injection protocol (SU McCormick, 1996). Patients presenting intra-oral and extra-oral KS are usually managed by systemic chemotherapy.

Lymphoma is another variety of cancer strongly associated with AIDS, and it is known that the most prevalent form of HIV-related lymphoma is the diffuse B-cell non-Hodgkin's Lymphoma (NHL). HL is increasing in incidence among HIV-related patients, although not being considered as being a specific AIDS-defining illness. There are two main types of AIDS-related non-Hodgkin lymphomas, and both are aggressive: the diffuse large B-cell lymphoma (including B-cell immunoblastic lymphoma and the Burkitt or Burkitt-like lymphoma. EBV has been detected in 50% of AIDS-related lymphoma cases. AIDS-related oral lymphomas appear as soft painless swellings that may be ulcerated by trauma. As stated earlier, HIV-infected patients are at increased risk to develop NHLs: these lymphomas progress rapidly and have a poor outcome (Castillo *et al*., 2012-Tirelli *et al*., 2000). Plasmablastic lymphoma- PBL is strongly associated with HIV infections and may occur in oral cavity: PBL, a diffuse, B- cell lymphoma, was first reported in HIV patients by Delecluse and co-workers in 1997. When it occurs in oral cavity, it involves especially both jaws, gingiva, and palate, and oral PBL accounts for 2.6% of all NHLs (Hansra *et al*., 2010). This neoplasm is also observed in lymph nodes, subcutaneous soft tissues, liver, bones, and anorectum (Corti *et al*., 2011). EBV is strongly associated (70% of cases) with the pathogenesis of PBL in patients with AIDS (Hamilton-Dutoit *et al*.,1993).

HIV serologic status should be evaluated in all patients with PBL of oral or extra oral sites. PBL is managed by R-CHOP chemotherapy

1. Rituximab (Mabthera®)
2. Cyclophosphamide
3. Hydroxydaunomycin (Doxorubicin)
4. Oncovir® (Vincristine)
5. Prednisolone (a steroid)

Rituximab, an anti-CD20 monoclonal antibody has demonstrated an efficacy in various lymphoid malignancies (Plosker and Figgitt., 2003- Marcus and Hagenbeek.,2007) :

this monoclonal drug belongs to a group of drugs called "targeted therapies" or "biological therapies". This group comprises monoclonal antibodies, angiogenesis inhibitors, cancer growth inhibitors, and cancer vaccines.Cervical lymphadenopathy is a strong feature but a deep investigation involving fine needle aspiration biopsy (FNAB) must be carried to distinguish it from adenopathy of non-neoplastic origin. Immunohistochemistry is strongly recommended to confirm definitive diagnosis. Recrudescent orofacial herpes simplex virus (HSV) infection is less common than candidiasis and can cause chronic ulcerations that may obscure the viral origin of the lesion.Varicella zoster and CMV reactivation are proportionate with progression from HIV infection to AIDS. Human Papilloma Viruses (HPV) can give rise to other mucosal lesions such as verruca vulgaris, condyloma acuminatum (Fig. 3), and focal epithelial hyperplasia-FEH (Heck disease). These benign HPV-associated oral lesions (v.vulgaris, c.acuminatum, and FEH) are collectively referred as oral warts.Verruca vulgaris, known as common wart, is a frequent skin lesion caused by HPV: it often affects epithelial tissues and mucous membranes, including oral ones, and it is most commonly induced by HPV-2, HPV-4, or HPV-40. Oral verruca vulgaris usually presents as polypoid mass, it is treated by either surgery, cryotherapy, electrocauterization, LASER, or topical agents (Condyloma acuminatum is a HPV-induced disease affecting the skin and mucosae of anorectum and genitalia: this lesion is rarely observed on oral mucosa and when it occurs in oral cavity it is usually treated by surgical removal and chemical cauterization with trichloroacetic acid (I Welter Henn, 2014). FEH (Heck disease) of oral mucosa affects tongue, oral mucosa, uvula, and lips (mostly lower lip): it is defined as circumscribed slightly elevated pink or white papules located mainly on lower lip and buccal mucosa (Archard, Heck, and Stanley, 1965): its diagnosis is based on HPV types 13 and 32. However, HPV types 1, 6-related, 11, 16, and 18 were also detected in FEH (Bodokh *et al.* ,1993-Cohen *et al.* ,1993). FEH was reported mostly among American Indians and Eskimos of Greenland, but it is sporadically reported in Caucasians (Bodokh *et al*., 1993). Oral FEH is very rare (Vilmer *et al*., 1994). Cutaneous FEH was successfully treated with an interferon-beta gel (Fiblaferon gel®) but oral FEH lesions are usually removed with CO2 LASER (M Luomanen, 1990).

Bacterial infections

They rarely affect the oral cavity regardless of immunodeficiency severeness. Escherichia coli and Klebsiella Pneumonia have been detected through culture of samples from oral lesions. Ulcer may be secondary to systemic infection as in case of Tuberculosis. Bacillary Angiomatosis (BA) is a vascular, proliferative form of Bartonella infection caused by Bartonella henselae.[7] It responds to antimicrobial therapy,as a main therapy, cryotherapy, electrodessication, curettage, and surgical excision of solitary cutaneous lesions, being considered as adjunctive therapies. Recognition of this disease is of utmost importance due to the possible occult dissemination of bacteria. HIV and AIDS-associated periodontal infections may be categorized as unusual, atypical, forms of gingivitis, periodontitis, and necrotizing AIDS-related opportunistic infections.

HIV-related periodontal disease

Common notable HIV-related periodontal conditions include linear gingival erythema and necrotizing ulcerative periodontitis. Linear gingival erythema, known as "red band gingivitis", presents clinically as red band along gingival margin: it is most frequently observed in association with anterior teeth but it commonly spreads to posterior ones. It also presents on non- attached and attached gingiva as petechial patches. It may or may not be accompanied by discomfort or occasional bleeding. Anti-fungals are not needed in this situation and treatments only includes debridement and daily rinces with 0.12% chlorhexidine gluconate solution for 2 to 4 weeks and improved home oral hygiene.

HIV-related gingivitis and periodontitis show a more aggressive behavior, compared to classical varieties of non HIV/AIDS-related gingivitis/periodontitis. Bone loss and gingival recession occur, regardless of patient's effort to maintain good oral hygiene manners. Necrotizing ulcerative periodontitis caused mainly by Spirochaetes is a strong indicator and marker of a severe immune depression: this condition features, bleeding, fetid odor (halitosis), ulcerated gingival papillae, severe pain, rapid loss of alveolar bone and periodontal soft tissues, and resulting loosening of teeth. Patients often complain of "deep jaw pain", and apart pain management, treatment consists of dental plaque and calculus removal, debridement of necrotic soft tissues, using 0.12% chlorhexidine digluconate. In most situations antibiotics are necessary (metronidazole 500 mg, 1 tablet twice daily for 2 weeks-other options may include clindamycin and amoxicillin). Follow-up visits based on scaling and root planning are of utmost importance for a good periodontal maintenance.

Murray and associates (1991) detected periodontal pathogensin HIV-associated periodontal lesions, using DNA probes. Subgingival plaque samples were obtained by the authors from both HIV-seronegative and HIV-seropositive homosexual menand from presumably uninfected heterosexuals and DNA probes were used to detect specific microbial agents. HIV-associated periodontitis sites showed a microbial profile qualitatively similar to that of conventional (non HIV/AIDS-related) periodontitis, except that Bacteroides gingivalis was much more prevalent in conventional periodontitis.And in contrast,HIV-related gingivitis sites showed a greater prevalence of all tested bacteria, among them: Actinobacillus actinomycetemcomitans, Bacteroides intermedius, Bacteroides gingivalis,and Eikenella corrodens.The authors concluded that HIV-related gingivitis is a precursor to HIV-related priodontitis,and that early detection and prophylactic treatment of high-risk individuals prevent the possible damage and destruction of deep periodontal tissues.

Lymphadenopathy

HIV-related lymphadenopathies are relatively common .In very specific cases; HIV-related lymph nodes need to be further investigated

1. rapid enlargement of a stable node
2. tender and fluctuant nodes
3. abnormally consistent nodes
4. asymmetrical nodes

5. group of enlarged nodes

Cervical lymphadenopathy is almost the most frequent head and neck manifestation. It is characterized by a lymph node superior to one centimeter in diameter. The major etiology is persistent follicular hyperplasia. It can present at any stage of HIV infection and does not necessary correlates with any progression toward AIDS condition. A biopsy is not indicated in the early stage of HIV infection, however it is a must once the patient presents with nodes that grow in size or become adherent to the underlying tissues in order to exclude associated systemic conditions such as Lymphoma.

Autoimmune phenomena

Thrombocytopenia is not a rare complication of HIV infection. The underlying pathophysiology includes accelerated peripheral platelet destruction and decreased production of platelets from the infected megakaryocytes.[35] In most cases, platelets count is still greater than 50000 cells/µl which allows conservative management of the condition. HIV-associated thrombocytopenia appears clinically as multiple purple patches that may be wrongfully diagnosed as simple pigmentations or other serious conditions such as Kaposi's sarcoma.

Other reported autoimmune diseases include lupus erythematosus and Sjögren- like salivary gland disease.

Oral ulcerations

In immunocompetent persons, oral aphthous ulcerations(Fig. 4), despite being painful and annoying constitute a self-limited problem, whereas in HIV infection, these ulcerations become progressive, destructive, and debilitating: indeed, they present as extremely painful, enlarging necrotic lesions, resembling the large aphthous ulcers observed in Behçet syndrome.[20] Oral ulcerative conditions related to HIV infection and AIDS may include HSV lesions, recurrent aphtous ulcers, and neutropenic ulcers. Their prevalence increase dramatically as the infection heads toward AIDS. They can be very annoying to the patient interfering with eating thus affecting the overall health of the patient. Diagnosis needs careful investigation for proper management. A biopsy is mandatory to rule out infectious agents such as cytomegalovirus. In these cases the patient responds well to antimicrobial drugs. In other cases, these ulcers may be major aphthae of unknown origin: in this case, thalidomide is the best potent treatment (100 mg capsule once a day/4 week course) but it is accompanied by undesirable side effects such as neurotoxicity. Patients whose aphthous ulcers had not completely healed by the end of the 4 weeks are usually offered the option of taking two 100 mg capsules for an additional 4 week course as tolerated.[20] Thalidomide is used by professionals only after an accurate diagnosis of major aphthae has been established.In case of sedation or other adverse effects(bilateral peripheral neuropathies), thalidomide course is reduced or discontinued, depending on the nature and grade of adverse effects. Thalidomide is strictly contraindicated in pregnant and lactating woman. Patients may benefit as well from granulocyte colony-stimulating factor (G-CSF) if receiving a systemic or topical steroid treatment: G-CSF is a glycoprotein that stimulates red bone marrow to produce granulocytes and stem cells, and release them into the bloodstream. G-CSF is given either subcutaneously (daily and at home) or intravenously. Oral aphthous ulcers in HIV infections often interfere with eating, and lead to malnutrition and wasting.[20] Apartoral cavity, hypopharynx and esophagus may be involved with aphthous ulcers in HIV-infected patients.

Neurological disorders

Facial palsy and trigeminal neuralgia are potential consequences.[7]

CONCLUSION

HIV infection is a global problem. Occurrence of oral lesions in HIV- infected patients could be a useful indicator in determining a depletion of immunological status of HIV-infected patients.[5] Rapid detection of HIV infection is of great importance as it reduces patient's morbidity and decrease srisk of transmission of virus to other patients. The dentist being responsible for the oral cavity must have adequate knowledge about different oral lesions that indicate HIV infection. In addition to clinical examination, dentists must be updated to different laboratory tests such as: ELISA (Enzyme-linked immunosorbent assay), Western blot, and PCR(Polymerase Chain Reaction)(Fig. 5).[14] Volunteer and Counseling test (VCT) is a new test of extreme sensitivity that can be used by dentists in dental clinics in case of suspicion. It is free and rapid. All what is needed is to prick the patient's finger to get a drop of blood which will be placed on the slide and the result will be obtained within 15 minutes.A positive result must be confirmed with further laboratory analysis such as:ELISA, Western blot, and PCR before the patient is subjected to HAART therapy which proved great success. Oral manifestations of HIV infection and AIDS have drastically changed after the advent and clinical use of HAART. As a result of an obvious improvement of the immune system, many opportunistic infections have resolved but the risk of hyperpigmentationin patients undergoing HAART has increased the prevalence of oral candidiasis whereas periodontal diseases were less observed in patients with HAART.[33, 30] In an Indian institutional study,[32] oral manifestations of HIV were studied in children treated in an HAART center: these manifestations were observed in children receiving HAART and they included dental caries(26%), periodontal diseases(23%), candidiasis(19%), hyperpigmentation(17%), ulcerative stomatitis(9%) and one case of mucocele. Authors[32] concluded that HAART had increased the disease-free states in HIV positive children, promising them better life span, they also stated that the incidence of oral manifestations can further come down with adequate oral hygiene measures in HIV- infected children. Another study[11] of oral manifestations of HIV- infected children in highly active HAART era concluded that HAART improves immune function and decreases mortality, morbidity, and opportunistic infections: frequency and severity of oral disease associated with HIV infection were considerably reduced, "although the use of HAART may be associated with an increased appearance of oral lesions associated with human papillomavirus and potentially increases the risk of later oral squamous cell carcinoma-OSCC".[11]

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How to cite this article:

Ziad Noujeim *et al* (2017) 'Oral Manifestations of Hivinfection and AIDS : An Update Onclinical Diagnosis and Management', *International Journal of Current Advanced Research*, 06(09), pp. 6256-6263.
DOI: http://dx.doi.org/10.24327/ijcar.2017.6263.0905

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