



A Rare Case: Recurrent Herpetic Gingivostomatitis in People with HIV/AIDS Who Treated with Single-Tablet Regimen of Anti Retro Virus

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Abstract

Oral manifestations are the earliest and most important indicators of HIV infection because they can be used to determine whether anti-HIV therapy is used in the staging and classification system and significantly reduces the quality of life of PLWHA. Purpose: This article aims to describe a rare case of recurrent herpetic gingivostomatitis in a PLWHA treated with a single tablet of ARV. Case: A 24-year-old male PLWHA came to the Dental and Oral Hospital of Jember University because of canker sores in the upper and lower mouth, bleeding gums, and itchy lesions on the left corner of the lips. In the left angular oris, there were 5 small vesicles. The upper and lower right retromolar had multiple ulcers, multiple $\varnothing \pm 2.5$ mm, painful, white, erythematous edges, and clearly defined. Posterior mandible left and right were edema, redness, and spontaneous bleeding. The patient was medicated with betadine gargle, oxy fresh spray 3x a day, and multivitamin tablets 1x a day. A week later, the check-up was done, and the canker sores healed and were no longer painful. The patient routinely used the medication, and there were no side effects. Extraoral examination showed that the angular oris sinistra vesicles had dried and formed crusts. In people living with HIV (PLWHA), although they may be young and consistently taking a single-tablet anti-retroviral (ARV) regimen and have a CD4 count of more than 200 cells/mm³, there is a significant risk of reactivating herpetic gingivostomatitis. In the case of our patient, this reactivation is likely linked to severe psychological conditions stemming from past abuse and his profession as a teacher. Therefore, providing psychological support to PLWHA is essential for enhancing their immune system and improving the effectiveness of their treatment.

Keywords: Acute Herpetic Gingivostomatitis Recurrent; HIV, Single-Tablet ARV, Gingival Bleeding

Introduction

The first verified case of HIV is from a blood sample taken in 1959 from a man who was living in what is now Kinshasa in the Democratic Republic of Congo. Since the beginning of the epidemic, 88.4 million [71.3–112.8 million] people have been infected with HIV, and about 42.3 million [35.7–51.1 million] people have died of HIV. Globally, 39.9 million [36.1–44.6 million] people were living with HIV at the end of 2023.

An estimated 0.6% [0.6-0.7%] of adults aged 15–49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions [1].

The human immunodeficiency virus (HIV) belongs to the Lentivirus genus within the Retroviridae family, specifically under the Orthoretrovirinae subfamily. Based on genetic composition and antigenic differences, HIV is categorized

into two types: HIV-1 and HIV-2. Similarly, immunodeficiency viruses found in non-human primates, known as simian immunodeficiency viruses (SIV), are also classified within the Lentivirus genus. Current epidemiological and phylogenetic studies suggest that HIV entered the human population between 1920 and 1940. HIV-1 originated from immunodeficiency viruses in Central African chimpanzees (SIVcpz), while HIV-2 traces its origins to West African sooty mangabeys (SIVsm) [2]. Oral manifestations are among the earliest and most significant indicators of HIV infection. Conditions such as oral candidiasis, oral hairy leukoplakia, and Kaposi's sarcoma are often present in the oral cavity and can serve as clinical markers for HIV progression. These manifestations are utilized in staging and classification systems for HIV, aiding in treatment planning and management [3]. Oral lesions can profoundly impact the quality of life for PLWHA, affecting their nutritional intake, speech, and overall well-being. Early recognition and management of these oral conditions are crucial in improving health outcomes and enhancing the quality of life for those affected. The most related oral manifestation of HIV is oral candidiasis [4]. Recurrent herpetic gingivostomatitis, an infection of the oral cavity caused by the herpes simplex virus type I, was rarely reported as manifestation of HIV. Herpetic gingivostomatitis appears as a diffuse, erythematous, shiny involvement of the gingival and the adjacent oral mucosa, with varying degrees of edema and gingival bleeding. Primary herpetic gingivostomatitis appears to occur in people who do not yet have antibodies to the herpes simplex virus [5]. This report aims to describe a case of recurrent herpetic gingivostomatitis in a PLWHA on STR and explore contributing

factors.

Case

A 24-year-old male patient, a teacher, came to the Department of Oral Medicine, Jember University Dental and Oral Hospital, on March 30, 2023, because of a sore mouth and bleeding from his gingiva. He was confirmed to have HIV/AIDS \pm 4 years ago. Since being diagnosed, the patient has routinely taken a Single Tablet Regimen (STR) of anti-retroviral (ARV), which varies depending on the availability of drugs at the hospital, the last STR-ARV was Dolutegravir sodium|lamivudine|Tenofovir Disoproxil Fumarate. The patient admitted that the CD4 level checked 2 years ago was above 200 cells/mm³ and three months ago the measurement of viral load was under 20 copies/ml. The clinical examination found that the posterior right gingiva had been bleeding, edema, and red. Two small ulcers were found on the retromolar pad and tuberosus maxilla. We also found five small vesicles in the corner of the left lip (Figure 2). Two days before the patient came to the hospital, the patient had a fever, followed by itching and burning in the side of the vesicles. The patient acknowledged that he frequently (almost once a month) experienced the same symptoms and healed without any treatment. The patient came to the hospital because the bleeding of the gum was more severe than usual. The patient admitted that he was often sad and desperate because he regretted his past. The patient said that he had experienced harassment when he was in junior high school, and because of that, when he was in college, the patient had free sex (Figure 1).



Figure 1: (a). Spontaneous bleeding on mandible right gingival posterior right. Gingiva showed edema and redness. (b) Two small ulcers on the right retromolar pad (c) Five small vesicles of skin on the lower corners of the lips.

From the anamnesis and clinical examination, we diagnosed that he had recurrent herpetic gingivostomatitis related to HIV infection. We prescribed povidone-iodine mouthwash and oxyfresh dental spray, which were sprayed on the sore gingiva after rinsing with betadine. For herpes lesions on the skin, we prescribed acyclovir cream, which was used 6 times

a day. As supportive therapy, we prescribed Becomzet® (which contains vitamin B complex, a high dose of vitamin C, and zinc minerals). On the second visit, 7 days later, all of the signs and symptoms in the mouth were completely resolved. On the left lip corner were multiple healing crusts.

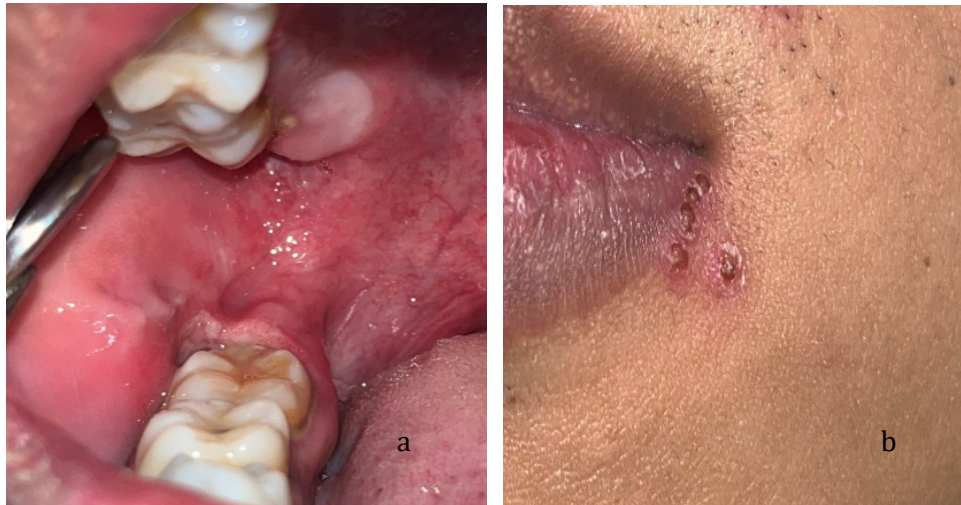


Figure 2: (a) The retromolar pad and gingiva completed healing at seven days of treatment. (b) At the corner of the mouth, the vesicles have turned into crusts

Discussion

Human Immunodeficiency Virus (HIV) infection leads to progressive immune suppression, rendering individuals susceptible to various opportunistic infections and neoplasms, many of which manifest in the oral cavity. Oral lesions in HIV patients are often among the first clinical signs of immunosuppression and can serve as diagnostic markers for disease progression.

Opportunistic infections (OIs) are a significant cause of morbidity and mortality among people living with HIV/AIDS (PLWHA). These infections arise due to the weakened immune system caused by HIV, leading to life-threatening conditions. Despite advancements in HIV diagnosis and treatment, OIs remain prevalent, especially in low and middle-income countries [6]. One of the most common oral manifestations of HIV infection is **oral candidiasis**, particularly pseudomembranous candidiasis, caused by *Candida albicans*. This condition is often an early indicator of immunosuppression and can present as white, curd-like plaques that can be wiped off, leaving an erythematous surface underneath [7]. Another significant finding is **oral hairy leukoplakia (OHL)**, which is strongly associated with Epstein-Barr Virus (EBV) reactivation. OHL presents as corrugated, white plaques on the lateral borders of the tongue that cannot be scraped off and is often indicative of

advanced HIV disease [8]. **Periodontal diseases**, including necrotizing ulcerative gingivitis (NUG) and necrotizing ulcerative periodontitis (NUP), are highly prevalent in HIV patients. NUP, characterized by severe gingival tissue destruction, rapid attachment loss, and bone resorption, is significantly associated with profound immunosuppression [9]. These conditions are often accompanied by severe pain and halitosis. HIV-associated **Kaposi's sarcoma (KS)** is another key oral manifestation, presenting as red, purple, or brown vascular lesions, commonly on the hard palate or gingiva. KS is linked to human herpesvirus 8 (HHV-8) and serves as an AIDS-defining illness [10]. Another neoplastic condition seen in HIV patients is **non-Hodgkin's lymphoma (NHL)**, which can manifest as rapidly enlarging, non-tender masses in the oral cavity, often affecting the gingiva, palate, or tonsillar region. NHL in HIV-positive individuals is associated with poor prognosis [11]. HIV-related **ulcerative lesions**, including those caused by herpes simplex virus (HSV) and cytomegalovirus (CMV), are also frequently observed. HSV-associated ulcers are often persistent and resistant to conventional therapy, while CMV-induced ulcers tend to appear as deep, painful ulcers in the oral mucosa [12]. **Xerostomia (dry mouth)** is a common complaint among HIV-positive individuals, primarily due to salivary gland disease or medication side effects. Reduced salivary flow increases the risk of opportunistic infections and dental caries [13].

Herpetic gingivostomatitis, caused by herpes simplex virus (HSV), is a common viral infection in both immunocompetent and immunocompromised individuals. However, in HIV-positive patients, the prevalence of recurrent and severe herpetic gingivostomatitis is significantly higher due to immune dysregulation. Studies indicate that HSV-associated lesions occur in up to 10-15% of HIV-infected individuals, with a higher incidence observed in those with advanced immunosuppression and lower CD4 counts [14]. In immunocompetent individuals, these lesions are typically self-limiting. However, in HIV-infected patients, especially those with significant immunosuppression (CD4 cell counts below 100 cells/mm³), herpetic gingivostomatitis can present with more severe, widespread, and prolonged lesions resembling primary herpetic infections [15]. The prevalence of herpetic gingivostomatitis in HIV-positive individuals varies, but studies have shown a significant reduction in its occurrence among patients receiving anti-retroviral therapy (ART). This fact suggests that effective ART not only improves immune function but also decreases the incidence of opportunistic infections, including herpetic lesions [16].

In our patient, the manifestation of herpes gingivostomatitis recurred very often with a frequency of almost every month since he was diagnosed with HIV, even though his CD4 count was above 200, the viral load was under 20 copies/ml and he routinely took one anti-retroviral tablet. The reactivation of HSV infection indicates that the body's resistance to HSV is still low, likely due to the patient's disturbed psychological condition, which worsens the immune system against HSV. Psychological conditions play a major role in the immune system against the virus [17]. Psychological problem particularly anxiety increased the glucocorticoid level in turn caused the suppression of immune system. Many of the effects of stress on disease are mediated by glucocorticoids released in response to the activation of the hypothalamic-pituitary-adrenal axis, which suppresses the immune response. Glucocorticoids will inhibit RU486, IFN- β and INF- γ expression which play a role in fighting HSV type 1 infection [18].

The weakened immune system induced reactivation of the dormant HSV [19]. Both innate and adaptive immunity play important roles in the process of latent HSV-1 infection and reactivation. The innate immune system recognizes viral components through pattern recognition receptors and initiates an antiviral response, although its role may be relatively limited during latent infection. In contrast, the adaptive immune system, particularly T and B cells, responds rapidly upon viral reactivation, controlling viral replication and transmission through cytotoxic effects, antibody production, and immune memory [20].

Single-tablet regimens (STRs) have revolutionized the management of HIV-1 infection by combining multiple anti-

retroviral agents into a single pill taken once daily. This approach simplifies treatment protocols, enhances patient adherence, and maintains effective viral suppression. STRs typically include a combination of drugs from different anti-retroviral classes to suppress HIV replication effectively [21,22]. However the STRs have **disadvantages**: Fixed-dose combinations may not allow for individualized dosing adjustments, which can be necessary in cases of drug-drug interactions, renal or hepatic impairment, or specific patient populations, combining multiple drugs into a single pill means that if a patient experiences an adverse reaction, it may be challenging to identify the causative agent without discontinuing the entire regimen, some components of STRs may interact with other medications the patient is taking, necessitating careful review and monitoring [23].

This report has limitation due to lack of the of virological confirmation of HSV from the patient and the acute necrotizing gingivostomatitis (ANUG) can be a diferential diagnose of this case.

Conclusion

For individuals living with HIV (PLWHA), even those who are young and responsibly taking a single-tablet anti-retroviral (ARV) regimen while maintaining a CD4 count above 200 cells/mm³, there remains a significant risk of reactivating herpetic gingivostomatitis. This challenge is often linked to deep psychological struggles that may arise from past trauma, as well as the pressures associated with their roles, such as being a teacher. It's crucial to acknowledge that providing compassionate psychological support to PLWHA can play a vital role in strengthening their immune systems and enhancing the overall effectiveness of their treatment. Being there for them emotionally can make a meaningful difference in their journey toward better health.

Ethics Approval and Informed Consent: Written and verbal consent has been obtained from the patients presented in this paper, including for publication.

Conflicts of interest: There are no conflicts of interest

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