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HIV-Related Oral Lesions, Demographic Factors, Clinical Staging and Anti-Retroviral Use

Velia Ramírez-Amador,[a] Gabriela Anaya-Saavedra,[a] Juan J. Calva,[b] Tirso Clemades-Pérez-de-Corcho,[c] Carlos López-Martínez,[c] Imelda González-Ramírez,[a] and Juan Sierra-Madero[b]

[a]*Universidad Autónoma Metropolitana−Xochimilco, México D.F., México*
[b]*Instituto Nacional de Ciencias Médicas y Nutrición, Salvador Zubirán, México D.F., México*
[c]*Clínica Especializada Condesa, México D.F., México*

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Background. The aim of the present study was to compare the prevalence of HIV-related oral lesions (HIV-OL) between two health centers for HIV in Mexico City and to analyze the factors that, in addition to combined antiretroviral therapy (CART) and low $CD4^+$, may be associated with possible differences in prevalence.

Methods. A cross-sectional observational study was performed between January 2000 and February 2003 at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ), a specialized referral center for HIV/AIDS patients and the Clínica Especializada Condesa (CEC), a primary care center for HIV-infected individuals without social security insurance. A consecutive sample of HIV-infected individuals had an oral examination based on established clinical criteria. Demographic, clinical and laboratory data were obtained. Independent association of each factor with specific HIV-OL was assessed by logistic regression modeling.

Results. Eight hundred fifty individuals were examined (INCMNSZ: 479; CEC: 371). Hairy leukoplakia (HL), periodontal disease (PD) and Kaposi's sarcoma (KS) were independently associated with the study site [odds ratio (OR) = 1.7 (95% confidence interval (CI): 1.1–2.4), OR = 4.2 (95% CI: 1.3–13), OR = 10.1 (95% CI: 2.7–38.2), respectively], being more frequent in CEC patients. HL was independently associated with men having sex with men OR = 1.7 (95% CI: 1.1–2.8). All HIV-OL were independently associated with $CD4^+$ counts and, with the exception of PD and KS, with time under CART.

Conclusions. The present comparative study showed that several factors were associated with a difference in prevalence of oral lesions found in two AIDS clinics located in Mexico City. Severe immune suppression, CART duration and the study site were associated with HIV-OL. Further investigation into factors such as socioeconomic determinants associated with HIV-OL is warranted.

Key Words: HIV, Oral lesions, Oral candidiasis, Hairy leukoplakia, Risk factors.

Introduction

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, the incidence of most AIDS-defining illnesses, opportunistic infections and Kaposi's sarcoma (KS) has declined (1–3). Similarly, a changing pattern in the overall prevalence of HIV-related oral lesions (HIV-OL) related to the use of HAART (4–8) has been observed. A decrease in the prevalence of oral candidiasis (OC), hairy leukoplakia (HL) and HIV-associated periodontal disease (PD) in adults has been noted (4,5,9,10), whereas in some series an increase in benign human papilloma virus-associated oral lesions and HIV-related salivary gland disease has been reported (4,9–11).

Address reprint requests to: Velia Ramírez-Amador, Camino Sta. Teresa 277-9, Col. Parques del Pedregal, 14010 México D.F. México; E-mail: rava1863@correo.xoc.uam.mx; veliaram@hotmail.com

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In developed countries where HAART is widely used, the prevalence of HIV-OL varies from 8% (9) to 37.5% (4). In contrast, in developing countries where the majority of HIV-infected patients live and antiretrovirals are not as widely used, the prevalence rate of HIV-OL remains high: 73% in Africa (12) and 90% in Asia (13). These variations could result from differences in several factors in addition to the availability of combined antiretroviral therapy (CART). Socioeconomic and demographic conditions, literacy, risk-group, access to, and utilization of available health facilities might play an important role in the spectrum of HIV-OL (14).

In Mexico City, there are two main referral centers for HIV-infected patients: the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ), a third level hospital where HAART has been used since 1996 (6), and the Clínica Especializada Condesa (CEC), a primary care center established in 2000, dedicated to the health care of HIV/AIDS patients who do not have social security insurance. The aim of the present study was to compare the prevalence of HIV-OL at both centers and to analyze the factors, in addition to CART and low $CD4^+$ counts, that may be associated with these lesions.

Materials and Methods

This was a cross-sectional observational study conducted at the HIV/AIDS Clinic of INCMNSZ and the CEC in Mexico City, between January 2000 and February 2003. A consecutive sample of HIV-infected individuals with the following inclusion criteria was enrolled: 1) age $\geq$18 years; 2) regular attendance at scheduled routine medical visits; and 3) informed consent to have an oral examination. HIV seropositivity for all patients was determined by ELISA and confirmed by Western blot. The study was approved by the Institutional Review Board of the participating institutions.

Demographic (age, gender, schooling, occupation), clinical and laboratory data (transmission category, clinical stage, type and duration of antiretroviral therapy, tobacco use, $CD4^+$ count and viral load determinations) were obtained from medical records. Occupation was classified in seven categories based on the Revised International Standard Classification of Occupation (15): professionals (health and teaching professionals, mathematicians, architects, engineers, writers and creative or performing artists, etc.); technicians and associate professionals (optical and electronic operators, nursing, teaching and social work associate professionals, artistic, entertainment and sports associate professionals, etc.); clerks (office and accounting clerks, secretaries, cashiers, customer service clerks, etc.); service and shop and market sales workers (travel attendants, restaurant service, personal care, fashion and other models, protective service workers, etc.); craft and related workers (miners, building frame and related trade workers, painters, handicraft workers, etc.) and elementary occupations (street vendors and related workers, domestic and related workers, messengers, agricultural, transport workers and freight handlers, garbage collectors, etc.).

Clinical stage for each patient was determined in agreement with the 1993 CDC Classification System (16), considering the $CD4^+$ lymphocyte count. According to this classification, patients in A_1, A_2, B_1 and B_2 stages were grouped as HIV/no-AIDS patients; individuals classified as A_3, B_3, and C_1 to C_3 were considered as having AIDS. Those patients in whom the $CD4^+$ cell counts were not available but had an AIDS-defining condition (16) were considered as having AIDS. HIV-infected individuals without clinical features of AIDS and without $CD4^+$ cell count were not included in the clinical staging. All patients were included in the data analysis.

Tobacco use was classified as a dichotomous variable. Patients were assigned to only one of two possible categories: smokers or non-smokers at the time of the oral examination; patients who were ex-smokers were considered as non-smokers.

For the purpose of the study, CART was defined as treatment with more than one antiretroviral agent for at least 1 month prior to the oral examination. CART included patients under highly active antiretroviral therapy (HAART), which included two nucleoside reverse transcriptase inhibitors (NRTIs) and at least one protease inhibitor (PI) and/or a non-nucleoside reverse transcriptase inhibitor. Also, the combination of three NRTIs was considered HAART, in agreement with the International AIDS Society−USA Panel (17). In addition, patients with dual therapy with NRTIs (non-HAART) were considered as receiving CART. The time of CART was calculated as the period between the date that a patient began to receive antiretrovirals without interruptions and for more than 3 months, and the date of the oral examination. An individual was defined as non-treated if he/she was not under CART or if the antiretroviral regimen was discontinued for 3 months or more before the oral examination.

The $CD4^+$ lymphocyte and viral load values considered in this study were those determined closest to the day of the oral exam, with a maximum of 6 months before or after; these measurements were named "$CD4^+$ cell count" and "viral load". In addition, the lowest $CD4^+$ count found in the medical records before the oral examination was registered and named "nadir $CD4^+$ count."

In both centers, HIV-OL was assessed by three experienced specialists (VRA, GAS, IGR) in the diagnosis of HIV-OL, who examined all participants based on established clinical criteria (18). There was an intraexaminer agreement of 84.7% (kappa = 0.80) and an interexaminer agreement of 79.5% (kappa = 0.71).

Clinical diagnosis of oral candidiasis (OC) was confirmed by the demonstration of *Candida hyphae* in oral smears of the affected oral mucosa. The diagnosis of hairy leukoplakia (HL) was confirmed by the lack of response to