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The Association between Skin Cancer and HIV Infection

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ABSTRACT

People affected by Human Immunodeficiency Virus (HIV) are burdened by a higher risk of developing malignancies as Non-Melanoma Skin Cancer (NMSC) and melanoma skin cancer. This is a cross-sectional retrospective study of HIV-infected and a matched comparison group, analyzing the associations between skin cancer and HIV infection. Our study used the computerized database of Gaffree&Guinle University Hospital – Rio de Janeiro, ensuring 38.164 subjects from 2005-2018, 594 HIV-infected and 37.570 HIV-uninfected patients. Compared to the HIV-uninfected, HIV-infected had 80% association with skin cancer (CI95%: 1,3-2,4; p<0,001). Squamous cell carcinoma has the strongest association, with statistical significance and prevalence ratio of 5,1 for HIV-infected when compared to HIV-uninfected (CI95%: 3.3-7.8; p<0.001). The mean age was 53.6 years (SD ± 16.4), and in the skin cancer group, it was 66.9 years (SD ± 13.7). In those who did not have skin cancer, it was 52.9 years (SD ± 16.2). No melanoma was found in HIV-infected. With this study, we have demonstrated that HIV-infected patients have an increased risk of Basal cell carcinoma and squamous cell carcinoma. Preventative dermatologic management is pivotal in the care of immune suppressed patients. These patients must perform the dermatological exam annually and should receive extensive counseling regarding sun avoidance, the use of sunscreens, and the use of sun-protective clothing.

KEYWORDS: HIV infection; Melanoma; Basal cell carcinoma; Squamous cell carcinoma

INTRODUCTION

The advent of Antiretroviral Therapy (ART) has markedly extended the survival rates of patients with Human Immunodeficiency Virus (HIV), leading to suppression even though not eradication of HIV. In HIV infected patients, cancer has become a growing problem,

representing the first cause of death. A large number of worldwide studies have shown that HIV infection raises the risk of many non-AIDS defining cancers, including melanoma and Non-Melanoma Skin Cancer (NMSC) [1, 2].

NMSC, defined as Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC), is the most common malignant condition in the world [3]. Among immune competent individuals, BCCs are more common than SCCs. However, among immune compromised persons, SCCs predominate over BCCs [4, 5].

The HIV-infected population has a risk of developing BCC and SCC that is increased 2-fold and 5-fold, respectively, of that of the general population. The risk of NMSC, especially SCC, increases further in patients with poorly controlled HIV, who are subsequently more immune suppressed (CD4 <200 cells/mL and/or HIV viral load of 10.000 copies/mL) [4, 6-10].

The incidence of melanoma in HIV-infected patients is 2.6 higher as compared to no HIV patients, which reflects both a decreased efficiency of the host immune response in eliminating potentially malignant cells and an improvement in the treatment of HIV patients - because of the development of new antiretroviral agents. The latter prolongs the survival of the infected patients increasing the time of immunodeficiency and the possibility of tumor development [11-14].

METHODS

Following the Gaffree&Guinle University Hospital – Rio de Janeiro Medical Ethics Committee (CAAE 08945019.0.0000.5258), we carried out this cross-sectional retrospective study of HIV patients and a matched comparison group, analyzing the associations between skin cancer and HIV infection.

Our study used the computerized database of Gaffree&Guinle University Hospital – Rio de Janeiro, ensuring 38.164 subjects from 2005-2018, 594 HIV-infected and 37.570 HIV-uninfected patients. The data collected were grouped into plain Microsoft Excel® spreadsheets and subsequently converted into the Stata®, version 15.1 (serial: 301506206729), to perform the statistical analysis.

The exposure considered was the presence of HIV, and the outcome was skin cancer. For this, the distribution of the absolute and relative frequencies of the categorical variables with cancer was carried out. The chi-square test was also applied, with a significance level of 5%.

The estimated association measure for exposure (HIV), and outcome (skin cancer) was the gross and adjusted Prevalence Ratios (PR), with the respective 95% confidence intervals. Logistic regression was used for this calculation, then the conversion of ODDS RATIO was performed due to prevalence through the ZHANG [15] and by the odds risk command in Stata® in version 15.1 (SERIAL: 301506206729). Besides, the Hosmer-Lemeshow test [16] assessed the quality of the adjusted model, considered adequate when the p-value was higher than 0, 10.

RESULTS

The study comprised 594 HIV-infected (1.6%), 37.570 (98.4%) HIV-uninfected persons (n=38.164), 1601 NMSC (43 HIV-infected vs 1558 HIV uninfected) and 107 cutaneous melanomas (all of them HIV-uninfected). The mean age was 53.6 years (SD ± 16.4), and in the skin cancer group, it was 66.9 years (SD ± 13.7). In those who did not have skin cancer, it was 52.9 years (SD ± 16.2).

We summarized the study characteristics in (Table1). The NMSC prevalence in males was 5.7% and, in females, 3.2% vs 94.3% male and 96.8% female. White individuals were 7.9%. HIV-infected had 1.7% BCC and 7.5%.

Among people who had BCC and HIV, the involvement of anatomical sites varied, with most cases occurring on the head (66.66%), followed by the trunk (23.80%), and lastly by the lesions diagnosed on the abdomen (4.76). The most common site of SCC was the genital region (68.18%), followed by the trunk (9.09%) and in lower proportions: face, lips, chronic sacral ulcer, upper limbs (22.73%).

Compared to the HIV-uninfected, HIV-infected had 80% association with skin cancer (CI95%: 1, 3-2, 4; p<0,001). The risk was 4, 5-fold higher by patients' age (CI95%: 3,3-5,9; p<0,001). When adjusted for patient age, sex and race, the risk was 6,4-fold higher of having cancer compared to the others (CI95%: 4,9-8,4; p<0,001) (Table 2).

Table 1: Characteristics of the Study.(n=38164)

CHARACTERISTICS	NMSC (%)	NO-NMSC (%)
Number of cases	1558 (4,1)	36606 (95,9)
Sex*3686		
Male	697 (5,7)	11560 (94,3)
Female	716 (3,2)	21505 (96,8)
Age,categorical(years)*13425		
18-49	129 (1,3)	9567 (98,7)
50-64	331 (4,0)	7836 (96,0)
>64	675 (9,8)	6201 (90,2)
Race/Color*25518		
White	646 (7,9)	7494 (92,1)
Medium/Black	94 (2,1)	4412 (97,9)
HIV		
HIV-infected	43 (7,2)	551 (92,8)
HIV-uninfected	1515 (4,0)	36055 (96,0)

*Number of lost information for each characteristic.

Table 2: Association between HIV positive and skin cancer.(n=38.164)

CANCER	PR	CI 95%	*p*	aRP*	CI 95%	p	aRP**	CI 95%	*p*
BCC	1,1	0,7 a 1,7	0,651	2,8	1,9 a 4,2	<0,001	4,4	2,9 a 6,3	<0,001
SCC	5,1	3,3 a 7,8	<0,001	12,3	7,9 a 18,7	<0,001	22,7	14,2 a 34,6	<0,001
BCC&SCC#	1,8	1,3 a 2,4	<0,001	4,4	3,3 a 5,7	<0,001	6,4	4,9 a 8,1	<0,001

PR: Prevalence ratio; **CI**: Confidence interval; a**RP***: Prevalence ratio when adjusted for patientage; a **RP****: Prevalence ratio when adjusted for patient age, sex, and race. #BCC and SCC
Model quality (2): BCC (*0,22; **0,12); SCC (*0,19; **0,21); BCC&SCC (*0,19; **0,21)

SCC has the strongest association, with statistical significance and prevalence ratio of 5,1 for HIV-infected when compared to HIV-uninfected (CI95%: 3.3-7.8; p<0.001). When adjusted for patient age, sex and race, the risk was 22,6-fold higher of having cancer compared to the others (CI95%:14,5-35,4; p<0,001). We used other GGHU laboratory databases to obtain laboratory test results (TCD4), but we found no association between TCD4 count <200 cells and large or more severe tumors.

We found 119 cases of cutaneous melanoma, but none of these individuals had HIV, so it was not possible to carry out a study with its characteristics.

DISCUSSION

Globally, 38.0 million people were living with HIV at the end of 2019.17 A large number of worldwide studies have shown that the HIV-infected population has an increased risk of developing BCC and SCC of that of the general population [4, 6, 7]. Our study presents the clinical features, epidemiology and laboratory markers in HIV-infected with NMSC to a better understanding of this condition.

This retrospective cross-sectional study of 38.164 pathology records from GGHU showed 1558 (4.1%) NMSC and 107 (0.28%) cutaneous melanoma. The HIV-infected who had some type of NMSC were 43 (21 BCC and 22 SCC); however, none of these individuals had melanoma. We believe that this was due to the rarity of this tumor. Also, our hospital is not a reference for cancer. The number of new cases of melanoma described in 2018 in the Brazilian territory was 6260, so it is possible to understand its rarity in our sample (594 HIV-infected) [18]. The results of our study were similar to the data in the literature, and HIV-infected with NMSC had a higher risk of tumor development compared to HIV-uninfected in the same hospital. SCC has the strongest association.

The sex prevalence among this sample was female. However, when we selected HIV-infected with NMSC, the majority were men (67.44% vs 32.55%). It is expected, as seen in this study, higher involvement in males than females, probably due to the greater number of cases of HIV infection being in men. The age group with the highest incidence of NMSC was older than 64 years, and HIV-infected was younger (50-64 years), suggesting that the virus may influence the development of NMSC.

Both groups had a prevalence of the white race. The prevalence of BCC in sun-exposed areas (95,22%) confirms the important role of ultraviolet radiation in the genesis of this tumor. In this investigation, the higher number of SCC was diagnosed in the genital area (68.18%) goes against this rationale and endorses the role of the Human Papilloma virus (HPV) in the genesis of SCC.

HIV-infected have a higher risk of contracting HPV, including oncogenic viruses, due to risk behavior and immunosuppression.19,20 Microscopy with H&E staining detected 54.5% cases with some histopathological alteration suggestive of HPV infection, such as koilocytotic atypia, cytopathic alterations of probable HPV-like viral lesion or diagnosis of Bowenoid papulosis.

A large number of GGHU patients use regular of ART, which may explain the TCD4 cell count of these individuals at higher levels. Considering that GGHU is a quaternary hospital that promotes prevention campaigns - like the National Campaign for the Prevention of Skin Cancer by the Brazilian Society of Dermatology annually - these patients may be protecting themselves, so we believe that this can influence the results.

The advent of ART has markedly extended the survival rates of patients with HIV, so cancer has become a growing problem, including melanoma and non-melanoma skin cancer. With this study, we have demonstrated that HIV-infected patients have an increased risk of BCC and SCC. Since there was no event of melanoma in the HIV-infected group, we cannot make a stronger conclusion regarding the risk of this tumor in these individuals.

Preventative dermatologic management is pivotal in the care of immune suppressed patients. These patients must perform the dermatological exam annually and should receive extensive counseling regarding sun avoidance, and the use of sunscreens and sun-protective clothing.

Further studies are needed to compare different geographical areas in the city of Rio de Janeiro and the Brazilian territory.

References:

1. Berretta M, Martellotta F, Di Francia R, Spina M, Vaccher E, Balestreri L, et al. Clinical presentation and outcome of non-AIDS defining cancers, in HIV-infected patients in the ART-era: the Italian Cooperative Group on AIDS and tumors activity. Eur Rev Med Phar-

macol Sci. 2015; 19: 3619-34.

2. Olsen CM, Knight LL, Green AC. Risk of Melanoma in People with HIV/AIDS in the Pre-and Post-HAART Eras: A Systematic Review and Meta Analysis of Cohort Studies. Plos One. 2014; 9: e95096.
3. Sociedade Brasileira de Dermatologia. Analise de dados das campanhas de prevençao ao cancer da pele promovidas pela Sociedade Brasileira de Dermatologia de 1999 a 2005. An Bras Dermatol. 2006; 81: 533-9.
4. Asgari MM, Ray GT, Quesenberry CP Jr, Katz KA, Silverberg MJ. Association of Multiple Primary Skin Cancers with Human Immunodeficiency Virus Infection, CD4 Count, and Viral Load. JAMA Dermatol. 2017; 153: 892-6.
5. Song SS, Goldenberg A, Ortiz A, Eimpunth S, Oganesyan G, Jiang SI. Nonmelanoma Skin Cancer With Aggressive Subclinical Extension in Immuno suppressed Patients. JAMA Dermatol. 2016; 152: 683-90.
6. Collins L 1, Quinn A, Stasko T. Skin Cancer and Immunosuppression. Dermatol Clin. 2019; 37: 83-94.
7. Omland SH, Ahlstrom MG, Gerstoft J, Pedersen G, Mohey R, Pedersen C, et al. Risk of skin cancer in HIV-infected patients: a Danish Skin Cancer and Immunosuppression 91 nationwide cohort study. J Am Acad Dermatol. 2018; 79: 689-95.
8. Chang AY, Doiron P, Maurer T. Cutaneous malignancies in HIV. CurrOpin HIV AIDS. 2017; 12: 57-62.
9. Coates SJ, Leslie KS. What's new in HIV dermatology? F1000Res. 2019; eCollection 2019.
10. Silverberg MJ, Leyden W, Warton EM, Quesenberry Jr CP, Engels EA, et al. HIV infection status, immunodeficiency, and the incidence of non-melanoma skin cancer. J Natl Cancer Inst. 2013; 105: 350-60.
11. Marra A., Scognamiglio G, Peluso I, Botti G, Fusciello C, Filippelli A, et al. Immune Checkpoint Inhibitors in Melanoma and HIV Infection. The Open AIDS Journal. 2017; 11: 91-100.
12. Facciola A, Venanzi Rullo E, Ceccarelli M, D'Andrea F, Coco M, Micali C, et al. Malignant melanoma in HIV: Epidemiology, pathogenesis, and management. Dermatol Ther. 2019; 26: e13180.
13. Ryska A, O Horky, J Berkovcova, Ticha I, Kalinova M, Matejckova M, et al. Malignant Melanoma - From Classical Histology Towards Molecular Genetic Testing. KlinOnkol. 2017; 3: 182-9.
14. Yanik EL, Hernández-Ramírez RU, Qin L, Lin H, Leyden W, Neugebauer RS, et al. Brief Report: Cutaneous Melanoma Risk Among People With HIV in the United States and Canada. J Acquir Immune DeficSyndr. 2018; 78: 499-504.
15. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998; 280: 1690-1.
16. Hosmer DW, Lemeshow S, Sturdivant RX. Applied Logistic Regression. New York: Wiley, 2013.
17. World Health Organization. HIV/AIDS, Data and statistics. 2019.
18. Instituto Nacional de Câncer (INCA). Tipos de câncer. 2019.
19. Donoso-Hofer F, Ampuero-Llanos S. HPV genotypes in oral papilloma in Hospital San Juan de Dios HIV (+) patients. Rev Chilena Infectol. 2019; 36: 469-74.
20. Wang J, Aldabagh B, Yu J, Arron ST. Role of human papillomavirus in cutaneous squamous cell carcinoma: a meta-analysis. J Am Acad Dermatol. 2014; 70: 621-9.