Hodgkin Lymphoma in HIV Positive Patients in Use of High-Effective Antiretrovirals

doi: https://doi.org/10.32635/2176-9745.RBC.2021v67n2.825

Linfoma de Hodgkin em Pacientes HIV Positivo em Uso de Antirretrovirais de Alta Efetividade

Linfoma de Hodgkin en Pacientes VIH Positivos en el Uso de Antiretrovirales de Alta Efectividad

Sávio da Silva Araújo[1]; Carlos Genilson Freire Monteiro[2]; Tiago Lima Sampaio[3]; Aline de Albuquerque Oliveira[4]

ABSTRACT

Introduction: The ability of the human immunodeficiency virus (HIV) of invading immune system cells, especially CD4+ to multiply and stay alive, when not reversed, has as inevitable outcome the acquired immunodeficiency syndrome (AIDS), an event in which patients start to develop secondary diseases such as opportunistic infections and cancer. **Objective:** To identify cases of Hodgkin's lymphoma in HIV+ patients using highly effective antiretrovirals. **Method:** Cross-sectional observational study with exploratory and descriptive design and qualitative and quantitative approach, carried out during the month of October 2018 based on the analysis of 57 HIV-infected patients' charts diagnosed with cancer and admitted to a hospital located in Fortaleza, CE. **Results:** A total of 21 non-AIDS-defining cancers were detected. Of these, skin cancer, with 14.3% (3) followed by breast cancer, with 9.5% (2), Hodgkin's lymphoma, 9.5% (2) and stomach cancer, with 9.5% (2) were the most common cases. **Conclusion:** The data obtained in the present study rank Hodgkin's lymphoma in second place among the non-AIDS-defining cancers encountered. However, while considering the small number of cases, due to the study limitations, these data are scanty to conclude the actual quantity of Hodgkin's lymphoma among the non-AIDS-defining cancers occurred in HIV-positive patients locally or to estimate the participation of HIV, viral load, immune condition and co-infection as risk factors.

Key words: Hodgkin Disease; HIV; Acquired Immunodeficiency Syndrome; Anti-Retroviral Agents/therapeutic use; Neoplasms.

RESUMO

Introdução: A capacidade do vírus da imunodeficiência humana (HIV) de invadir células do sistema imunológico, principalmente células T CD4+, para se multiplicar e manter-se vivo, quando não revertido, possui, como desfecho inevitável, a síndrome da imunodeficiência adquirida (SIDA), evento no qual os pacientes começam a apresentar doenças secundárias como infecções oportunistas e câncer. **Objetivo:** Identificar casos de linfoma de Hodgkin em pacientes HIV+ em uso dos antirretrovirais de alta efetividade. **Método**: Estudo do tipo observacional transversal com delineamento exploratório e descritivo e abordagem quali-quantitativa, realizado durante o mês de outubro de 2018, a partir da análise de 57 prontuários de pacientes HIV+ diagnosticados com câncer e internados em um hospital localizado em Fortaleza, CE. **Resultados:** Foi identificado um total de 21 cânceres não definidores de SIDA. Destes, os mais comuns foram o câncer de pele com 14,3% (3); seguido do câncer de mama com 9,5% (2); linfoma de Hodgkin com 9,5% (2); e o câncer de estômago com 9,5% (2) dos casos. **Conclusão:** Os dados obtidos no presente estudo colocam o linfoma de Hodgkin em segundo lugar entre os cânceres não definidores de SIDA encontrados. Contudo, ao considerar o baixo número de casos, resultante das limitações da pesquisa, essas informações não permitem concluir sobre a real quantidade de linfomas de Hodgkin entre os demais cânceres não definidores de SIDA ocorridos em pacientes HIV+ na localidade, tampouco estimar a participação do HIV, carga viral, condição imunológica e coinfecções como fatores de risco.

Palavras-chave: Doença de Hodgkin; HIV; Síndrome de Imunodeficiência Adquirida; Antirretrovirais/uso terapêutico; Neoplasias.

RESUMEN

Introducción: La capacidad del virus de inmunodeficiencia humana (VIH) para invadir las células del sistema inmunitario, especialmente las células T CD4 + para multiplicarse y mantenerse con vida, cuando no se revierte, tiene el resultado inevitable del síndrome de inmunodeficiencia adquirida (SIDA), evento en el que los pacientes comienzan a presentar enfermedades secundarias como infecciones oportunistas y cáncer. **Objetivo:** Identificar los casos de linfoma de Hodgkin en pacientes VIH+ utilizando los antirretrovirales de alta eficacia. **Método:** Este es un estudio observacional transversal con diseño exploratorio y descriptivo y enfoque cualitativo, realizado durante octubre de 2018 a partir del análisis de 57 registros médicos de pacientes VIH + diagnosticados con cáncer y hospitalizados en un hospital ubicado en Fortaleza, CE. **Resultados**: Se identificaron un total de 21 cánceres que no definen el SIDA. De estos, los más comunes fueron cáncer de piel con 14,3% (3), seguido de cáncer de seno con 9,5% (2), linfoma de Hodgkin 9,5% (2) y cáncer de estómago con 9,5% (2) de los casos. **Conclusión**: Los datos obtenidos en el presente estudio colocan al linfoma de Hodgkin en segundo lugar entre los cánceres no definitorios de SIDA encontrados. Sin embargo, considerando el bajo número de casos resultantes de las limitaciones de la investigación, esta información no nos permite concluir acerca de la cantidad real de linfoma de Hodgkin entre los otros cánceres no definitorios de SIDA en pacientes VIH + en la localidad, ni estimar la participación del VIH, la carga viral, la condición inmune y las coinfecciones como factores de riesgo.

Palabras clave: Enfermedad de Hodgkin; VIH; Síndrome de Inmunodeficiencia Adquirida; Antirretrovirales/uso terapéutico; Neoplasias.

[1,2]University Center Fametro (Unifametro). Fortaleza (CE), Brazil. E-mails: saviosaviosi@gmail.com; genilson.monteiro09@gmail.com. Orcid iD: https://orcid.org/0000-0001-5491-5319; Orcid iD: https://orcid.org/0000-0002-4217-4039
[3]Federal University of Ceará (UFC). Fortaleza (CE), Brazil. E-mail: tiagosampaio91@gmail.com. Orcid iD: https://orcid.org/0000-0002-3962-6508
[4]Christus University Center (Unichristus). Fortaleza (CE), Brazil. E-mail: alinealbuquer@hotmail.com. Orcid iD: https://orcid.org/0000-0002-5998-2606
Corresponding author: Sávio da Silva Araújo. Rua Conselheiro Estelita, 500 - Centro. Fortaleza (CE), Brazil. CEP 60010-260. E-mail: saviosaviosi@gmail.com

INTRODUCTION

When untreated, the human immunodeficiency virus infection (HIV) results in immunosuppression because of the capacity the virus has of invading immune system cells, mainly CD4+ T, multiply and keep alive. If not reversed, this mechanism has the acquired immunodeficiency syndrome (AIDS) as its inevitable outcome, from which secondary diseases as opportunistic infections and cancer start to appear[1].

After the introduction of HAART – Highly Active Antiretroviral Therapy and the increase of HIV+ patients life expectancy because of AIDS reduction, a new scenario involving pathologies of this population was noticed, mainly for non-AIDS defining cancers as Hodgkin lymphoma, liver, anal, prostate and lung whose incidence increases when compared with AIDS-defining cancers as Kaposi's Sarcoma, invasive cervical cancer and non-Hodgkin lymphomas[2].

From 2007 to 2017 in Brazil, 192,217 cases of HIV-infection were notified in the "*Sistema de Agravos de Notificação (Sinan)"* (System of Notification of Health Harms) with the biggest number of infected individuals[3] found in the Southeast (49.65%), South (20.73%) and Northeast (15.59%) regions.

For AIDS, the notifications accounted from 1980 to June 2017 reached a total of 882,810 cases, the mean is 40 thousand registries in the last five years. 316,088 deaths were notified until 2016 in Brazil since the beginning of the epidemics (1980), and from 2014 on, after the policy of treatment for all, there was a drop of 11.9% of the AIDS death rate for the whole country[3].

Regarding some non-AIDS defining cancers from 2000 to 2015 in Brazil, the incidence and the number of deaths obtained from the Population-Based Cancer Registry (PBCR) were respectively 7,403 and 7,499 for Hodgkin lymphoma, 12,611 and 113,973 for liver cancer, 3,897 and 4,086 for anal cancer, 57,677 and 320,912 for lung cancer and 116,321 and 181,251 for prostate cancer[4,5].

Among the risk factors typically quoted for most of the non-AIDS defining cancers are ageing, smoking and family history[6-8], except Hodgkin lymphoma that has HIV-infections, human T-lymphotropic virus type 1 (HTLV-1) and Epstein-Barr virus (EBV) as major contributors for its development in addition to the risk factors already mentioned[9-11].

A result of the action of the HIV virus, lymphocytopenia works as a stimuli for the bone marrow which, in attempting to revert the immunosuppression status, stimulates the dependent lymphopoiesis of the interaction of CD34 cells with CD4+ infected cells, resulting in the exhaustion and failure in producing new cells B. The perturbation of hematopoiesis associated with the increased volume of precursors cells of new cells B raises the odds of genetic errors and incidence of lymphomas in HIV+ patients[12].

Another factor related to the high production of cells B occurs by the presence of protein p-17 in the envelope of HIV. This protein is able also to stimulate the formation of new blood vessels and can promote, in addition to the lymphomagenesis, the dissemination of the lymphoma[12].

Taylor et al.[13] infer yet that according to the chronicity of the HIV-infected patient due to the efficacy of the antiretrovirals, Hodgkin lymphoma can become an increasing complication in these individuals.

Although currently some countries are discussing the HIV infection and the non-AIDS defining cancers, in Brazil the information from cross-checking these data are still scarce, mainly when the characteristics of HIV patients affected with specific types of cancer need to be obtained.

Based in this necessity and in risk factors already mentioned, the objective of this article is to identify cases of Hodgkin lymphoma among the non-AIDS defining cancers diagnosed in HIV+ patients followed up in a reference hospital of Fortaleza, CE while in use of highly active antiretroviral therapy, characterizing these patients per age, gender, CD4+ count, viral load, history of coinfections and antiretroviral regimen utilized until cancer diagnosis.

METHOD

Retrospective, cross-sectional study attempting to analyze the factor (HIV+ patients in use of antiretrovirals) and the effect (Hodgkin lymphoma) in the same historical moment and observational because the investigators did not intervene. In addition, it is an exploratory study since it was tried to collect data not provided locally, and descriptive, considering that the results of the cases of the patients who matched the inclusion criteria will be detailed.

The approach was quali-quantitative. Under the qualitative perspective, the characteristics as gender, age-range, type of antiretroviral treatment of these patients were described and coinfections when applicable. In the quantitative approach, all the cases of non-AIDS defining cancers registered in HIV+ patients' charts in use of antiretroviral therapy were estimated in order to obtain the number of cases of Hodgkin lymphoma for this population.

The study was conducted in "*Hospital São José de Doenças Infecciosas*" (HSJ) (Infectious Diseases Hospital)

of Fortaleza, CE, through review of the charts of HIV+ patients hospitalized from January 2013 to September 2018. The chart's data were collected and reviewed in the Medical and Statistical Service (SAME) of HSJ during October 2018.

As initial source to obtain the number of charts to be reviewed, the books of discharges and deaths available at HSJ's SAME were consulted. Thus, it was possible to access all the charts of HIV+ patients hospitalized who were diagnosed with AIDS defining and non-AIDS defining cancers from January 2013 to September 2018.

The inclusion criteria were charts of HIV+ patients in use of antiretrovirals diagnosed with non-AIDS defining cancers with information about viral load and CD4+ T cells count, the later was not necessary for patients with indetectable viral load due to clinical protocols which recommend to not request CD4+ T cells count after the first indetectable viral load was obtained. The justification for the criteria is that the understanding about the immune condition, the HIV-infection through the quantity of copies of the virus in the blood and the use of antiretrovirals can potentially indicate whether the cases of neoplasms encountered, mainly Hodgkin lymphoma are related to the serologic condition of the study population.

In compliance with the inclusion criteria, 21 charts of HIV+ patients with history of use of high active antiretrovirals who were diagnosed with any non-AIDS defining cancer were selected. Next, the investigation about the following variables commenced: gender (identify whether the mean age range and gender match the profile reported in other countries); type of non-AIDS defining cancer (identify whether there is predominance for Hodgkin lymphoma); first viral load count and first CD4+ T cells count after the diagnosis of HIV+; last viral load count and last CD4+ T count cells before the diagnosis of cancer (understand the immune and serologic evolution after the diagnosis of HIV until the diagnosis of non-AIDS defining cancer); history of coinfections (presuppose relation of the infectious agent with cancer or potentializing of predisposition of cancer); antiretroviral regimen utilized until the diagnosis of cancer (discuss whether the use during the treatment of Hodgkin lymphoma has any impact in the treatment efficacy and/or safety of the patient) and history of adherence to the antiretroviral treatment evaluated from the medical records in the charts and associated with the results of the CD4+ T cells and viral load count after the beginning of the treatment.

For further analysis, ten charts of HIV+ patients with cancer were selected but without specification of subtype, for instance, lymphoma and malignant neoplasm, continuing in the study only the confirmed cases of non-AIDS defining cancers, after investigation.

Charts of HIV+ patients diagnosed with AIDS-defining cancer or who failed to meet the inclusion criteria were excluded.

For not meeting the inclusion criteria of this study, the charts of HIV+ patients diagnosed with AIDS-defining cancer (Kaposi's Sarcoma, non-Hodgkin lymphoma, invasive cervical cancer) and charts of patients diagnosed with cancer whose subtype was unspecified or who in any moment used high active antiretrovirals were excluded.

A follow up form of the variables was elaborated to obtain and organize the information based in the full analysis of each chart. The data collected were exported to a Microsoft® Excel (2013) software spreadsheet, updated according to the progress of the study and analyzed. In addition to the descriptive statistical data, some were also converted in figures and tables to present the results achieved.

The Institutional Review Board of the Fametro University Center (Unifametro) approved the study, CAAE 99291718.6.0000.5618 and report 2.925.389.

RESULTS

The present study conducted with secondary sources of data of all the HIV+ patients hospitalized in a period of six years resulted in 57 charts to be investigated. Of these, 26 were patients diagnosed with AIDS-defining cancers, other ten were patients with unspecified cancer type, reaching 36 charts not selected for the study.

Of the charts selected, 21 non-AIDS defining cancers were encountered (Figure 1). Of these, 14.3% (3) with skin cancer, followed by 9.5% (2) of breast cancer, 9.5% (2) with Hodgkin lymphoma and 4.8% (1) for pleural, lung, oropharynx, colon, rectum, penis, prostate, mouth, esophagus, anaplastic carcinoma, multiple myeloma and leukemia .

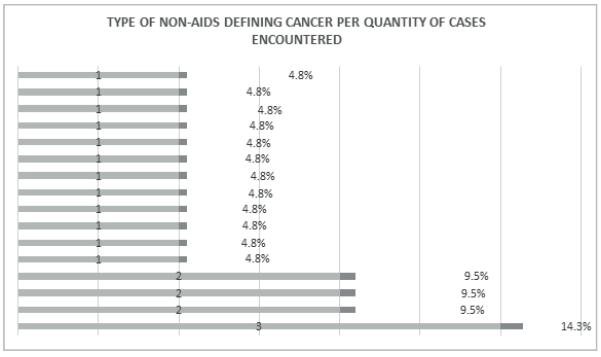

Figure 1. Number of cases per type of non-AIDS defining cancer in HIV+ patients admitted in a reference hospital in Fortaleza, Ceará, January 2013 to September 2018.

81% (17) were males and 19% (4) females. For males, the age ranged from 37 to 70 years, mean of 52 years. The variation for females was from 37 to 65 years with mean of 50 years. For the patients with Hodgkin lymphoma, 100% (2) were males, minimum age of 40 years, maximum of 49 years and mean of 45 years.

Of the 21 charts analyzed, only 13 provided information about the variables: "first CD4+ count after the diagnosis of cancer"; "last CD4+ count before the diagnosis of cancer" and last viral load count before the diagnosis of cancer. Only 12 reported the "first viral load count after the diagnosis of HIV+. The justification for the absence of these variables in the other charts is due to the fact that these are patients that other State's STI/AIDS specialized care follow up; the history of these patients in HSJ is just for services of admission and whose outcome was death or referral to other care unit before the retrieval of the CD4+ history and/or viral load.

Considering the information mentioned in the charts analyzed about the first CD4+ cells count after the diagnosis of HIV+ (Figure 2), a variation of 54 cells/dL (skin cancer) to 660 cells/dL (stomach cancer) was found with mean equal to 317.85 cells/dL. For the first quantification of the viral load after the diagnosis of HIV+ (Figure 2), the minimum value was indetectable (carcinoma) and the maximum value equal to 4,300,00 copies/mL (penis cancer), the mean is equal to 462,474 copies/mL. In the cases of Hodgkin lymphoma, these data were obtained only in 50% (1) of the charts with CD4+cells count equal to 596 cells/dL and viral load equal to 5,000 copies/mL.

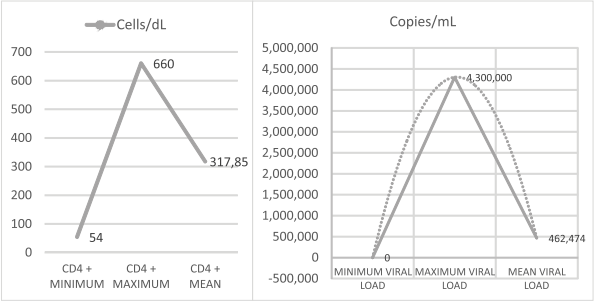

Figure 2. First CD4+ cells and viral load count after the diagnosis of HIV+ in patients admitted in a reference hospital of Fortaleza, Ceará, January 2013 to September 2018

The last CD4+ counts obtained before the diagnosis of cancer (Figure 3) ranged from ten (oropharynx cancer) to 765 cells/dL (stomach cancer) with mean equal to 342.23 cells/dL. Among the cases of Hodgkin lymphoma, the maximum count before the diagnosis of cancer was 549 cells/dL and minimum equal to 398 cells/dL, with mean of 473.5 cells/dL. The variation of the viral load count before the diagnosis of cancer (Figure 3) ranged from indetectable (Hodgkin lymphoma; rectum and colon cancer) to 9,027,157 copies/mL (Hodgkin lymphoma) with mean equal to 1,016,270 copies/mL.

Of the 21 patients diagnosed with non-AIDS defining cancers, only 33.33% (7) reported some type of coinfection. The main agents involved were the viruses varicella-zoster 28.57% (2); cytomegalovirus 14.28% (1); fungus *Candida sp* 14.28% (1); bacteria *mycobacterium tuberculosis* 14.28% (1); *acinetobacter* 14.28% (1) and parasite *leishmania sp* 14.28% (1). No case of coinfection with Hodgkin lymphoma was described in the patients' charts.

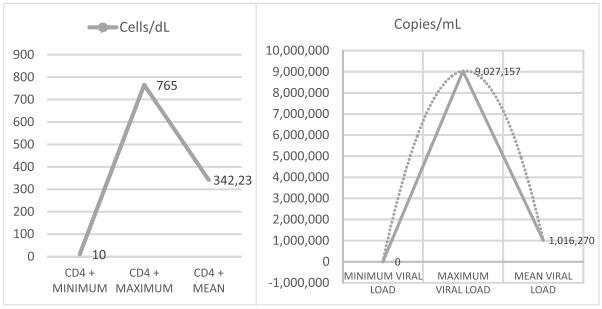

Figure 3. Last CD4+ and viral load count of HIV+ patients admitted in a reference hospital of Fortaleza, Ceará before the diagnosis of cancer, January 2013 to September 2018

The therapeutic regimen of each patient in use of antiretrovirals (Figure 4), 33.3% (7) had two nucleoside reverse transcriptase inhibitors associated with protease inhibitors; 9.52% (2) utilized two nucleoside reverse transcriptase inhibitors associated with one protease inhibitors; 42.86% (9), two nucleoside reverse transcriptase associated with one non-nucleoside reverse transcriptase; 4.76% (1), two nucleoside reverse transcriptase inhibitors associated with one integrase inhibitor and 4.76% (1) only two protease inhibitors. Only in 4.76% (1) of the charts (anaplastic carcinoma) no information about the therapeutic regimen was found because the patient did not know which antiretrovirals were taken. For the cases of Hodgkin lymphoma, one (50%) used two nucleoside reverse transcriptase inhibitors associated with two protease inhibitors and one (50%) used the regimen with two nucleoside reverse transcriptase inhibitors associated with one non-nucleoside reverse transcriptase inhibitor as therapeutic regimen.

The nucleoside reverse transcriptase inhibitors most commonly described were tenofovir (TDF) associated with lamivudine (3TC), present in 40% (8) of the 20 therapeutic regimens reported. For protease inhibitors, the most common was the association between lopinavir (LPV) and ritonavir (RTV), present in the regimen of 25% (5) of the patients. Among the non-nucleoside reverse

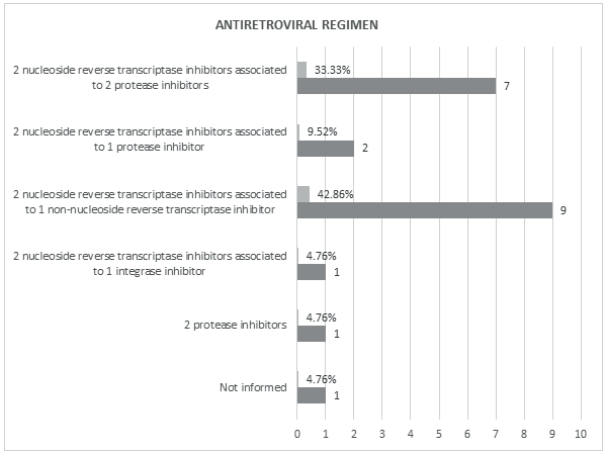

Figure 4. Antiretroviral regimen of the HIV+ patients diagnosed with non-AIDS defining cancer admitted in a reference hospital of Fortaleza, Ceará, January 2013 to September 2018

transcriptase, efavirenz (EFV) was the only prescribed, included in the regimen of 45% (9) of the patients. Dolutegravir was the only protease inhibitor prescribed, a component of the regimen of 5% (1) of the patients.

The following data were obtained about the adherence of the patients to antiretrovirals after investigating the evolution the physicians described in the charts: 61.9% (13) of the patients claimed the main reason for non-compliance with the treatment was forgetfulness; 9.52% (2) started antiretroviral therapy only after the admission to the hospital, when the patient, apart from the cancer diagnosis, became aware of the anti-HIV positive serology; 4.76% (1) have completely abandoned the treatment; 23.81% (5) of the charts failed to report the assiduity of the patients to the anti-HIV treatment.

The main data obtained in the two HIV+ patients before the diagnosis of Hodgkin lymphoma found in this study are shown in Table 1 where it is possible to observe CD4+ equal to 549 cells/dL in one of the cases, indetectable viral load and, although there are no information about the history of adherence to the treatment, possibly it is a patient with good adherence to the proposed antiretroviral therapy. In the second case, the patient has CD4+ equal to 398 cells/dL, elevated viral load and non-compliance with antiretrovirals use.

DISCUSSION

Among the non-AIDS defining cancers found in HIV+ patients, Hodgkin lymphoma ranked second in this study with the same quantity of cases of breast and stomach cancer, below only skin cancer. Vaccher et al.[14], in their epidemiologic studies about cancer in HIV+ patients, from the studies of linking registries in the United States of America, Italy and Switzerland which obtained 1,078 cases of non-AIDS defining cancers, reported the likelihood of elevated relative risk 50-fold higher for cancers related to infections by oncogenic agents, with special emphasis for anal cancer, Hodgkin lymphoma, hepatocellular carcinoma and lung cancer. These authors informed there were scarce evidences of increased risk for epithelial cancers as breast, colon and prostate cancer.

The characteristics related to the patients' gender and age and type of Hodgkin lymphoma found in this study have similar profile to the data of a review Uldrick and Little[15] conducted with the objective of describing the epidemiology of Hodgkin lymphoma in HIV+ patients whose result was median age of 40 to 44 years and for this same age range, a correlation between classic Hodgkin lymphoma and HIV in 14% of the cases occurred in the United States.

According to Cobucci et al.[16], one of the contributing factors for the increase of the incidence of Hodgkin lymphoma after HAART is because Reed Sternberg cells present in this type of malignant neoplasm depend on CD4+ cells to keep active, concluding that this would be a type of cancer whose odds of appearance would be diminished in individuals with severe

Table 1. Data obtained from HIV+ patients after diagnosis of Hodgkin lymphoma and admitted to a reference hospital in Fortaleza, Ceará

INDICATORS	CASE 1	CASE 2
Gender	Male	Male
Age	40 years	49 years
Type of Hodgkin Lymphoma	Classic	Classic
Viral load before the diagnosis of cancer	Indetectable	9,027,157 copies/mL
CD4 + count before the diagnosis of cancer	549 cells/dL	398 cells/dL
Antiretrovirals utilized	TDF + 3TC + ATV/RTV	D4T + DDI + EFV
History of treatment	Not informed	Non-compliance

Captions: TDF (tenofovir); 3TC (lamivudine); ATV (atazanavir); RTV (ritonavir); D4T (stavudine); DDI (didanosine); EFV (efavirenz).

immunosuppression and increasing in cases of moderate immunosuppression.

Consequently, when the immune condition of the patients before the diagnosis of Hodgkin lymphoma was investigated in the present study, considering CD4+ lower than 200 cells as non-AIDS defining cancer as the Ministry of Health determines, none of the two cases was immunosuppressed. Some authors attribute the parameter of normality for CD4+ count in individuals with HIV and cancer associated with highly active antiretroviral therapy[17].

While considering the main objective of antiretrovirals which is to promote the reduction of HIV replication, the monitoring of the viral load, a test which permits to quantify the RNA of the circulating virus in the bloodstream, becomes an important clinical marker, able to reflect the dynamic of the retrovirus after the beginning of the treatment[18].

In this study, a contrast among two cases of Hodgkin lymphoma was obtained. One of the cases had indetectable viral load during the diagnosis of cancer while the second showed very high viral load (9,027,157 copies/mL), this count was the biggest among all the non-AIDS defining cancers identified while the study was being conducted and possibly justified because the patient had a history of non-compliance in using antiretrovirals.

Although in this study none of the patients with Hodgkin lymphoma was immunosuppressed and only one patient had elevated viral load, it is important to emphasize that histories of coinfections with microorganisms as EBV, human herpesvirus 8, hepatitis B and C virus and human papilloma virus (HPV) can favor the appearance of cancers[19].

Carroll and Garzino-Demo[12] concluded that the capacity of HIV induced hyperactivation of cells B can be potentialized when EBV coinfection occurs, increasing the risk of erroneous recombination of genes. The joint actions of these viruses result in alterations of the somatic hypermutations and classes of immunoglobulins, favoring the appearance and survival of the lymphoma.

In addition, coinfections in any of the charts of the patients investigated with Hodgkin lymphoma were reported. Taylor et al.[13] informed that EBV coinfection would be the main difference of the Hodgkin lymphoma among anti-HIV negative serology and HIV+ individuals, suggesting important differences in the subjacent physiopathological mechanisms.

The multifactorial aspect involved in the process of manifestations of Hodgkin lymphoma in HIV+ individuals, quite often ends up in diagnosis at more advanced and aggressive stages of the disease and intensifies the complexity of the oncologic clinical management of these patients. Therefore, it is paramount to evaluate all the parameters (viral load, CD4+ counts) typically monitored in patients living with HIV, including the antiretrovirals in use for better multi-professional health conduct in cancer treatment[20].

A case report involving a HIV+ patient diagnosed with Hodgkin lymphoma stage IV B treated with ABVD (adriblastina, bleomycin, vinblastine and dacarbazine), without interruption of antiretrovirals (TDF associated with 3TC + RTV-boosted atazanavir), resulted in history of adverse reactions to antineoplastic therapy as neutropenic fever grade 4 and neuropathy grade 2. The professionals involved in the case concluded that the complications occurred in the initial treatment resulting from pharmacokinetic interactions of protease inhibitors over vinblastine and the switch to another class of antiretroviral with minimum effects over the enzyme CYP4A3 would make chemotherapy safer[15].

Therefore, the use of classes of antiretrovirals as non-nucleoside and nucleoside reverse transcriptase inhibitors associated with first line treatment (protocol ABVD) for Hodgkin lymphoma is safer because of lower risk of pharmacokinetic interactions[15].

In the present study, the antiretroviral regimen of one of the patients diagnosed with Hodgkin lymphoma included protease inhibitors RTV-boosted atazanavir. To avoid adverse reactions that may compromise the clinical management of HIV+ patient in use of antiretrovirals during cancer treatment, multi-professional care including clinical pharmacy through anamneses, that is, collection of the pharmacotherapy history and the inter-professional relation of all the players of the oncologic care to the patient are essential.

The study had limitations regarding the access to ambulatory charts of the HIV+ patients. Thus, the trial proceeded based in the admission charts of the patients who during the hospital stay were diagnosed with non-AIDS defining cancer. The lack of data usually filled out in the outpatient consultation of these patients as CD4+ count and viral load, further to the necessity of transference of the patients to oncology specialized centers hampered the collection of some data for this research. However, for the cases of Hodgkin lymphoma found in this study, only one information (first CD4+ and viral load count after the HIV+ diagnosis) was unable to be obtained.

CONCLUSION

Several factors continue to be evaluated while pursuing alternatives for the increased risks of the appearance of cancer in persons living with HIV in use of highly active antiretrovirals.

The data obtained in the present study rank Hodgkin lymphoma in second place among the non-AIDS defining cancers encountered. The variables gender, age and even the subtype of Hodgkin lymphoma presented are similar to the data encountered in international studies, the current main source of the literature.

Regarding the immune condition of patients with Hodgkin lymphoma, although it has been obtained the first CD4+ after the diagnosis of HIV+ in only one of the two patients of the present study, the last count before the diagnosis of cancer allowed to understand that, contrary to the patients diagnosed with skin, rectum, penis and oropharynx cancer, none of the cases of Hodgkin lymphoma went through severe or moderate immunosuppression status, which contradicts one of the required factors to favor malignant cells of this lymphoma.

The same argument applies to the variables viral load and antiretrovirals because the non-adherence to the antiretroviral treatment as indicated in one of the cases of Hodgkin lymphoma can unchain viral resistance and increase the replication of HIV; it can favor the risk of coinfections, in addition to the necessity of switching the antiretroviral with possible negative influence over the extension of life expectancy of these patients and hampers the clinical management of infection and cancer concomitantly because of the risk of increasing the toxicity of the antineoplastic utilized in the first line of treatment of the lymphoma. It is necessary to expand the knowledge of multi-professional care, including pharmacy follow-up due to the great likelihood of polymedication after antineoplastic chemotherapy and possible support medications.

At last, the limitations of the present study do not ensure the conclusion about the actual quantity of cases of Hodgkin lymphoma among non-AIDS defining cancers in HIV+ patients locally, or to estimate the participation of HIV, viral load, immune condition and coinfections as risk factors as already well documented in the international literature. However, they allow to incentive new studies encompassing data obtained from outpatient and specialized centers in oncology and onco-hematology and then permit a better description of the profile not only of the cases of Hodgkin lymphoma, but also of other non-AIDS defining cancers in HIV+ patients.

CONTRIBUTIONS

All the authors contributed for the study conception and/or design, collection, analysis and interpretation of the data, wording, critical review and approved the final version to be published.

ACKNOWLEDGMENTS

To the HSJ SAME team.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

None.

REFERENCES

1. Stanfield CL. Fisiologia Humana. 5ed. São Paulo: Person; 2014. Capítulo 23, Sistema imune; p. 811
2. Clifford GM, Polesel J, Rickenbach M, et al. Cancer risk in the swiss hiv cohort study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. J Natl Cancer Inst. 2005;97(6):425-32. doi: https://doi.org/10.1093/jnci/dji072
3. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde. Boletim epidemiológico HIV AIDS: 2017. Brasília, DF: Ministério da Saúde; 2017.
4. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2018: incidência de câncer no Brasil [Internet]. Rio de Janeiro: INCA; 2017 [acesso 2018 jul 10]. Available from: http://www.epi.uff.br/wp-content/uploads/2013/08/estimativa-incidencia-de-cancer-no-brasil-2018.pdf
5. Atlas on-line de mortalidade [Internet]. Rio de Janeiro: INCA; c1996-2014 [acesso 2018 jul 10]. Availabe from: https://mortalidade.inca.gov.br/MortalidadeWeb/pages/Modelo01/consultar.xhtml;jsessionid=16D87A70D7BB5F0772AB31D83C7DA767#panelResultado
6. Howlader N, Noone AM, Krapcho M, et al. SEER cancer statistics review, 1975-2014 [Internet]. Bethesda: National Cancer Institute; 2017 [cited 2018 Aug 1]. Available from: https://seer.cancer.gov/csr/1975_2014/
7. Arnold M, Sierra MS, Laversanne M, et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-91. doi: http://doi.org/10.1136/gutjnl-2015-310912
8. Canadian Cancer Society. Canadian cancer statistics 2015 special topic: predictions of the future burden of cancer in Canada. Toronto, CA: Canadian Cancer Society; 2015 May.
9. American Cancer Society [Internet]. Atlanta: American Cancer Society; c2021. Non-Hodgkin Lymphoma Risk Factors [revised 2020 June 9; cited 2018 Aug 1]. Available from: https://www.cancer.org/content/cancer/en/cancer/non-hodgkin-lymphoma/causes-risks-prevention/risk-factors/

10. Centers for Disease Control and Prevention (US) [Internet]. Atlanta (GA): Centers for Disease Control and Prevention (US); [date unknown]. Lymphoma [revised 2018 May 29; cited 2018 July 10]. Available from: https://www.cdc.gov/cancer/lymphoma/
11. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2020: incidência de câncer no Brasil. Rio de Janeiro: INCA; 2019.
12. Carroll V, Garzino-Demo A. Hiv-associated lymphoma in the era of combination antiretroviral therapy: shifting the immunological landscape. Pathog Dis. 2015;73(7):ftv044. doi: https://doi.org/10.1093/femspd/ftv044
13. Taylor JG, Liapis K, Gribben JG. The role of the tumor microenvironment in HIV- associated lymphomas. Biomark Med. 2015;9(5):473-82. doi: https://doi.org/10.2217/bmm.15.13
14. Vaccher E, Serraino D, Carbone A, et al. The evolving scenario of non-aids-defining cancers: challenges and opportunities of care. Oncologist. 2014;19(8):860-7. doi: https://doi.org/10.1634/theoncologist.2014-0024
15. Uldrick TS, Little RF. How I treat classical Hodgkin lymphoma in patients infected with human immunodeficiency virus. Blood. 2015;125(8):1226-35. doi: https://doi.org/10.1182/blood-2014-08-551598
16. Cobucci RNO, Lima PH, Souza PC, et al. Assessing the impact of HAART on the incidence of defining and non-defining AIDS cancers among patients with HIV/AIDS: a systematic review. J Infect Public Health. 2014;8(1):1-10. doi: https://doi.org/10.1016/j.jiph.2014.08.003
17. Totonchy J, Cesarman E. Does persistent HIV replication explain continued lymphoma incidence in the era of effective antiretroviral therapy? Curr Opin Virol. 2016;20:71-7. doi: https://doi.org/10.1016/j.coviro.2016.09.001
18. LeMessurier J, Traversy G, Varsaneux O, et al. Risk of sexual transmission of human immunodeficiency virus with antiretroviral therapy, suppressed viral load and condom use: a systematic review. CMAJ. 2018;190(46):E1350-E60. doi: https://doi.org/10.1503/cmaj.180311
19. Freitas JB, Gagliani LH, Caseiro MM, et al. Perfil epidemiológico dos pacientes infectados pelo HIV com e sem câncer em um hospital público na Baixada Santista - SP - Brasil. Rev. UNILUS Ensino Pesqui. 2017;14(34):17-24.
20. Bachanova V, Connors JM. Hodgkin lymphoma in the elderly, pregnant, and hiv-infected. Semin Hematol. 2016;53(3):203-8. doi: https://doi.org/10.1053/j.seminhematol.2016.05.002

Recebido em 31/7/2020
Aprovado em 23/11/2020