Clinical and laboratory characteristics, staging, and outcomes of individuals with AIDS-associated Kaposi’s sarcoma at an university hospital

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Abstract: BACKGROUND: Kaposi’s sarcoma continues to be the most common human immunodeficiency virus - associated neoplasm with considerable morbidity and mortality.

OBJECTIVE: To describe the clinical and laboratory characteristics, initial staging, and outcomes of aids patients with Kaposi’s sarcoma at an university hospital of Recife, Pernambuco.

METHODS: This is a descriptive study with analytic character, retrospective, of a case series between 2004 and 2014.

RESULTS: Of the 22 patients included in the study, 20 were aged <40 years (72.7%). The majority had CD4+ T lymphocyte counts of <200 cells/mm³ (77.3%) and human immunodeficiency virus loads of <100,000 copies/mL (78.9%). Lesions were most commonly observed on the skin (90%), and internal organs were affected in 11 of the 22 patients. Only 7 (31.8%) of the 22 patients were undergoing antiretroviral therapy (ART) at the time of Kaposis sarcoma diagnosis, and the initial disease staging classification was high risk (Aids Clinical Trials Group Oncology Committee) in 19 of the 22 patients (86.4%). Regarding Kaposi’s sarcoma treatment, 17 of 22 patients (77.3%) underwent systemic chemotherapy + ART and 5 were treated exclusively with ART. Eight of the 22 patients died (36.5%); of these, 87.5% had died within one year of Kaposi’s sarcoma diagnosis.

LIMITATION OF THE STUDY: Without a control group, this study cannot be used to generate hypotheses.

CONCLUSIONS: Despite the association between aids and late Kaposi’s sarcoma diagnosis in the study population, including an unfavorable risk at the time of staging, a lower mortality rate was observed relative to other studies; this might be related to access to a specialized health service.

Keywords: Acquired immunodeficiency syndrome; HIV; Neoplasms; Sarcoma, Kaposi

INTRODUCTION

AIDS-associated Kaposi’s sarcoma (KS) remains a serious public health problem in emerging countries, with a high mortality rate, even in patients presenting the cutaneous form of the disease.¹ Before the advent of antiretroviral therapy (ART), KS was 20,000 times more common in AIDS patients than in the general population.² Currently, the incidence of KS has decreased dramatically in the United States and Europe. However, it remains the second most frequent tumor in patients infected with the human immunodeficiency virus (HIV) in the world, being the most common cancer in sub-Saharan Africa.³⁴

The World Health Organization (WHO) estimated that about 5 million people infected with HIV would be receiving ART in sub-Saharan Africa by the end of 2010, with an estimated coverage rate of 56% of patients.⁵ ART has been used successfully in the treatment of KS in the earliest stages, thus reducing the mortality of this neoplasia.

In Brazil, some researchers published data about the clinical-epidemiological characteristics, as well as the geopolitical distribution of KS in the different regions of the country, however, we did not observe, in these studies, the inclusion of the clinical follow-up of the patients.⁶ Therefore, this study intends to fill these gaps, reporting the clinical-laboratory characteristics, initial staging according to the AIDS Clinical Trials Group Oncology Committee (ACTG) and what the clinical outcome of these patients.
METHODS

A retrospective, descriptive study with an analytical character, case series, conducted between 2004 and 2014, at the Hospital das Clínicas de Recife-Pernambuco, which attends patients in the public healthcare system - Sistema Único de Saúde (SUS).

Patients aged 18 years or older with AIDS and histopathological examination demonstrating Kaposi’s sarcoma were included. The study was approved by the Research Ethics Committee of the University Health Sciences Center.

A specific form was used, containing the following variables: age, sex, T-CD4+ cell count, viral load, lesion classification, most affected organs, ART use, presence of B symptoms, opportunistic infection, treatment with exclusive ART or chemotherapy + ART, which chemotherapy medications were used and the clinical outcome.

Patients included in the study were organized into two groups during the classification of staging by ACTG. The first was by individuals who were already using ART at the time of diagnosis of Kaposi’s sarcoma and the second by patients with a recent diagnosis of HIV infection who had not yet started ART or by those who dropped out treatment.

The description of the characteristics of the study population was presented by frequency distribution. In the analysis of the associations regarding the use of ART, the variables were tested by Fisher’s exact test. The significance of the test was 5% (p <0.05). The software used in the analysis was STATA, version 12.0.

RESULTS

Twenty-two patients were included in the study, 20 (90.9%) of them were men and the majority aged <40 years (72.7%). In 77.3% (17) of the investigated cases, the T-CD4+ cell count was below 200 cells/mm³, noting that nine patients had a diagnosis of AIDS concomitant with the diagnosis of KS, as well as HIV viral load <100,000 copies/mL was present in 78.9% (15) of the patients, whereas only one case had an undetectable viral load (Table 1).

In 90.0% (20/22) of the cases, KS lesions involved the skin, and in addition to these cutaneous lesions, half of the patients (11) had organ involvement. Only one case (4.5%) presented minimal oral lesion, and in four cases (18.18%) patients had extensive oral lesions, some of them vegetative. The organs most affected were the stomach and intestines. Previous opportunistic infections were identified in seven cases and, at the time of diagnosis, in 16 cases (72.7%), and orospongial candidiasis more frequent both at the time of diagnosis and in the diagnosis. Of the nine patients who had a diagnosis of AIDS concomitant to the diagnosis of KS, eight also had an opportunistic infection. In 77.3% of the cases, B symptoms were found, and only seven patients used ART at the time of KS diagnosis (Table 2).

Regarding Kaposi’s sarcoma treatment, 17 (77.3%) of the 22 patients underwent chemotherapy + ART, and the remaining five, exclusive ART. There was no record of irradiation, intralesional or surgery treatment. Liposomal doxorubicin and bleomycin-vincristine (BV) were the most commonly used medications, with a case of adriamycin-bleomycin-vincristine (ABV) and paclitaxel; in two patient records, no information regarding medications was found (Table 3).

Of the 22 patients studied, 19 (86.4%) had initial staging of the high-risk disease, of which, 71.4% were using ART, and 93.3%
were not. There was no significant association between the initial staging and the use of ART (Table 4).

Regarding the outcome of Kaposi’s sarcoma after treatment with chemotherapy + ART or exclusive ART, 40.9% (9/22) of patients had complete remission, and in one case the remission was partial. One case presented stable disease; in two cases, the disease progressed; and in one case, there was healing after five years. Among the researched cases, eight died (36.5%), seven in the first year of treatment and one death after the first year. Associating the outcome of the case with the use of ART, there was no statistical significance, in which it was observed that the distribution of outcomes was similar between patients with and without ART use (Table 4).

DISCUSSION

KS is a multifocal malignant neoplasm resulting from the abnormal proliferation of the vascular endothelium, which occurs mainly in individuals with immune deficiency, and this cancer is most commonly associated with AIDS. Since its initial description by the Hungarian dermatologist Moritz Kaposi, remains a clinical and therapeutic challenge. After the introduction of ART in the mid-1990s, there was a significant decline of this neoplasia in developed countries, a fact not observed in the emerging countries where KS remains with high incidence and high mortality rate. In a study published by Saraceni et al. in 2013, the prevalence of KS decreased after the introduction of ART in all regions of Brazil, suggesting an individual protection of the antiretroviral medication.

Regarding the demographic characteristics, a predominance of the male population was observed, a result similar to other studies. This is probably due to the high frequency of human herpes virus type 8 (HHV 8) infection, also called KS-associated herpes virus (KSHV) in men who have sex with men (MSM), a group predominantly affected by HIV infection in Brazil and in the state of Pernambuco. Mean age was 33 years, with 32% of the patients being under 25 years of age. This finding may be partly explained by the shift in the diagnosis of HIV/AIDS infection to younger age groups, particularly in Northeast Brazil. Recent data from the Ministry of Health show that most new HIV infections occur in men who have sex with men (MSM) under the age of 25 years.

More than half of the patients had a T-CD4+ cell count below 200 cells/mm³, in agreement with most studies found where the mean T-CD4+ cell count was below 200 cells/mm³. In a retrospective comparative analysis conducted at the Evandro Chagas National Institute of Infectious Diseases in Rio de Janeiro and at the Comprehensive Care Center for HIV/AIDS patients in Nashville, it was shown that immunosuppression was associated with an increased risk of developing neoplasias defining AIDS.

This fact signs for late diagnosis of HIV infection, often only when there are opportunistic infections or neoplasms such as KS. Most of the research subjects did not use ART at the time of KS diagnosis, demonstrating that, despite the educational campaigns and universal availability of ART, those most vulnerable to infection still delay its diagnosis and treatment.

In the present study, the cutaneous lesions were predominant in the individuals, being the disseminated form the most observed, and when there was involvement of deep organs, the stomach was the most affected. Similar results were described by Rezende et al. in a retrospective study with patients presenting KS in stomach, of which 80% had concomitant skin lesions. On the other hand, in a survey conducted in the city of Rio de Janeiro/Brazil by Corriça & Caldas, the involvement of skin and organs was lower, reaching around 54.8%.

Although the presence of KS in the oral cavity is particularly common and may be the initial symptom of the disease, these findings were only observed in five of the 22 patients, reinforcing that the cutaneous manifestations represented the most common presentation form of the neoplasia. Many of these patients with characteristic skin lesions reported care by a non-dermatologist physician months before the definitive diagnosis of the disease, and that they did not recognize KS. An unusual finding observed was exclusive visceral involvement without skin or palate lesions in two patients, corroborating findings reported in the literature. In such cases, the diagnosis of KS can be difficult due to systemic manifestations and may lead to confusion with other diseases, especially in the scenario of a compromised immune system.

Because a large number of individuals had T-CD4+ cells <200 cells/mm³, some opportunistic infections were observed at the time of KS diagnosis. Oroesophageal candidiasis was the most diagnosed opportunistic infection in this group of individuals, fol-
lowed by pulmonary and extrapulmonary tuberculosis. Similar results were demonstrated by Keller et al. in a multicenter study in which it was shown that the most frequent opportunistic infections in patients with KS were oroesophageal candidiasis followed by pulmonary and extrapulmonary tuberculosis.20 These findings point to the late diagnosis of HIV infection, and to the fact still not explained that these patients present a higher risk of tuberculosis than the general population.

In the literature, ART use has been associated with a substantial decline in the incidence of KS among AIDS patients.27-29 This can be explained both by the direct action of ART on KSHV as well as by the suspension of the progression of HIV infection and, consequently, the immunodeficiency that predisposes KS. In case series, few patients used ART at the time of KS diagnosis, similar to the data found by Saraceni et al., in which 57% of KS cases were diagnosed before the individual started antiretroviral treatment.12 Among individuals not using ART, many presented old - but newly diagnosed - HIV infections. De Boer et al., in a survey conducted in South Africa with 161 patients, describes the relation of delayed diagnosis of HIV and the presence of advanced KS.31

Regarding KS treatment, most (17/22) subjects underwent treatment with ART associated with chemotherapy, while only five were treated exclusively with ART. The subjects had their treatment conducted in a university hospital in one of the poorest regions of Brazil, where, despite the limitations, almost half of the individuals (46.6%) were treated with liposomal doxorubicin, and the other part was treated with combined regimen of BV (bleomycin-vincristine) or ABV (adriamycin-bleomycin-vincristine). When the combined regimen chosen was BV over ABV, the choice was made because many patients had KS at later stages of the disease, with low immunity, presence of opportunistic diseases, and a Karnovsky Performance Status <70.

In this study, despite the late diagnosis of KS associated with AIDS in the studied population, including unfavorable risk at the time of staging, a lower mortality rate (36.5%) was found than that reported by Chu et al. in a study conducted in South Africa, where the mortality rate was 70/100 person years (95% CI 42-117).10 This relative low lethality can be explained, in part, by the fact that these patients attend specialized health services.

CONCLUSION

The findings of the present study allow a better clinical-epidemiological understanding of the clinical staging and outcome of KS cases associated with AIDS in our region. The research points to a population of men who have sex with men, young, with an advanced state of immunodepression, reflected in the prevalence of disseminated lesions and opportunistic infections associated with KS. It is important to note that the fact that the study was conducted in a university hospital may have directed a sample of more serious cases and that, despite this fact, the availability of chemotherapy with first-line drugs may have influenced a lower mortality than that reported in the literature, even though there is a delay in the diagnosis and treatment of KS.

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