Kaposi’s sarcoma, syphilis and neurocryptococcosis in an HIV-positive patient

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ABSTRACT

Human immunodeficiency virus (HIV) infection has become a worldwide public health problem in recent decades. The main characteristic of HIV is the suppression of the immune system by attacking CD4+ T lymphocytes, which weakens the immune system and makes the individual susceptible to opportunistic infections, secondary neoplasms, and neurological diseases. This study aims to report and discuss the case of an HIV-positive patient who presented concomitantly Kaposi’s Sarcoma (KS), primary syphilis, and neurocryptococcosis, all HIV-related. This is a 31-year-old male patient who sought care at the reference hospital with violaceous skin lesions on the face, upper limbs and chest, with a three-month evolution. Dermatological examination showed infiltrative erythematous-violet plaques, with regular, elevated, scaly edges and varying diameters. He obtained positive serology for anti-HIV and VDRL antibodies, initiating antiretroviral therapy (ART) and treatment protocols for primary syphilis. The patient returned to the service 30 days after hospital discharge, complaining of severe headache, refractory to analgesia with opioids, associated with persistent vomiting. Cranial computed tomography was performed and did not demonstrate alterations; later CSF puncture showed the presence of cryptococcus. A therapeutic scheme for neurocryptococcosis was started, and two other CSF punctures were performed to relieve the pain. This report agrees with the medical literature, reaffirming that HIV-positive patients present a greater predisposition to conditions such as KS, syphilis, and neurocryptococcosis. Thus, the study illustrates with uniqueness the simultaneous occurrence of complex clinical manifestations in the same immunosuppressed patient.

Keywords: Opportunistic infections, Sarcoma Kaposi, Cryptococcosis, Acquired Immunodeficiency Syndrome, HIV.

INTRODUCTION

Human immunodeficiency virus (HIV) infection has become a global public health problem in recent decades. It is estimated that by the end of 2019, 38 million people worldwide were living with HIV, and among them, approximately 7.1 million were unaware of their infection¹. The main characteristic of HIV is the suppression of the immune system due to the attack on CD4+ T lymphocytes, which weakens immunity and makes the individual susceptible to opportunistic infections, secondary neoplasms, and neurological diseases².

Acquired syphilis (AS), a sexually transmitted infection (STI) prevalent in HIV-positive patients, caused by the spirochete Treponema pallidum, leads to clinical manifestations such as genital ulcers, skin lesions, fever, meningitis, neurological syndromes, and others, in the three clinical stages if not adequately treated. Although syphilis does not have defining characteristics that determine the advanced stage of HIV infection, such as opportunistic diseases and secondary neoplasms, the presence of ulcerative lesions caused by syphilis increases the risk of HIV co-infection by approximately 18 times³. This correlation is reinforced by risky sexual behaviors that expose the sexually active population to STIs, as well as the increase in syphilis cases in Brazil over the past five years⁴,⁵.

In addition to the aforementioned co-infection issue, this study highlights Kaposi’s Sarcoma (KS) among the opportunistic diseases secondary to HIV. KS, first described in 1872 by Moritz Kaposi as an angioproliferative tumor in elderly men, is the most common neoplasm associated with Acquired Immunodeficiency Syndrome (AIDS). Therefore, it is one of the main indicators for suspecting the disease. KS has been stigmatized among HIV-positive patients due to its characteristic visible cutaneous manifestation. While most cases have a benign
course with a good response to various treatments, severe cases can lead to complications.

Among the opportunistic diseases, HIV also predisposes the individual to cryptococcosis, a systemic mycosis caused by two etiological agents: Cryptococcus gattii and Cryptococcus neoformans. The latter is responsible for the majority of cases with meningoencephalic presentation, affecting nearly all immunosuppressed patients. It is estimated that neurocryptococcosis has an annual incidence of 223,000 cases and 180,000 deaths among individuals infected with the human immunodeficiency virus, with most of these cases occurring in the African continent.

The most severe clinical presentation, also discussed in this study, affects the central nervous system. Transmission usually occurs through inhalation of infected propagules or spores found in the feces of pigeons of the Columba livia species. Subsequently, they reach the lungs and then spread to the central nervous system (CNS). This form is considered the most dangerous due to its neurological repercussions, often accompanied by intracranial hypertension. If left untreated, it can lead to complications such as amaurosis.

Therefore, this review aims to highlight, through a case report, the unprecedented occurrence of these aforementioned pathologies infecting the same individual, causing synergistic and conflicting repercussions. The project was approved by the Ethics and Research Committee of Univás (Opinion number 4,845,542) and the participant signed the Free and Informed Consent Form authorizing their participation and the future use of the data generated.

CASE REPORT

WCG, male, 31 years old, physical educator, without previous comorbidities, born in a city in the south of Minas Gerais (MG), currently resident in the state of Rio de Janeiro (RJ), phenotype III according to the Fitzpatrick Classification.

He presented violaceous skin lesions on his face, upper limbs, and posterior thorax, with three months of evolution. He sought medical care in the city of origin, where serology tests revealed positive antibodies for HIV and a positive rapid test for syphilis. He then returned to MG to initiate antiretroviral therapy (ART) and was hospitalized for further investigation and evaluation by the Oncology team.

The patient had the necessary medications, as he had been in consultation at an Infectology outpatient clinic before returning to MG, but had not started it. During hospitalization, a VDRL test was performed, resulting in a positive titer of 1:32. As he had not yet been treated for syphilis, he received two doses of Benzathine Penicillin, 2,400,000 units each. For further investigation, the following tests were requested: bronchoscopy, upper digestive endoscopy (UGE), biopsy of skin lesions, and computed tomography (CT). The head CT showed subcutaneous nodules, the chest CT revealed mediastinal lymphadenopathy and focal consolidations in the right and left regions, as well as subpleural micronodules. The abdominal CT indicated lymph node enlargement in the pelvic, mesenteric, and retroperitoneal regions. Serological tests were also performed to screen for other potential opportunistic infections, including cytomegalovirus, toxoplasmosis, hepatitis B and C, and sputum bacteriology to detect Koch’s bacillus. All these serologies yielded negative results, and no Koch’s bacillus was found. Lymphocyte count and viral load were monitored to assess immune function, with the following results: CD3: 1176 cells/mm³ (718-2494), CD4: 43 cells/mm³ (456-1492), CD8: 1064 cells/mm³ (272-1144), and viral load: 1320 copies/mm³.

Dermatological examination revealed erythematous violaceous infiltrative plaques with regular, raised, scaly, non-pruritic edges and variable diameters. The most prominent lesion was located on the nasal region of the face (Figure 1), and another smaller lesion was observed on the upper part of the posterior chest (Figure 2). The anatomopathological and immunohistochemical exams showed moderate capillary proliferation of the superficial and reticular dermis, branching, and cytological atypia in endothelial cells associated with chronic inflammatory infiltrate and hemosiderin deposits. Macroscopically, the findings are characteristic of dermal KS, plaque stage. Following evaluation by the Oncology team and investigation of the KS progression, the patient was discharged.
However, he returned to the hospital 30 days later, complaining of a severe unresponsive headache to opioid analgesics. He also had persistent vomiting but no fever. Cranial CT was performed at the time, and it showed no abnormalities compared to the previous scan performed on the first hospitalization. It was opted to perform a cerebrospinal fluid puncture (CSF). A China ink test on the CSF sample revealed the presence of cryptococcus. The patient was started on Amphotericin B at a daily dose of 40 mg, with a target dose of 800 mg. Due to ongoing severe headache despite analgesic treatment, two additional CSF punctures were performed to alleviate the pain. Symptoms started improving. After reaching the target dose, a search for cryptococcus using China ink in the CSF sample yielded negative results. Consequently, the patient was discharged. He is currently undergoing outpatient follow-up at the Oncology service and the STD-AIDS clinic in the municipality.

**DISCUSSION**

Briefly, due to the natural history of the disease, in the first weeks, the virus infects the CD4+ T lymphocytes in the lymphoid tissues, spreads throughout the body, and there is the development of the host’s immune response specific to HIV. Even in a state of stable viremia, the period is silent until around the first to third weeks, when some non-specific clinical manifestations, such as fever, headache, and pharyngitis, illustrate the acute retroviral syndrome (RAS). It is self-limited and very similar to other viral infections, comprising the acute phase of the disease. In untreated patients, it is estimated that ten years is the average time between infection and the onset of the disease. Chronic infection encompasses the clinical latency phase and the symptomatic phase, which have repercussions due to the actions of HIV. During this time, HIV kills a significant number of mucosal CD4+ T lymphocytes, leading to manifestations such as mild leukopenia, frequent bacterial infections, low fever, fatigue, oral lesions, and enteropathies. These manifestations result in diarrhea, increased gastrointestinal permeability, inflammation, and malabsorption. Without proper treatment, this
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syndrome weakens the patient and may lead to
a progressive condition characterized by weight
loss, anemia, dehydration, malnutrition, and oth-
er manifestations. This scenario increases the
risk of several opportunistic infections, espe-
ially cryptococcosis, and secondary neoplasms like
KS and neurological diseases. The manifestation
of opportunistic infections and neoplasms is de-
cisive and defines the last phase of the disease: 
acquired immunodeficiency syndrome (AIDS)¹³.

It is worth noting that, although there is no
cure for HIV infection, drug treatment with an-
tiretrovirals prevents the multiplication of the vi-
rus in the body, avoiding damage to the immune
system and, consequently, increasing the lifespan
and quality of life of infected individuals. This drug
treatment has been free of charge by the Unified
Health System (SUS) since 1996 and is part of
the therapeutic itinerary along with other behav-
ioral and structural interventions, such as access
to information, counseling, adherence support,
and follow-up with a multidisciplinary team¹².

KS originates from endothelial and immune
cells infected with human herpesvirus type 8
(HHV-8), also known as Kaposi’s sarcoma-associ-
ated herpesvirus (KSHV). The condition is divided
into four types: epidemic (associated with AIDS),
iatrogenic, classic, and endemic, with HHV-8
being the common causative agent, present in
more than 95% of all cases. The clinical course
of each form is different; therefore, it is believed
that there is an influence of other factors, such
as the extent of immunosuppression. HIV-asso-
ciated KS has worse evolution compared to oth-
er types because the infection leads to increased
HHV-8 replication. Presentation is less aggressive
in patients already receiving highly active anti-
teroviral therapy (HAART). It usually has a variable
clinical course, ranging from indolent mucocuta-
aneous lesions to extensive visceral involvement¹³.

The multicentric nature of the tumor con-
tributes to the fact that KS cutaneous lesions can
occur simultaneously in any region of the body,
although they are generally concentrated in the
lower extremities and the head and neck region.
They are pigmented, painless, palpable, and non-
itchy. They may appear pink and red initially, and
with the progression of the disease, they can
turn violet and brown, evolving from a macular
appearance to plaques that can further develop
into larger nodules (tumor lesions) and vary in
size from millimeters to centimeters in diameter.
Tumors can also involve lymph nodes and visceral
organs, such as the gastrointestinal and respira-
tory tracts. Differential diagnoses for KS include
cutaneous lymphoma, bacillary angiomatosis,
pyogenic granuloma, aneurysmal fibrous histiocy-
toma, and acroangiodermatitis, among others¹⁴,¹⁵.

The report also studied the presence of neu-
cryptococcosis, a common opportunistic fungal
infection in patients with AIDS. Neurocryptococ-
cosis is caused by the fungi Cryptococcus neoformans
or Cryptococcus gattii, with meningitis and menin-
goencephalitis being the most common manifesta-
tions². The patient experienced an atypical head-
ache that was unresponsive to medications due to
the neurotropism of the fungus in the body. Addi-
tionally, fever may present from the early stages
of the infection and worsen when lying down. Oth-
er typical manifestations include intracranial hy-
pertension, nausea, vomiting, blurred vision, and
drowsiness. While there have been reports of co-
existence between KS and infections such as cryp-
tococcosis in HIV-infected patients, the incidence
of such cases has decreased in developed coun-
tries since the introduction of ART. Cryptococcal
disease usually develops when the CD4+ lympho-
cyte count drops below 100 cells/µL¹⁶.

Co-infection between syphilis and HIV has
great clinical relevance, given its increasing inci-
dence and the synergy between these two sexually
transmitted infections¹⁷. This phenomenon can be
attributed to the fact that HIV accelerates the nat-
ural progression of syphilis by altering components
of the infected individual’s immune system. In ad-
dition, syphilis facilitates the transmission and ac-
quisition of HIV, as demonstrated in several studies
where infection with Treponema pallidum nearly tri-
pled the risk of acquiring HIV. This correlation can
be explained by the syphilitic ulcers in the genitalia,
which significantly increases the transmission and
acquisition rates of HIV due to the compromised
protective epithelial barrier. Moreover, the ulcer site
is rich in macrophages and activated lymphocytes,
creating an immune microenvironment with highly
expressed receptors for HIV¹⁸.

Since the literature is quite clear about the
relationship between HIV and syphilis, we know
that both STIs can often occur associated with co-infection situations. According to studies, there is a predominance of 9.5% of cases of syphilis in patients with HIV. In contrast, patients infected with *Treponema pallidum* are between 2 and 9 times more likely to be contaminated with HIV, mainly due to the lesions in the mucous membranes and epithelial damage caused by syphilis, illustrating the opportunistic characteristic of this disease. This can be explained because HIV accelerates the natural history of syphilis by modifying elements of the infected individual's immune system. Furthermore, the injury site is rich in activated macrophages and lymphocytes, which serves as an immuno-microenvironment for highly expressed HIV receptors18,19.

As indicated in the literature, the patient under discussion presents the proven co-infection simultaneously in his pathological history. Despite the early diagnosis and rapid intervention of the case, the correlation between the STIs may lead to a temporary condition of increased HIV viral load and a decrease in the CD4 T cell count - mainly in secondary syphilis -, opening up room for a greater probability of developing neurosyphilis18,19.

Additionally, the diagnosis and, consequently, the therapeutic management of these STIs is impaired due to HIV infection falsifying serology for syphilis and modifying its classic manifestations, making it difficult to differentiate its stages, creating challenges in decision-making. There are also obstacles in controlling the “cure” of syphilis in people co-infected with HIV, as it alters parameters to guide successful treatment20,21.

No similar reports were found regarding the occurrence of the three pathologies in the context of immunosuppression in the main databases of the medical literature, evidencing the originality of the presented case. Thus, it reinforces the importance of thoroughly investigating all possible pathologies and clinical manifestations in immunosuppressed patients. It also recommends adopting a therapeutic approach based on scientific evidence to enable early detection of patients and implement measures that enhance their quality of life.

Finally, discussing this case emphasizes and illustrates the variety of each clinical manifestations and their correlations, as presumed by the medical literature. It reaffirms that patients who test positive for HIV have a more significant predisposition for manifestations such as Kaposi’s sarcoma and/or neurocryptococcosis.

**REFERENCES**


A case report entitled Kaposi’s sarcoma, syphilis, and neurocryptococcosis in an HIV-positive patient for publication in Revista Medicina (Ribeirão Preto). An original article, which has not been previously published and is not currently under consideration for publication in another journal. The work must be attributed to the institution Irmandade do Hospital da Santa Casa de Poços de Caldas, Department of Internal Medicine. The financing was own, that is, there was no source of support for the research.

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1. Collection of clinical history;
2. Substantial contribution to the study design;
3. Analysis and interpretation of data, laboratory and imaging tests;
4. Organization of collected data;
5. Research on topics in the medical literature;
6. Writing of the preliminary version;
7. Preparation of the introduction, case report and discussion;
8. Resume writing;
9. Final revision;
10. Standardization in the norms according to the magazines;
11. Compliance with being responsible for the integrity of any part of the study.

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