Kaposi sarcoma in the lower limbs: case report

Sarcoma de Kaposi em membros inferiores: relato de caso

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Abstract

The Kaposi sarcoma is an angio-proliferative malignant neoplasm that mostly affects the skin and subcutaneous tissue, although it can present in a more aggressive form, involving the oral cavity, lungs and gastrointestinal tract (visceral Kaposi sarcoma). It is classified into 4 clinical-epidemiological types: classic, endemic, iatrogenic and epidemic, all of them associated with the human herpes virus 8. We report a rare case of Kaposi sarcoma in an elderly immunodepressed female patient, not related to the acquired immunodeficiency syndrome, that evolved fatally in five months, since the appearance of hematic necrotic bullous lesions which progressed with intense local exudation, dehydration, renal insufficiency and worsening of the clinical status, ending in death, caused by multiple organ failure.

Keywords: Sarcoma, Kaposi; herpesvirus 8 human; neoplasms.

Resumo

O sarcoma de Kaposi é uma neoplasia angioproliferativa maligna que na maioria das vezes se restringe à pele e ao tecido subcutâneo; porém, pode aparecer de forma mais agressiva, atingindo a cavidade oral, o trato gastrointestinal e os pulmões (sarcoma de Kaposi visceral). É classificado com quatro variantes clínco-epidemiológicas: clássica, endêmica, iatrogênica e epidêmica, todas associadas ao herpes vírus humano tipo 8. O objetivo desta publicação foi relatar um caso raro de sarcoma de Kaposi em paciente idosa imunossuprimida, não relacionado à síndrome da imunodeficiência adquirida, que evoluiu de forma desfavorável em um período de cinco meses a partir do aparecimento de lesões bolhosas hemáticas e necróticas que, posteriormente, progrediram com intensa exsudação local, desidratação, insuficiência renal e piora do estado geral, evoluindo então a óbito, tendo como causa mortis a falência de múltiplos órgãos.

Palavras-chave: Sarcoma de Kaposi; herpesvirus humano 8; neoplasias.

Introduction

Kaposi Sarcoma (KS) was first described in 1872 by Moritz Kaposi as an “idiopathic multiple pigmented sarcoma”. It is a malignant multicenter angio-proliferative neoplasm characterized macroscopically by the development of wine-colored, frequently elevated, tumors. Such tumors are often restricted to the skin and subcutaneous tissues, but visceral dissemination may occur as well. Microscopic analysis shows endothelium-lined channels and vascular portions associated with aggregations of fusiform cells of different sizes.

There are four known clinical-epidemiological tumor types with the same histological characteristics that seem to be associated with type 8 human herpes virus (HHV8) infection, according to the criteria by Stebbing et al. (2003), which classifies clinical manifestations as to their presentation1,2:

3. Iatrogenic/immunosuppression: frequent in patients who suffered transplantation or who are using immunosuppressive drugs.

4. Epidemic/associated with human immunodeficiency virus (HIV): more frequent in homosexual and bisexual young male adults.

Lesions are mediated by inflammatory cytokines and angiogenic factors that are unleashed or amplified by the HHV8 infection, referred to as Kaposi sarcoma-associated herpes virus (KSHV). Its genome codifies proteins involved in cell proliferation, antiapoptotic functions and inflammation.

When associated with HIV, it is more aggressive and presents as the first symptom of the acquired immune deficiency syndrome (AIDS).

**Objective**

To present a rare case of Kaposi Sarcoma not related to AIDS in an immunosuppressed patient, and to briefly review the literature.

**Case description**

Case of an 88-year-old female patient, Brazilian, of Portuguese descent, with Alzheimer disease and chronic lymphocytic leukemia (CLL). In February 2007 she was admitted to the emergency of Hospital e Maternidade São Luiz (HMSL) with thrombocytopenia and gastrointestinal bleeding. The diagnosis of CLL was confirmed by bone marrow biopsy.

In July 2007 she was readmitted to HMSL Emergency Room with left femoropopliteal deep venous thrombosis (DVT), which was diagnosed by color Doppler ultrasound. She was treated with low-molecular-weight heparin (LMWH) for six days and oral anticoagulation (warfarin) for three months. Then, she developed severe bullous lesions with hematic content on the lower limbs, mainly on legs and feet. She was then admitted to the Intensive Care Unit (ICU) and had satisfactory outcome. After hospital discharge, she repeatedly presented disseminated petechiae on the lower and upper limbs and needed transfusion of platelets, which controlled the hemorrhagic complications. Oral anticoagulants were interrupted and the patient was referred for treatment of the bullous lesions.

In October and November 2007, she had two episodes of erysipelas on the lower limbs and was hospitalized for treatment with crystalline penicillin (30,000,000 U/day) for seven days and debridement of the necrotic and hematic bullous lesions. (Figures 1 and 2). After the operation, warfarin 5 mg/day was prescribed and controlled by coagulogram, with the International Normalized Ratio (INR) maintained between 2.0 and 3.0.

The material collected at surgery was sent to anatomicopathological examination, which indicated ulcerated Kaposi Sarcoma in nodular stage. The material was friable, constituted by hemorrhagic tissue. Histological evaluation demonstrated aggregation of fusiform cells, angiogenesis, endothelium-lined channels, fibrin and hemorrhagic areas (Figure 3). Serology was negative for HIV, but positive for HHV8.

Figure 1 – Preoperative aspect of the lesions

Figure 2 – Preoperative aspect of the lesions
The patient was discharged in November 2007 and referred to radiotherapy for local control of the disease. About one month after hospital discharge, she had recurrent skin and subcutaneous tissue necrosis in the malleolar regions with intense local exudation. Her clinical status worsened and she developed severe dehydration and prerenal acute renal failure (ARF). The patient died of multiple organ failure on December 25, 2007.

Discussion

The etiology of Ks can be attributed to several factors, such as endothelial growth factor, oncogenic expression and genetic predisposition associated with possible environmental cofactors\(^6\); however, its etiology remains unclear. Studies point to the existence of a transmission agent as the cause of KS that may or may not be related to HIV infection\(^5\).

According to Friedman-Kein et al.\(^4\), KS used to be known as a very rare disease that became epidemic among male homosexuals, for they are more prone to conditions that facilitate HIV transmission, as well as to the KS agent. HIV-induced immunosuppression in carriers of the etiologic agent enables the development of KS and may be the first manifestation of AIDS.

The incidence is higher in patients of extreme age groups and it is probably related to low immunity. It is, however; less frequent in HIV-positive children, unlike the endemic form (Sub-equatorial African type). Men are more affected than women, in a proportion of 15:1\(^7,9\). The annual incidence is 0.02 to 0.06% of all malignant tumors\(^7\). KS rarely affects American or European heterosexuals, but heterosexuals from Africa or the Caribbean are frequently affected\(^10\).

Sexual transmission of HHV8 is predominant in developed countries and is mainly related to anal coitus and the high number of sexual partners. Infection may also occur during labor or by placental transmission in endemic areas. However, cases in children and adolescents have been reported in these countries, which suggests ways of transmission other than sexual. There is no consensus about the etiology and mode of virus transmission, however KS-related herpes virus has frequently been found in saliva and semen of infected patients\(^11,12\).

KS starts in a context of immune deregulation characterized by CD8+ T cell activation and production of cytokines stimulated by Th1 cells, which induce activation of endothelial cells. These cells cause adhesion and extravasation of lymphomonocytes, production of fusiform cells and angiogenesis. This phenomenon is unleashed or intensified by HHV8 infection, which is reactivated by these very cytokines\(^5\).

HHV8 dissemination is favored by immune deregulation and evasion by the viral agent, which makes it hard to effectively eliminate the virus, but paradoxically, exacerbates the reaction process. The circulating cells infected by the virus are then recruited to the tissues, where the KS lesions are triggered\(^5\).

Safai et al. evaluated patients with AIDS-related KS without opportunistic infections and observed a 28-month survival after diagnosis in 80% of them, while in patients with opportunistic infection this period of time dropped to approximately six months\(^13\). The tumor may remain stable, without any significant repercussions or progress,
which occurs in nearly half of the patients who develop cutaneous and visceral involvement.

In the case described, death ensued five months after the first lesions appeared in the lower limbs, even though she had neither HIV and its opportunistic infections, nor visceral involvement, which indicates high severity of the illness. Therefore, this was an atypical manifestation of KS.

Differential diagnosis must be done with cutaneous lymphoma, hemosiderotic hemangioma, benign lymphangioendothelioma (BLAE), cutaneous angiosarcoma, fusiform cell hemangioendothelioma and angiolipoma. Heparin- and warfarin-induced cutaneous lesions (rare complications related to these anticoagulants) are also included in the differential diagnosis of this patient, because she was given anticoagulant therapy to treat DVT.

In this case report, we emphasized the atypical circumstances of KS development. The patient, a Portuguese-desendant Brazilian, did not fit into any of the four clinical and epidemiological classifications of the disease. In terms of geography, the classic KS is predominant among men of the Mediterranean, Eastern European and North American lineages, while the endemic KS is frequent among Africans, especially young men and children. Epidemic KS is directly related to HIV patients, mainly homosexual young males. The patient of our case was elderly and HIV-negative.

Iatrogenic KS and immunosuppression occur more frequently in patients who have been transplanted (kidney mainly) or those receiving immunosuppressive therapy.

The only association between CLL and KS besides immunosuppression is the presence of HLA-DR5 major histocompatibility complex, described as possibly associated with KS in rare cases. Nevertheless, this is a hypothesis that needs to be studied and confirmed.

Conclusion

The high incidence in immunosuppressed patients reinforces the need for early recognition of KS in the differential diagnosis of cutaneous lesions. The diagnosis of KS in HIV-negative patients is a challenge due to its low incidence and prevalence. In some patients, warfarin- and heparin-induced cutaneous lesions must be considered in the differential diagnosis.

References

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