CASE REPORT

Fatal outcome in classic Kaposi's sarcoma

Sarcoma de Kaposi clássico fatal

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Abstract: First described in 1872, Kaposi's sarcoma is defined as a rare multifocal tumor that originates in the endothelial cells and presents with cutaneous and extracutaneous manifestations. The classic form is most common in elderly men and progression is slow. This tumor responds well to chemotherapy and radiotherapy. This report describes a classic case of Kaposi's sarcoma in a woman with skin and visceral manifestations in whom the disease rapidly progressed to a fatal outcome.
Keyword: Herpesvirus 8, human; Sarcoma, Kaposi; Skin tumors

Resumo: Descrito em 1872, o sarcoma de Kaposi é neoplasia multicêntrica rara originária de células endoteliais com manifestação cutânea e extracutânea. A forma clássica é muito mais frequente em homens idosos, com evolução prolongada e boa resposta a quimioterapia e radioterapia. Apresentaremos um caso de sarcoma de Kaposi clássico com comprometimento cutâneo e visceral em paciente do sexo feminino com rápida evolução fatal.
Palavras-chave: Herpesvirus humano 8; Neoplasias cutâneas; Sarcoma de Kaposi

INTRODUCTION

Kaposi's sarcoma (KS) is a rare tumor described by Moritz Kaposi as a benign disease of the elderly. Four clinical forms are currently recognized: classic KS, African endemic KS, iatrogenic transplant-related KS and epidemic AIDS-associated KS. Although the four types have different forms of progression, they have similar phenotypical characteristics.

Classic KS is more common in elderly males of Jewish, European or Mediterranean descent. [1,2] Two studies conducted in Italy, for example, have confirmed the difference in incidence rates between men and women, Dal Maso et al. reporting a male-to female ratio of 1 to 0.4 per 100,000 inhabitants/year. [3,4]

This tumor is characterized by slowly progressing, purple macules on the distal portion of the limbs that may acquire nodular or tumoral characteristics as the disease progresses. Dissemination to internal organs may occur in the more advanced forms.

This report describes an aggressive case of classic KS with rapid progression and fatal outcome in a female patient from the northeast of Brazil.

CASE REPORT

A 61-year old, white, female patient from the Brazilian state of Pernambuco, who had been living in the state of São Paulo for more than 30 years, sought medical attention for lesions that had appeared around 18 months previously on her right lower limb. She had a history of arterial hypertension.

She had begun treatment with a rheumatologist four months previously based on a diagnostic hypothesis of erythema nodosum and had used hydroxychloroquine and 20 mg of prednisone daily. She reported a progressive increase in the lesions over the previous two months, with dissemination to the left leg and the presence of purulent secretion and a fetid odor.

Initial physical examination revealed single and confluent papules, nodules and tumoral lesions forming infiltrated plaques and affecting almost the entire right lower limb and the distal third of the left lower limb. There was a hardened edema over the entire right lower limb, intense exudation and a purulent secretion in lesions on the homolateral foot, in addition to areas of necrosis on both feet (Figures 1 and

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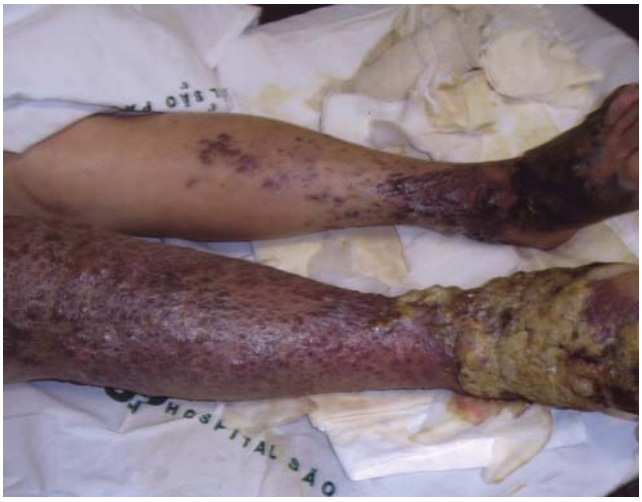

Figure 1: Lesions of Kaposi's sarcoma on the lower limbs: papules, nodules, tumoral lesions and infiltrative plaques. Intense exudation, purulent secretion and areas of necrosis

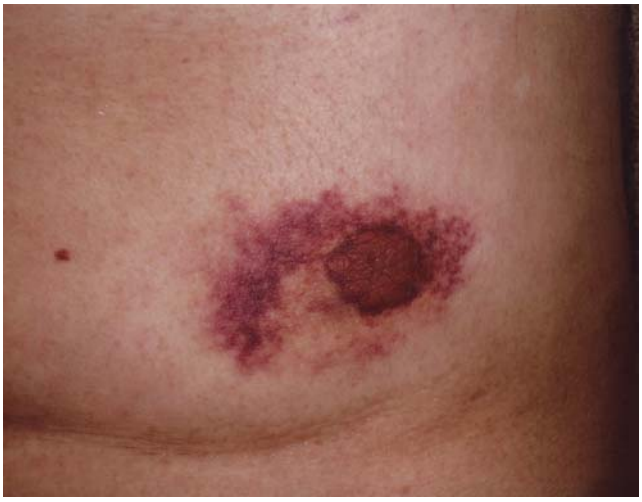

Figure 3: Recent lesion of Kaposi's sarcoma: violet-colored nodule with a purplish halo on the left side of the patient's chest

2). A violet-colored nodule with a purple halo was also found on the left chest region (Figure 3), which was reported by the patient to have appeared within the last week. While in hospital, a new purplish, erythematous lesion appeared in the right retroauricular area. No lesions were found in the oral cavity, and there were no adenomegaly, hepatomegaly or splenomegaly.

Histopathology of the lesion on the left chest region showed a morphological appearance compatible with a KS lesion in an initial phase, with a predomination of vascular channels and discretely atypical proliferations of capillary vessels and areas without nuclear atypia (Figure 4). Histopathology of the lesion on the patient's right leg showed morphology characteristic of the more advanced phase of the disease, with an intense proliferation of cells, atypical fusiform nuclei and mitotic figures involving vessels and vascular channels (Figure 5).

Bronchoscopy revealed wine-colored lesions bordered by accentuated hyperemic lines in the proximal and mid trachea, suggestive of Kaposi's sarcoma.

Serology for HIV and hepatitis B and C was negative. Laboratory workup showed creatinine 4.1 and urea 219. Ultrasonographic evaluation of the kidneys revealed signs of parenchymatous nephritis and a bilateral increase in the renal cortex. The patient was

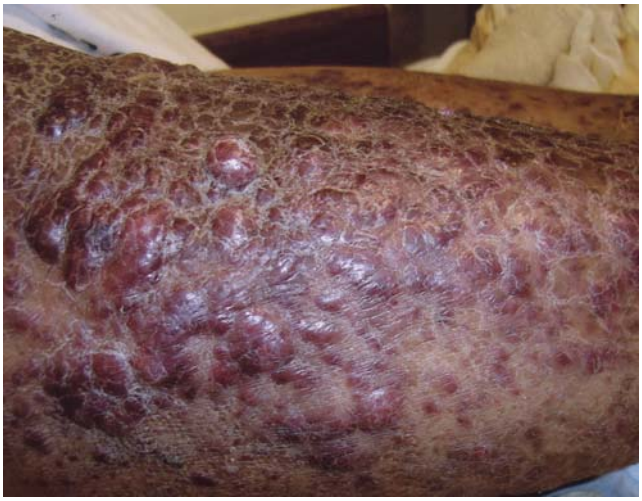

Figure 2: Detail of the lesions of Kaposi's sarcoma on the right leg: multiple nodules and hardened purple erythematous papules

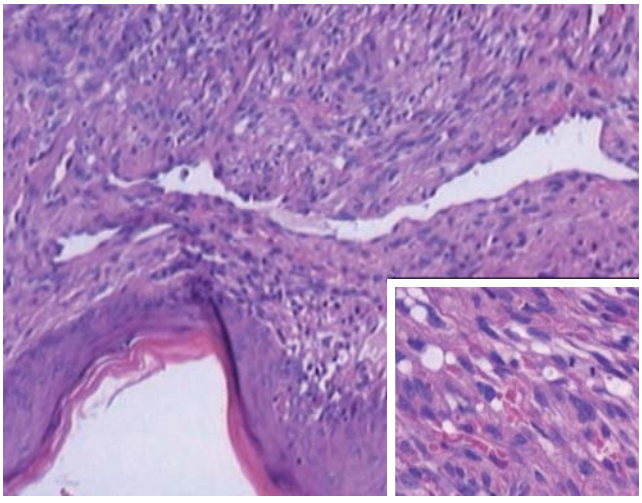

Figure 4: Left intercostal lesion: discretely atypical proliferation of vascular channels and capillary vessels and areas with no nuclear atypia (HE; magnification 100x). Note the extravasated erythrocytes in the middle of vascular channels (HE; magnification 200x)

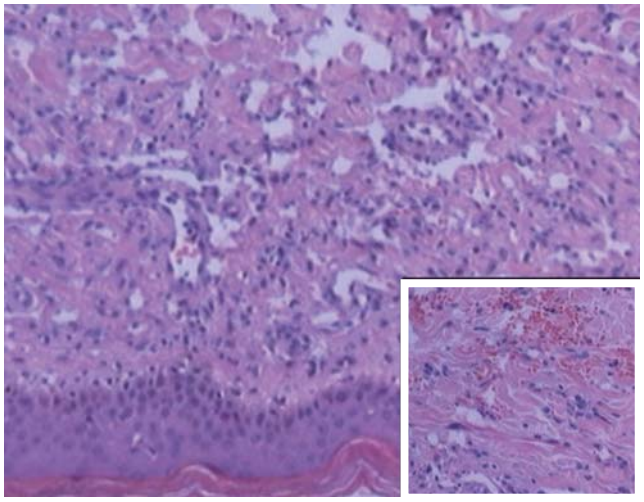

Figure 5: Lesion on the right leg: intense cell proliferation, atypical fusiform nuclei and mitotic figures involving vessels and vascular channels (HE; magnification 100x). Note the proliferation of fusiform cells with nuclear atypia (HE, magnification 200x)

being followed up by a nephrology team under the hypothesis of acute on chronic renal failure. Kidney biopsy was planned but was not performed. No significant abnormalities were found in any of the other tests performed.

The patient remained in hospital for only ten days and, despite the use of wide spectrum antibiotics throughout the entire duration of her hospitalization, she developed a severe skin infection, which progressed to septic shock and death. It was not, therefore, possible to perform clinical staging of the tumor or initiate chemotherapy.

DISCUSSION

KS is a multifocal endothelial tumor of low malignant potential. It was considered rare until the beginning of the AIDS epidemic. From 1981 onwards, its incidence increased considerably, principally in male patients who have sex with men (AIDS-associated Kaposi's sarcoma). In 1994, the involvement of a virus of the herpes group (HHV-8 or KSHV) in the etiopathogeny of KS was identified. [5] More recent studies have shown three factors most commonly involved in the etiopathogeny of this disease: infection by the human immunodeficiency virus (HIV), HHV-8 infection and the role of cytokines. [1,6,7] In HIV-positive patients, the introduction of combined, highly active antiretroviral therapy (HAART) resulted in a significant reduction in the number of new cases of epidemic KS from 1996 onwards. [8-10]

Endemic KS occurs throughout all of equatorial Africa, particularly in sub-Saharan Africa. It affects children and adults, predominantly males, and is not associated with immunodeficiency. Its clinical variants are: nodular, florid, infiltrative and lymphadenopathic KS. In children, the condition tends to be fatal.

Patients undergoing immunosuppressive therapy, particularly solid organ transplant patients, have an increased risk of developing iatrogenic KS, which, according to Tesari et al. may reach a hundred-fold. [11] It occurs typically in the first two years of treatment with immunosuppressive drugs and clinical severity is generally proportional to the degree of immunosuppression. Its principal characteristic is the reversibility of the condition with suspension of the immunosuppressors.

Classic KS is a rare condition, which progresses slowly and is benign. It affects principally males of 40-70 years of age. [1-4] Its incidence varies from region to region, being more common in Italy, Greece, Turkey and Israel. In the case described here, it should be emphasized that the patient was originally from the northeastern region of Brazil and she reported no family history of predecessors of Mediterranean or Jewish descent.

Lesions typically start as purple macules in the distal portion of the lower limbs, progressing very slowly (over years or even decades) to nodules, plaques and tumorous lesions. Because they are multifocal, new lesions may appear at other sites. As the disease progresses, the lesions harden, becoming brown-colored with an irregular surface. Ulceration and perilesional edema may be present. The mucosa is affected in around 15% of patients and the visceral form of the disease most commonly affects the lymph nodes and the digestive tract; [12] however, the liver, lungs and heart may also be affected, as well as other organs. In the case described here, the lesions were extremely aggressive. In a little over a year, the lesions spread to cover almost the entire right leg of the patient and lesions had also appeared at distant sites. In the ten days of hospitalization in which the patient was followed up, progression of the older lesions was noted, as well as the appearance of a new retroauricular lesion. Due to the severe clinical condition of the patient, it was impossible to evaluate the extent of the disease in the internal organs; however, lesions were found in the lung, an unusual site for a more indolent disease.

Histopathology findings vary in accordance with the clinical stage of the lesions. The initial KS lesions (macules and plaques) are characterized by a slight increase in dermal vessels with little endothelial atypia, associated with surrounding hemosiderin deposition. This feature may be confused with granulation tissue, which hampers histopathological diagnosis. In the more advanced phases of the disease, cell proliferation is numerically greater and has a fusiform appearance, with the formation of irregular vascular channels that may contain whole and degenerated

extravasated erythrocytes. Mitotic activity is more prominent. The histopathological differences between the distinct chronological and morphological stages of the disease were clearly present in this case.

The response of KS to the various therapeutic strategies is good. [13] For localized lesions, surgical excision, cryotherapy and radiotherapy may be used. For larger skin lesions, multiple lesions or those affecting internal organs, systemic therapy may be indicated. Of these forms of treatment, chemotherapy is used when the disease is disseminated, and is effective both on skin and visceral lesions. There are various active chemotherapy agents with response rates of around 60-80%, including the liposomal anthracyclines (doxorubicin, daunorubicin), paclitaxel, vinblastine and etoposide. Immunotherapy with interferon may be indicated in certain cases.

The present report described the case of a female patient from the northeastern region of Brazil with classic KS presenting with extensive skin and pulmonary involvement. Progression of the disease was rapid, leading to a fatal outcome. ❑

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