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Case Presentation

Kaposi Sarcoma of the eyelid as an initial manifestation of AIDS

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ABSTRACT

Kaposi sarcoma (KS) is a multifocal systemic disease that originates in the vascular endothelium related to Human Herpes Virus 8 (HHV-8). In the early 1980s the first series of cases of disseminated Kaposi Sarcoma in HIV infected patients were reported. However, with the advent of highly active antiretroviral therapy (HAART) since 1997, these cases are less frequently observed by clinicians. We report the case of a 40-year-old woman, presenting with two asymptomatic purpuric nodules localized in the superior and inferior left eyelids, occluding the palpebral fissure, which were present for 4 months prior to presentation. The eyelid nodules were determined to represent KS, but there were no additional cutaneous lesions. Pulmonary and gastric KS involvement was documented. Antiretroviral therapy was initiated along with pegylated liposomal doxorubicin. The nodules gradually disappeared and her immune status eventually improved. Ocular and periorbital involvement of KS associated with HIV-1 infection as the initial clinical manifestations is a rare advent. This case is important as it illustrates that disseminated KS was not to be predicted by the number or the extension of cutaneous lesions.

Keywords: kaposi´s sarcoma, disseminated, AIDS

INTRODUCTION

Kaposi sarcoma (KS) is a multifocal systemic disease that originates in the vascular endothelium and is etiologically related to Human Herpes Virus 8 (HHV-8) [1,2]. KS is traditionally grouped into four different types: classic, endemic, epidemic or AIDS-associated, and transplantation-associated KS [3]. It commonly involves the skin, particularly the lower limbs, but can also involve the mucous membranes, lymphatic system, and other organs, especially the lungs, liver, intestines and stomach [1].

In the early 1980´s Friedman-Kien *et al* [4] reported the first series of cases of disseminated Kaposi Sarcoma in HIV-1 infected patients. However, with the introduction of highly active antiretroviral therapy (HAART) in 1997, these cases became increasingly less frequently observed by clinicians especially in developed countries [5]. We report a case of disseminated KS with atypical cutaneous manifestations that led to the diagnosis of HIV-1 infection.

Case synopsis

A 40-year-old woman, presented with two asymptomatic purpuric nodules localized in the superior and inferior left eyelids, which were present for the 4 months prior to presentation. They had an insidious onset and gradual size increase. On the inferior left bulbar and palpebral conjunctiva, a reddish nodule loosely connected to the underlying tissue was also present for

the same period of time (Figure 1). Small brown papules with a central umbilication were seen in both malar areas; these had been present for the same period of time. The remaining physical examination revealed severe xerosis affecting the entire integument. The patient also noted a non-quantified weight loss in the previous six months. She had no history of systemic disease nor allergies. She was not taking any medications. No relevant family history was apparent.

Figure 1. Clinical picture showing the eyelid nodules.

A skin biopsy of one of the nodules was performed, revealing the presence, in the dermis, of spindle shaped cells separated by vascular spaces containing erythrocytes (Figure 2).

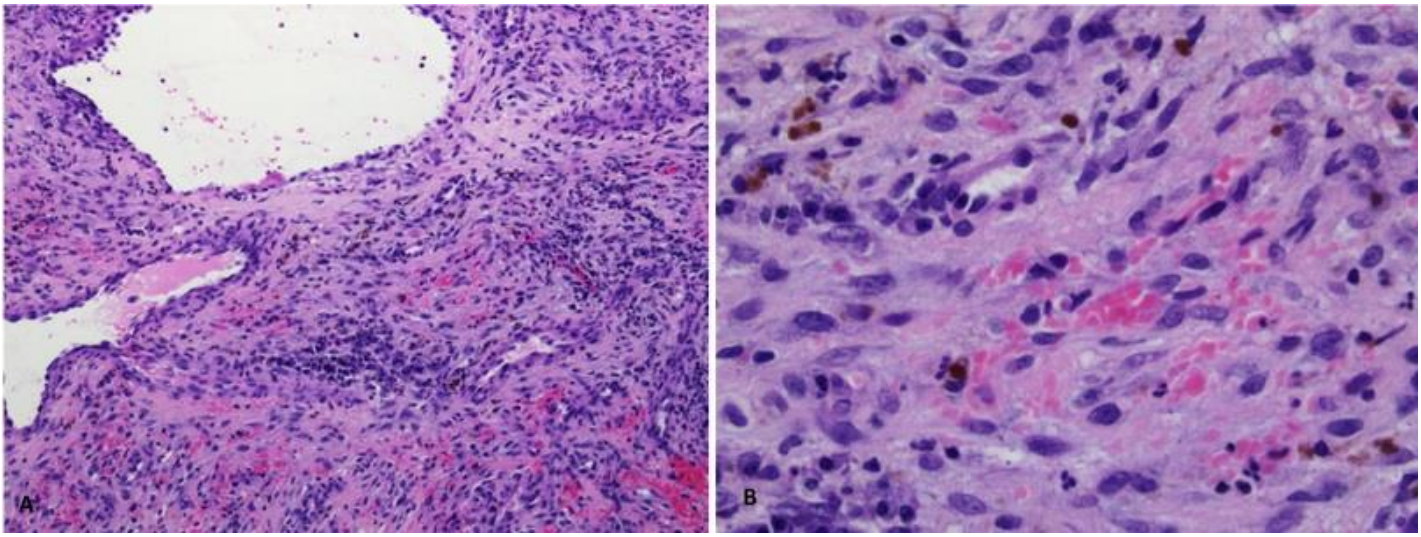

Figure 2. Histopathology stained with hematoxylin-eosin 100X magnification (A) and 400X magnification (B), showing spindle-shaped cells separated by vascular spaces containing erythrocytes.

These cells expressed human herpes virus 8 (HHV-8) antigens as shown by a positive immunostaining for HHV-8 (Figure 3). The histopathological examination of one of the small malar papules revealed the diagnosis of molluscum contagiosum. Laboratory investigation revealed HIV-1 infection with a T CD4 lymphocyte count of 88 cells/mm3 and a viral load of 128700 copies/mL.

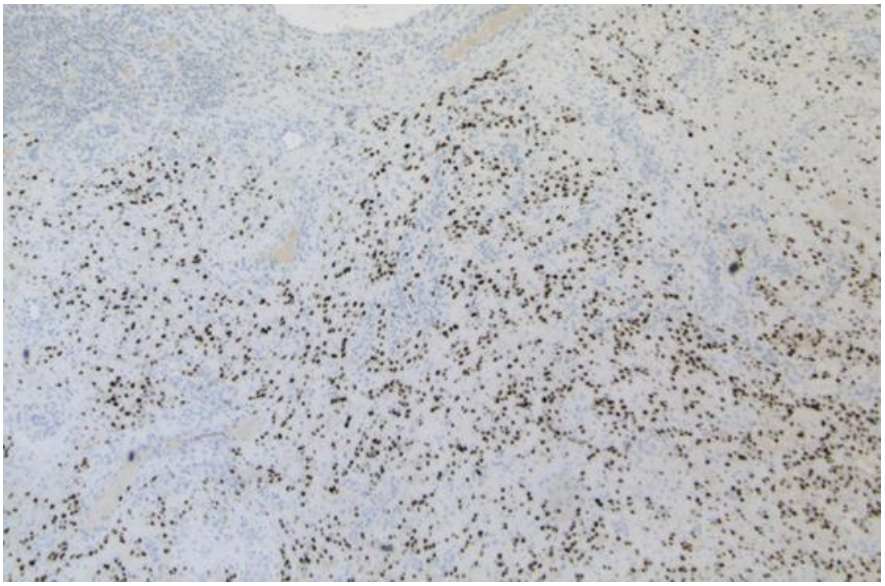

Figure 3. Immunohistochemical detection of the human herpes virus 8 (HHV8).

Imaging tests were carried out to stage the disease, starting with a chest x-ray that showed diffuse bilateral cotton-like infiltrates that were further characterized by a chest computed tomography scan (CT) as multiple bilateral parenchymal nodularities in a peribronchovascular distribution suggesting the diagnosis of tumors (Figure 4). A tissue sample was obtained by bronchoscopy, which was compatible with KS. No adenopathies nor pleural abnormalities were observed.

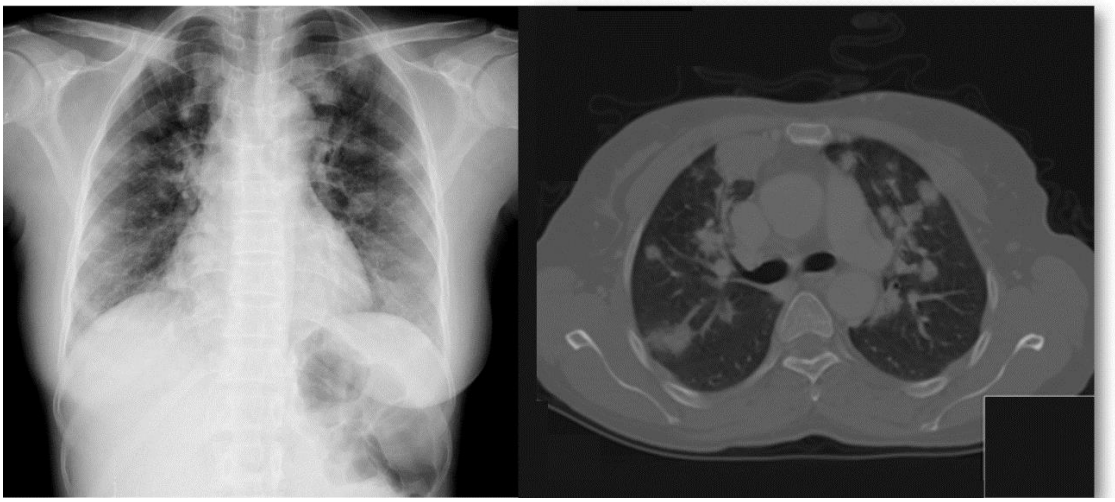

Figure 4. Multiple nodules scattered throughout the lung parenchyma bilaterally suggesting secondary deposits. A-chest radiography; B-Chest CT-scan

An esophagogastroduodenoscopy revealed the presence of an antral polypoid lesion which was positive for HHV-8 on immunohistological examination. The abdominal and pelvic CT scans did not show any relevant alterations.

Combined antiretroviral therapy (cART) with boosted darunavir, emtricitabina, tenofovir, and raltegravir was initiated (because of an unexpected broad resistance profile). In addition, pegylated liposomal doxorubicin 20mg/m^2 three times weekly was initiated. After the completion of eight cycles of chemotherapy in association with cART her skin nodules and pulmonary lesions progressively regressed along with gradual improvement of immune status. A thoracic CT scan and esophagogastric endoscopy performed 7 months after therapy showed complete regression of the pulmonary and gastric lesions. No further ophthalmologic intervention was needed and no recurrence was apparent after a two years follow-up period.

Discussion

KS is the most frequent tumor associated with HIV infection [6]. It relates closely with the immune status of the patient, namely T CD4 lymphocyte count, and is considered by WHO as an AIDS-defining disease [7,8,9]. Since the introduction of HAART its incidence has declined significantly in the HIV population with access to it, remaining very high in some African populations [5]. In AIDS patients with disseminated KS, ocular presentations have an incidence of 15-20%, but only in a small percentage of cases (2 to 4%) this location is the revealing manifestation of the disease [10,11]. In our case it was the ocular lesions that led to the diagnosis of both KS and HIV infection.

Skin lesions are the most frequent manifestation of AIDS associated KS and between 33-40% of these patients also present with visceral spreading of the disease [12]. The cutaneous lesions are known to frequently precede the visceral involvement. However, there are no published works determining predictive clinical factors (as extension, type and location of cutaneous lesions) for visceral involvement. Our case illustrates that disseminated KS might not be predictable by the number or the extension of cutaneous lesions, since our patient had no involvement of the remaining integument. The dissemination mechanism involved in KS still remains a point of debate: the lack of a clear primary site in many cases makes KS different from other neoplasms. Perhaps other mechanisms and stimulatory factors are involved in the progression of this particular neoplasm, such as immunosuppression status as measured by T CD4+ lymphocyte count, HIV, or HHV-8 viral load [13, 14].

Coinciding with the above, other factors than the tumor load were included in the staging system initially proposed by the AIDS Clinical Trials Group Oncology Committee (ACTG) in 1989. This staging system includes measure of tumor extent (T), severity of immunosuppression (I), and other systemic HIV-associated illness (S). In the presence of any of the following: edema or ulceration associated with the cutaneous tumor or disseminated disease (T1); T CD4 lymphocyte count inferior to $200/mm^3$ (I1); presence of B symptoms, presence of any other HIV related disease, or previous history of opportunistic infections (S1), the patients are classified as "*Poor risk*" and require treatment with a combination of cART and chemotherapy [9].

In recent studies, however, the prognostic value of this staging system has been questioned resulting in no international consensus on which parameters should be taken into account to select the patients that should receive cART alone and which should receive cART plus chemotherapy, or chemotherapy alone.

A few authors defend that only tumor load (T) and the presence of systemic illness(S) identify patients with poor survival [15], whilst others state that only immune status (I) and the presence of systemic illness (S) are of prognostic significance [16]. Stebbing *et al* identified four different prognostic factors: KS as the first AIDS-defining illness, T CD4+ lymphocyte count, age greater than 50 years, and the presence of any other HIV related disease. Based on these parameters a prognostic index can be calculated which can guide therapeutic options [17]. More recently, Bower *et al*, conducted a 15-year-long prospective study in which patients were staged at diagnosis according to the ACTG system and the decision of initiating cART in combination with chemotherapy was made solely based on tumor load (T). This study demonstrated excellent outcomes for treatment of KS confined to skin and lymph nodes with cART alone (T0), and validated the use of cART plus chemotherapy in patients with edema or ulceration associated with the cutaneous tumor or disseminated disease (T1) [18]. In all these studies, liposomal anthracyclines have been the chemotherapy of choice, namely pegylated liposomal doxorubicin or daunorubicin [19, 20, 21].

In conclusion, we describe a rare presentation of KS associated with HIV-1 infection that illustrates the dissociation between the number and extension of cutaneous lesions and visceral involvement.

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