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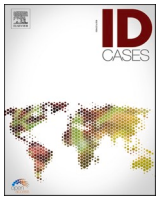

Case report

Kaposi sarcoma in an individual recently diagnosed with HIV

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ABSTRACT

Kaposi Sarcoma (KS) commonly manifests with multiple vesicular cutaneous and mucosal nodules, with four subtypes clinically recognized. Although commonly seen in younger men, our patient presented with presumed epidemic KS at an older age. Additionally, our patient presented with Kaposi sarcoma during primary HIV infection which is atypical for Kaposi sarcoma presentation. The patient's clinical course is important to follow, as his rectal involvement indicates the patient would benefit from systemic therapy. Furthermore, our case highlights the need for a keen clinical index of suspicion in all patients with new HIV diagnosis and new onset suspicious lesions, regardless of age.

Introduction

A rare multifocal angioproliferative neoplasm of endothelial cells, Kaposi Sarcoma (KS) commonly manifests with multiple vesicular cutaneous and mucosal nodules. It develops due to infection with Kaposi sarcoma-associated herpesvirus (KSHV), otherwise known as human herpesvirus 8 (HHV-8) [1].

There are several other clinical entities of note that are associated with KSHV [16,17]. These similar conditions include Kaposi inflammatory cytokine syndrome (KCIS), Multicentric Castleman Disease (MCD) and immune reconstitution inflammatory syndrome (IRIS). KCIS mimics sepsis and is marked by features of respiratory failure, HIV and KSHV viremia, lymphadenopathy, pancytopenia [16]. MCD has a very similar clinical feature that can be distinguished from KCIS through a biopsy of the bone marrow, lymph node or spleen. IRIS is characterized by the presence of AIDs with a CD4 count of less than 100 prior to treatment as well as a positive virologic or immunological response soon after initiating antiretroviral therapy [16].

We present a case of epidemic KS in an older gentleman recently diagnosed with HIV.

Case description

An 81-year-old man with a past medical history of type 2 diabetes, primary syphilis (previously treated), and benign prostatic hyperplasia presented with a painful rash on his bilateral lower extremities as well as purple lesions on his hard palate and abdomen (Fig. 1a). He had initially developed small lesions on his feet one month prior to his hospital presentation (Fig. 1b). He reported new onset of pain with ambulation but denied any sensory or motor deficits in his lower extremities. Of note, the patient had a history of unprotected sex with multiple male partners in Costa Rica and had been diagnosed with Human Immunodeficiency Virus (HIV) the same month that these lesions appeared. He also reported a 20-pound weight loss over a one year period. Notably, he had tested negative for HIV less than four months prior to his initial presentation.

On admission, the patient was afebrile and normotensive. His physical exam was remarkable for bitemporal wasting, bilateral lower extremity edema, as well as diffuse violaceous papules and plaques on his lower extremities, abdomen, and hard palate (Fig. 1a-b). He also reported persistent diarrhea but denied any fever, chills, shortness of breath, hematochezia or hematemesis. Labs on admission were notable for an HIV-1 Viral load of 83,307 and a CD4 count of 520. Given his new diagnosis of HIV, he was started on Biktarvy during this admission. CT imaging showed mild axillary, intrathoracic and pelvic lymphadenopathy as well as splenomegaly.

Differential diagnoses included endemic KS, cutaneous metastases, secondary skin manifestations of inadequately treated syphilis, leukemia/lymphoma cutis, and bacillary angiomatosis. Diagnoses such as vasculitides and autoimmune diseases were felt to be less likely but were

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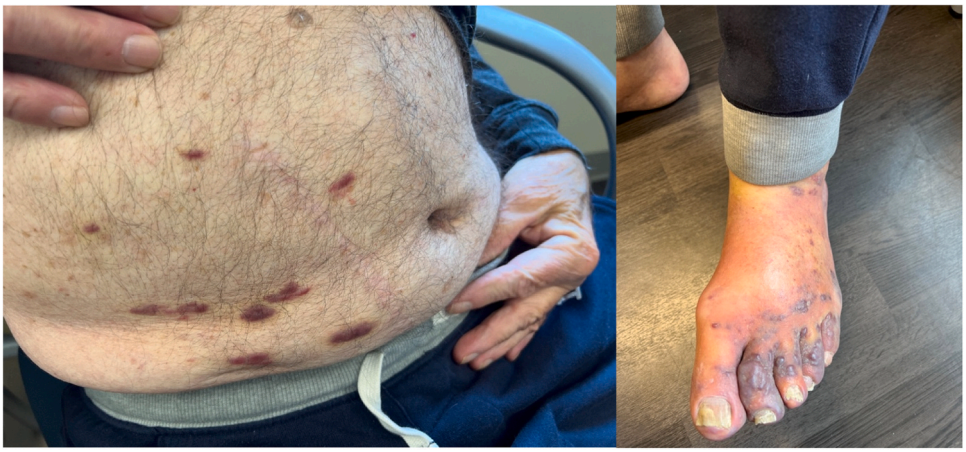

Fig. 1. Violaceous plaques seen on ventral abdomen (Fig. 1a) and left foot (Fig. 1b). These lesions are typical for what can be seen in Kaposi Sarcoma which features lesions on the skin or mucocutaneous surfaces that are typically violaceous pink to purple. The lesions are also commonly seen on the feet as seen with this patient.

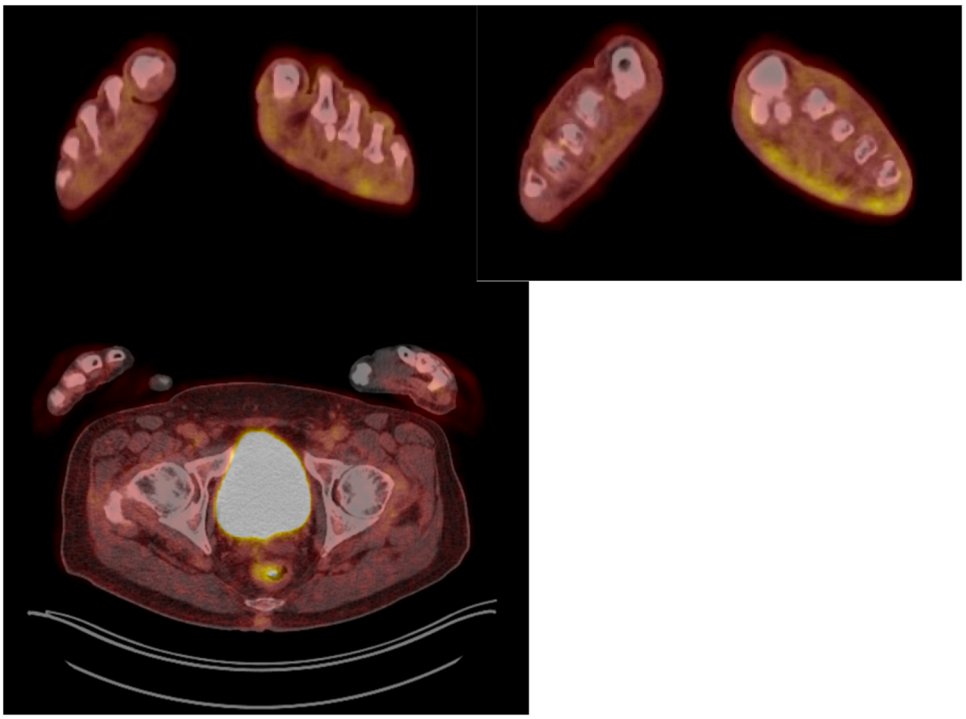

Fig. 2. PET CT showing hypermetabolism in left foot (Fig. 2a) and rectum (Fig. 2b) PET CT can be used to assess the extent of disease involvement. The yellow regions pinpoint the areas where there is high metabolic activity. The involvement of the rectum is a poor prognostic indicator.

also considered. The patient was seen by Dermatology and underwent a punch biopsy of an abdominal lesion. This showed dense lymphocytic infiltrate associated with increased vascular channels and spindle cells infiltrating the dermis as well as focal hemorrhage (Fig. 2). The endothelial cells and spindle cells were positive for D2–40, ERG and HHV-8. These findings were consistent with the diagnosis of Kaposi sarcoma. He was seen by hematology oncology as an inpatient and was scheduled for outpatient oncologic follow up and palliative radiation therapy for treatment of his cutaneous lesions on his feet.

He was seen in clinic shortly after discharge, and was recommended to continue antiretroviral therapy (ART) and undergo palliative radiation therapy as previously mentioned. He expressed a desire to avoid chemotherapy. In addition, he underwent PET CT staging which showed hypermetabolism in the left leg and foot, as well as hypermetabolism of the posterior rectal wall concerning for neoplasm (Fig. 3). He was seen by gastroenterology and underwent colonoscopy, which identified a localized area of moderately altered vascular, congested and erythematous mucosa in the rectum. This lesion was biopsied and stained positive for D2–40, ERG, and HHV-8, supporting diagnosis of Kaposi sarcoma involving rectal mucosa and submucosa.

The patient has continued to follow with infectious diseases and oncology as an outpatient. He has been compliant with his ART therapy. His current HIV-1 Viral load is less than 20 and his CD4 count is 618. He currently does not need any immediate systemic chemotherapy. The palliative radiation therapy of his feet significantly improved his pain. His most recent imaging did not show any systemic disease.

Discussion

Kaposi sarcoma is a malignant neoplasm of lymphatic endothelial cell origin associated with HHV-8 that can occur in the setting of uncontrolled HIV. Four subtypes of KS are clinically recognized: Epidemic

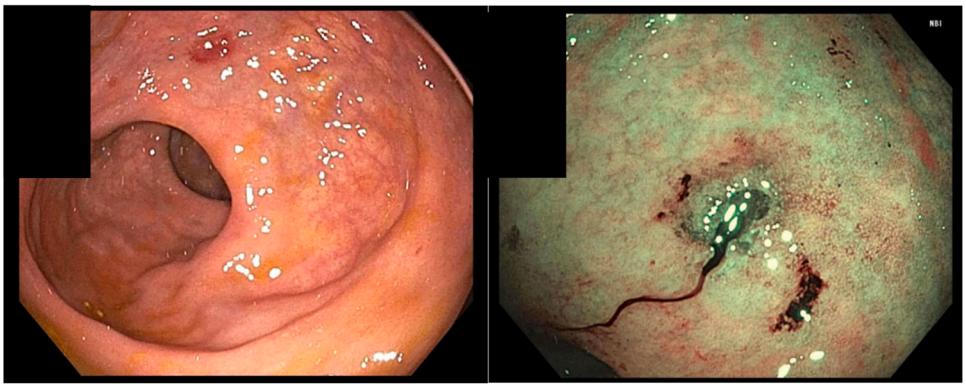

Fig. 3. Colonoscopy showing rectal involvement. The colonoscopy images show a localized area of moderately altered vascular, congested and erythematous mucosa in the rectum.

(HIV/AIDS) KS, Classic KS, Endemic (African KS), and Immunosuppression Associated KS [2]. Of these subtypes, Epidemic KS is seen in men who have sex with other men (MSM), and usually presents in younger patients compared to other subtypes of KS. HIV-related KS is an AIDS defining illness and it is the second most common tumor that can be found in HIV patients with CD4 counts less than 200 cells/mm3 [3]. HIV positive males who have sex with males have a 5 to 10 times greater risk of developing Kaposi sarcoma. Of the HIV patients who do not take ART 30% will go on to develop Kaposi sarcoma [4,5].

Classic KS is predominantly seen in males over 50 years of age of Eastern European or Mediterranean descent [15]. These patients are at a high risk for developing a secondary malignancy. Endemic KS is common throughout Eastern and central Africa. Immunosuppression Associated KS is seen in patients with bone marrow, solid organ peripheral blood stem cell transplants. These patients have a 400 to 500 fold increased risk of developing this malignancy over the general population [15].

Kaposi sarcoma is a vascular lesion that appears as a violaceous pink to purple plaque [1]. Most lesions appear on the limbs, face and trunk. HHV8 infects endothelial cells and activates the mTOR pathway which promotes aberrant angiogenesis [6]. Another 20% of these patients will have visceral involvement most typically in the gastrointestinal tract and lungs. Both presentations are commonly associated with lymphedema.

While there is no universal staging system for Kaposi sarcoma, the disease is classified as localized, nonaggressive, or locally aggressive and disseminated [7,8]. The AIDS Clinical Trial Group staging system assesses extent of the tumor, their immune status and the severity of their systemic illness [9,10]. Factors predictive of poor outcomes include tumor associated edema or ulcer, extensive oral lesions, and lesions in the gastrointestinal tract or other visceral organs, especially the lung [11,12]. Additional poor prognostic factors include history of opportunistic infections, fever, night sweats, weight loss greater than 10% of patient's body weight and diarrhea persisting more than 2 weeks. Patients with CD4 counts less than 200 also have a worse prognosis. While our patient did not have an initial CD4 count less than 200, his visceral organ involvement would suggest a worse prognosis.

Treatment depends on the extent of the involvement. Local symptomatic lesions can be treated with intralesional chemotherapy and radiation. Skin lesions can be removed via local excision, liquid nitrogen or injection of vincristine. Conversely, systemic therapy is indicated for patients with limited cutaneous disease that is symptomatic or cosmetically unacceptable, advanced cutaneous disease, or disease that involves the oral cavity, viscera, or lymph nodes. For these cases, first line systemic chemotherapy is usually liposomal doxorubicin [2,13]. Epidemic Kaposi sarcoma is very responsive to ART and treatment with ART can result in complete resolution of their symptoms [3].

Our patient's presentation is unique due to his late diagnosis of HIV and subsequent atypical late manifestation of HIV-associated Kaposi sarcoma. As detailed, the patient tested negative for HIV less than four months prior to his presentation to the hospital. He first tested positive for HIV when the lesions initially appeared. One month later, he received the biopsy that revealed the additional diagnosis of KS. The patient tested positive Kaposi sarcoma can occur as quickly as 24 months after the primary HIV infection but it is extremely rare to see Kaposi sarcoma during the primary HIV infection [14]. Based on the patient's clinical presentation, it is most likely that he has classic KS rather than AIDS-related KS. At the time of diagnosis, the patient had a CD4 count of 520 making classic KS the more likely diagnosis since he did not demonstrate the profound CD4 cytopenia seen with AIDS-related KS.

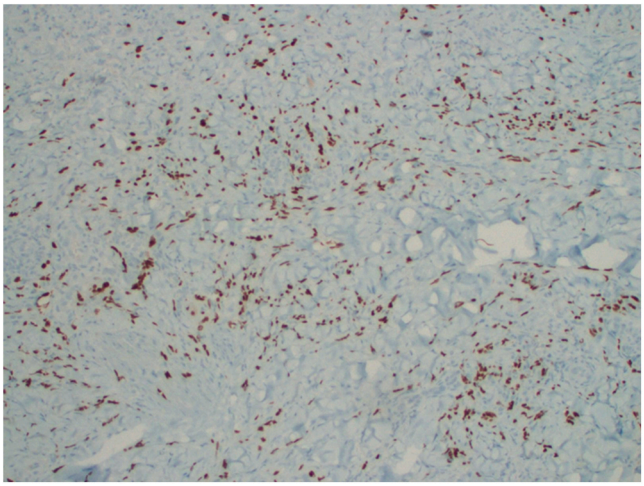

Fig. 4. Immunostaining for HHV-8 is positive in the spindle cells confirming the diagnosis as Kaposi sarcoma. Lesions are composed of cells that have become infected with HHV8 and can be characterized by spindle cell proliferation.

To our knowledge, only a single other case report discusses KS diagnosis during the period of primary HIV infection. However, that patient's symptoms appeared 11 weeks after HIV diagnosis [14] whereas our patient's symptoms of Kaposi Sarcoma happened 4 to 5 weeks prior to diagnosis of HIV. Review of the literature revealed a case of an individual diagnosed with AIDS and KS simultaneously [18]. This individual had the violaceous plaques characteristic of KS for 2 years prior to presentation. A skin biopsy at the time of his presentation revealed the diagnosis of KS and his CD4 count at that time was 173 [18]. This case also differs from our patient as our patient's lesions appeared in quick succession to him receiving a diagnosis of HIV. His disease was also not as advanced classifying him as classic KS rather then

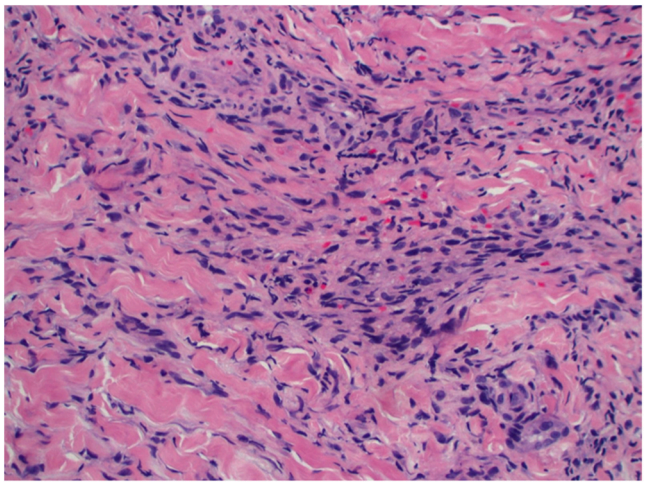

Fig. 5. Atypical spindle cell proliferation is associated with focal extravasated red blood cells and crush lymphocytes. HHV8 can result in angiogenesis as well as cytokine production.

this other patient who demonstrates epidemic KS. Figs. 4 and 5.

Ethical approval

The research described in this manuscript has been approved by the relevant ethics personal and all procedures followed ethics guidelines.

CRediT authorship contribution statement

Gabriela Contino: Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Kim Hookim:** Resources, Investigation, Formal analysis, Data curation. **Akshay Desai:** Writing – review & editing. **Keri Morgan Cronin:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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Informed Consent

Informed consent was obtained by the patient described in this study.

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