Skin Lesions and Lower Extremity Edema in a newly diagnosed HIV patient

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ABSTRACT

The differential diagnosis of skin lesions in human immunodeficiency virus patients is diverse and includes both infectious and non infectious causes. In this case presentation, a 37 year old male newly diagnosed with HIV presented to a hospital in the United States with skin lesions and worsening lower extremity swelling. After presentation, he developed respiratory distress and was found to have disseminated Kaposi sarcoma with cutaneous and pulmonary involvement. Kaposi sarcoma has decreased in incidence in the era of highly active antiretroviral therapy. However, it remains an important acquired immunodeficiency syndrome defining illness which may be the presenting complaint in a patient with occult HIV infection. Kaposi sarcoma has substantial mortality and morbidity and should be included in the differential diagnosis of skin lesions in a HIV positive patient.

INTRODUCTION

In this case report, we describe a patient recently diagnosed with human immunodeficiency syndrome (HIV) who presented with progressive lower extremity swelling. During his hospitalization his respiratory status deteriorated and was found to have Kaposi Sarcoma (KS) with cutaneous and pulmonary involvement. KS remains an important acquired immunodeficiency syndrome (AIDS) defining illness and must be included in the differential diagnosis of skin lesions in HIV patients. In the setting of HIV, it is treated with initiation of highly active antiretroviral therapy (HAART) and in some cases systemic chemotherapy. KS continues to be an important cause of morbidity and mortality in HIV patients.

CASE REPORT

A 37 year-old Ghanaian male diagnosed with HIV three weeks prior presented with one month of worsening bilateral lower extremity edema and stiffness to a Boston area hospital in the United States in February 2010. He was admitted to an outside hospital three weeks prior to presentation with nonproductive cough, shortness of breath and chills. At that time, he was found to be HIV positive and was treated with azithromycin for community acquired pneumonia and trimethoprim-sulfamethoxazole (TMP-SMX) and prednisone for presumed Pneumocystis jirovecii pneumonia. His CD4 count and viral load were not available. On his presentation to our hospital, he described a one month history of worsening lower extremity edema which gradually worsened to extend to his bilateral hips. On review of systems, he noted a two to three month history of weight loss and decreased appetite. He also stated that the non productive cough and dyspnea on exertion had not resolved. He denied fevers, chills, nausea, vomiting, diarrhea or history of trauma to either lower extremity. He emigrated from Ghana to the United Kingdom 10 years ago and moved to Boston two years ago.

In the emergency department, his temperature was 38.4 degrees Celsius, blood pressure of 108/62 mm Hg, heart rate of 106 beats per minute and oxygen saturation of 92% on 6 liters by nasal cannula. On physical examination, he was alert and oriented and in no acute distress. His cardiovascular exam revealed tachycardia without murmurs or rubs. On pulmonary exam, he had crackles at his right base. His abdominal exam was unremarkable. His bilateral lower extremities showed pitting oedema which extended to the hips bilaterally. On skin exam there were multiple, hyper pigmented, irregular plaque-like lesions which could be seen on his chest, nose and back (Figure 1). His admission laboratory studies revealed a white blood cell count of 15.7 K/μL, haemoglobin of 9.5 g/dL, platelet count of 75 K/μL, sodium of 128 mEq/L and creatinine of 1.29 mg/dL.

Shortly after admission to the hospital, the patient became acutely short of breath. A chest radiograph from the day of admission revealed bilateral interstitial infiltrates (Figure 2). He was subsequently intubated, transferred to the intensive care unit and started on high dose TMP-SMX and methylprednisolone. Bronchoscopy revealed multiple vascular lesions in the main stem bronchus (Figure 3). All sputum and bronchoscopy specimens were nega-

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tive for Pneumocystis jirovicii cysts. Skin biopsy was diagnostic of Kaposi sarcoma (Figure 4). His CD4 count was 193 with a viral load of 141,992 copies/mL. He was started on HAART and liposomal doxorubicin. His course was complicated by immune reconstitution inflammatory syndrome, cytomegalovirus viremia and ventilator associated pneumonia and after a prolonged course in the intensive care unit, the patient died.

DISCUSSION

Moritz Kaposi was the first to describe what is now known at Kaposi sarcoma (KS) as a multicentric cutaneous disease in five elderly patients in 1872.[1] In the 1940s, a similar vascular neoplasm was described in Africa, but appeared to have a more aggressive clinical course. With the introduction of organ transplantation in the 1970s, KS was again seen but in this case was a complication of iatrogenic immunosuppression. Finally, in the early 1980s, reports of clusters of KS and Pneumocystis jirovecii pneumonia in New York City and Los Angeles heralded the first clusters of HIV infection in the United States.[2]

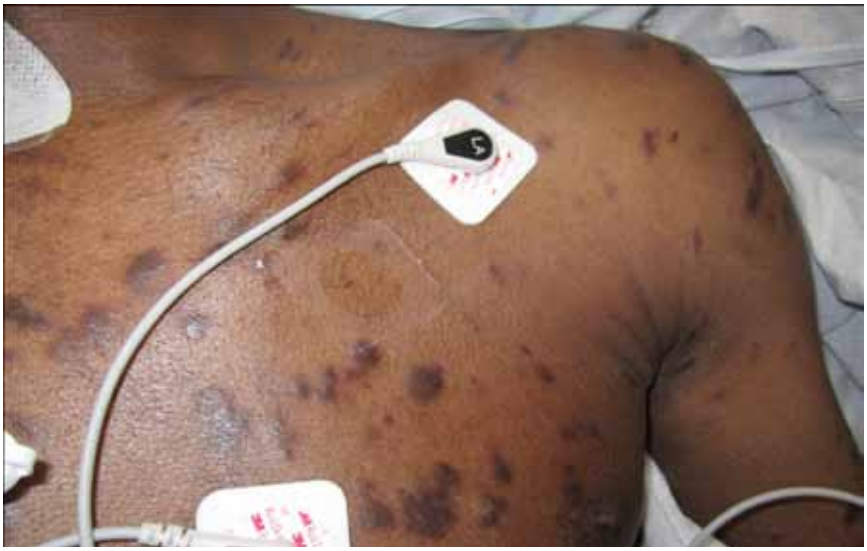

Figure 1. **Multiple hyperpigmented plaque-like skin lesions noted on physical examination of the chest of the patient on admission to the hospital**

Kaposi sarcoma is a multifocal, systemic neoplasm of endothelial origin which is thought to be caused by human herpesvirus-8 (HHV-8) infection. There are four clinical variants of KS: classic KS, endemic African KS, KS associated with immunosuppressive therapy and AIDS-related KS.[3]

Classic KS typically occurs in older men, usually of Mediterranean or Jewish origin, who present with local skin lesions. Lesions usually develop first on the lower extremities as unilateral or bilateral bluish-red macules which progress in size into plaques and may become nodular and ulcerate. In general, progression is slow and can occur over decades.[3] Systemic involvement usually occurs only after several years of progression and is rarely symptomatic.[4]

Endemic African KS differs from the classic form in that there is a subset of patients who demonstrate an invasive and rapidly progressive lymphadenopathic variant. In some Central African countries, KS is the most common neoplasm and can account for up to 10% of malignancies in men in this region.[3] African KS can present as nodular, infiltrative or lymphadenopathic types. The infiltrative subtype can aggressively invade skin and soft tissue, muscle and bone.[5,6]

KS in patients on immunosuppressive medications is thought to be a complication of their effect on the host immune system. In transplant patients, recipients of kidney transplants are most commonly affected and skin involvement is more common (85% in one series) than visceral disease.[7] Skin lesions seen in patients on immunosuppressive medications are similar to those seen in classic and AIDS-related KS.

AIDS-related KS is generally multifocal, rapidly progressive and occurs commonly with visceral involvement. Although it was present as an AIDS defining illness in more than 20% of European patients early in the HIV epidemic, its incidence has decreased in the era of HAART.[8] However, KS is still the most common AIDS

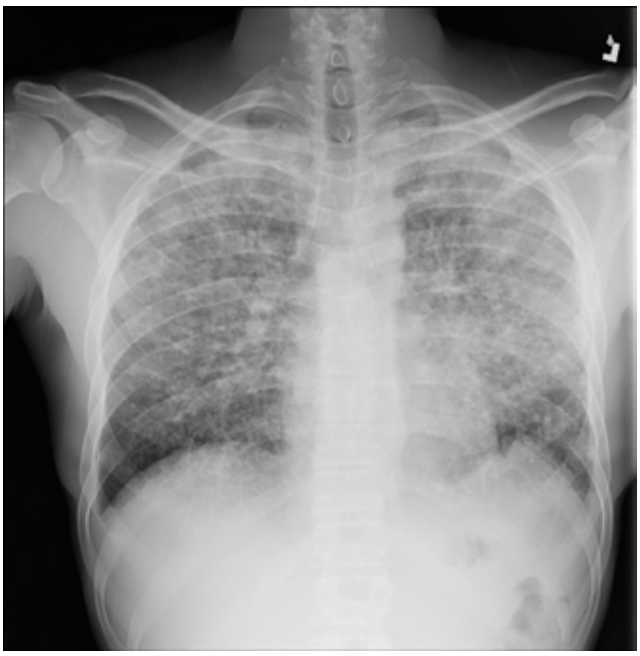

Figure 2. **Chest radiograph on admission to the hospital showed extensive diffuse bilateral interstitial infiltrates**

related tumor seen in men who have sex with men.[9] AIDS-related KS is clinically more aggressive than classic KS. Early skin involvement consists of violaceous macular lesions that rapidly develop into plaques and nodules. They are frequently seen in the face, eyelids, ears, chest and trunk. Oral mucosal involvement is seen in 10-15% of AIDS- related KS patients. The differential diagnosis of skin lesions includes bacillary angiomatosis, pyogenic granuloma and angiosarcoma. The differential diagnosis of oropharyngeal lesions includes squamous cell carcinoma, bacillary angiomatosis and Non-Hodgkin lymphoma.[3] Visceral disease most frequently involves lymph nodes, the gastrointestinal tract and lungs. Gastrointestinal involvement can be complicated by bleeding and illeus[10] while pulmonary involvement can be complicated by bronchospasm, cough and respiratory compromise.[11]

Treatment options for KS depend on the type and extent of involvement. Localized cutaneous disease of any clinical subtype can be treated with surgical excision, liquid nitrogen, laser therapy, or topical 9-cis retinoic acid. Radiation therapy is used when local topical therapy is difficult.[3] Progressive cutaneous disease or visceral disease often requires systemic therapy.
Common chemotherapeutic agents used include doxorubicin, daunorubicin or paclitaxel. In the cases of KS in patients receiving immunosuppressive medication and AIDS-related KS, it is thought that suppression of the immune system is a key factor in the pathogenesis of KS. Therefore, reducing immunosuppression is a cornerstone of therapy.[7] Similarly, in AIDS-related KS, HAART is key to therapy since its goal is immune reconstitution. However, in AIDS patients who have extensive disease, HAART alone may not be adequate to treat KS and chemotherapy may also be required.[3]

The majority of studies describing outcomes of AIDS-related KS are from early in the HIV epidemic when HAART was not available. One such study described 212 patients with AIDS-related KS in New York City initially diagnosed between 1979 and 1983 who were followed prospectively. After five years of follow up, 174/212 (82%) had died. Of these, 84% were thought to have died from an opportunistic infection (OI) while the remaining 16% were thought to have died as a direct complication of visceral involvement of KS (78% had pulmonary involvement). Variables found to be independently predictive of mortality were presence or history of an OI, presence of systemic symptoms and absolute

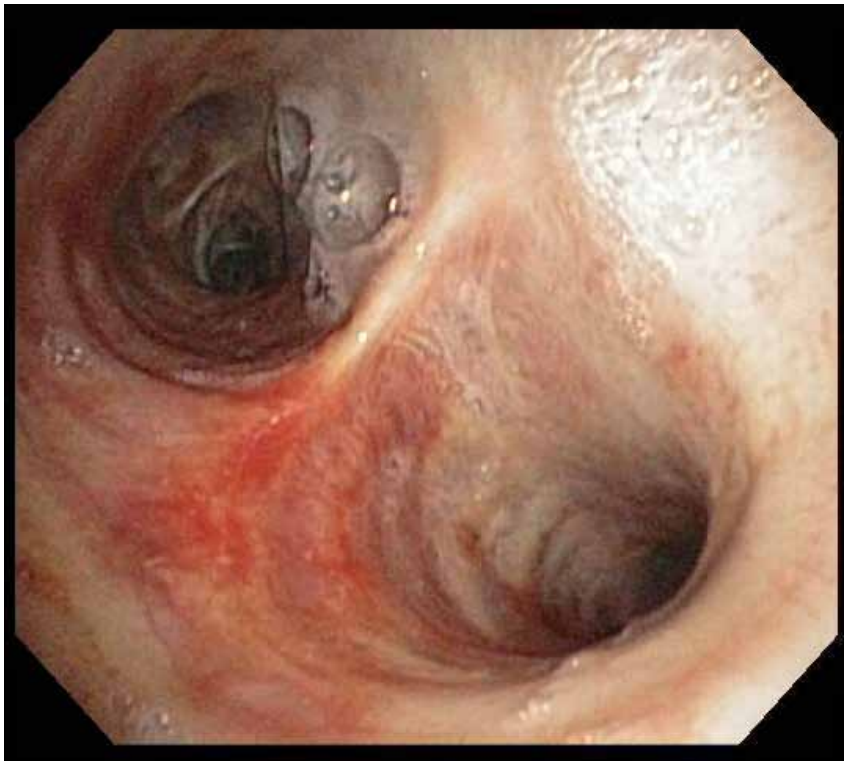

Figure 3. **Bronchoscopy showed multiple erythematous plaque-like lesions in both main stem bronchi which were highly suggestive of pulmonary involvement of Kaposi Sarcoma**

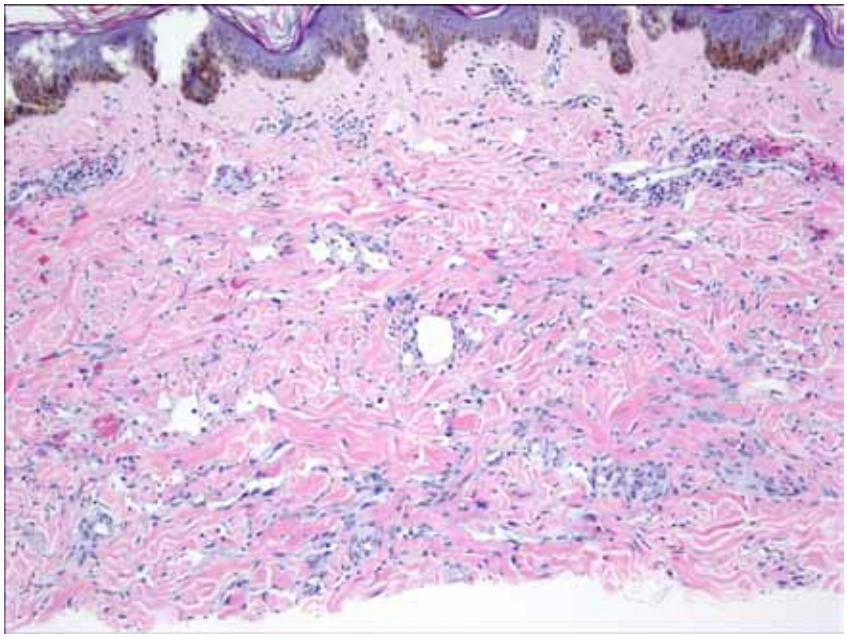

Figure 4. **Pathologic appearance of skin biopsy specimen of skin lesions seen on the chest of the patient which demonstrate atypical vascular proliferation with red cell extravasation and lymphoplasmacytic infiltration characteristic of Kaposi sarcoma. Immunohistochemical staining for HHV-8 was positive.**

CD4 count of < 300 cells/μL.[12] A more recent study by Nasti et al found that when compared to patients on HAART, patients who were not on HAART at time of diagnosis of KS had more widespread cutaneous involvement and more visceral involvement (particularly gastrointestinal involvement). Three year survival in both groups, after all patients were started on HAART, was higher than rates seen in the pre-HAART era.[13]

Although the incidence of AIDS-related KS has declined in the era of HAART, it remains an important AIDS related malignancy with substantial morbidity and mortality. KS must be included in the differential diagnosis of skin lesions in HIV patients and it is important to recognize common extracutanous sites of involvement.

KS may be the initial presentation of a patient with occult HIV infection and it is critical that HIV infection be ruled out in any patient in which KS is considered. AIDS-related KS is treated primarily with institution of HAART in order to promote immune reconstitution, but in advanced disease, systemic chemotherapy may also be required.

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