

Metastatic Kaposi sarcoma with osseous involvement in a patient with AIDS

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Kaposi sarcoma is an AIDS-defining illness associated with human herpes virus-8 (HHV-8) co-infection. It was described in 1872 by the Hungarian dermatologist Moritz Kaposi, and was an isolated and sporadic occurrence before the emergence of HIV infection and AIDS.¹ It was first affiliated as an AIDS-associated neoplasm in 1981.¹ Kaposi sarcoma is a systemic disease that can present with cutaneous lesions with or without internal involvement. There are four subtypes: Classic, African endemic, AIDS-related (CD4 count, <200), and Kaposi sarcoma in iatrogenically immunosuppressed patients. The disease has the propensity to manifest in the skin and gastro-intestinal and respiratory tracts, and osseous involvement is rarely encountered. We present here the case of an AIDS-positive man with generalized bone pain as a result of metastasis from Kaposi sarcoma. Our discussion includes the epidemiological, clinical, pathological, and radiological facets of AIDS-related Kaposi sarcoma, and the anomaly of osseous involvement.

Case presentation and summary

A 26-year-old African American man with a history of AIDS (CD4 count, 13 cells/mm³ [normal, 500-1,600 cells/mm³]) who was noncompliant with HAART (highly active antiretroviral therapy), presented to the emergency department in January 2016 with chest, abdominal, and back pain. His HAART regimen included darunavir 8 mL oral suspension daily, emtricitabine 4 mL oral suspension daily, and ritonavir 100 mg tab daily. A computed-tomography (CT) scan of the man's abdomen revealed axillary, mediastinal, and abdominal lymphadenopathy, with splenomegaly and innumerable osseous lucent spinal lesions. A left axillary lymph node biopsy was posi-

tive for Kaposi sarcoma; pathology showed fascicles of spindle, oval- to round-shaped atypical cells positive for HHV-8 (granular nuclear staining), CD31, and CD34 (partial; Figure 1). Serum and urine protein electrophoresis showed no paraproteins.

He restarted his previous HAART regimen in March 2016, and was subsequently started on chemotherapy with liposomal doxorubicin (50 mg [20 mg/m²] in 250 ml D5W IV every 2 weeks) because of his extensive disease.² He completed 6 cycles by June 2016. However, he returned in July 2016 with worsening back pain. A repeat CT scan revealed significant improvement in the disseminated lymphadenopathy, but worsening osseous metastatic disease was seen in the lumbar, thoracic, and pelvic regions. A pelvic lytic lesion biopsy revealed Kaposi sarcoma; pathology showed spindle cells positive for CD34, CD31, and HHV-8 (Figure 2). The patient received palliative radiation to the spine, aiding in pain management and ambulatory dysfunction. He continued with his noncompliance with all medications and outpatient follow-ups, and after XXX succumbed to his disease burden.

Discussion

Kaposi sarcoma is a low-grade mesenchymal tumor that involves the blood and lymphatic vessels.³ Its association with AIDS was revealed in the early 1980s at the start of the HIV epidemic in the United States. In 1994, Chang and colleagues discovered the association between Kaposi sarcoma and HHV-8 by isolating DNA fragments of HHV in Kaposi sarcoma tumors from AIDS patients.⁴ The mode of transmission of HHV-8 has not been fully decoded. It has been presumed that adult homosexual contact continues to be an important route of transmission, inferring a common route of infection. In 1990, the

Accepted for publication April 17, 2017. Correspondence: Mariola Vazquez-Martinez, MD; mariolavazquez89@gmail.com. Disclosures: The authors report no disclosures or conflicts of interest. JCSO 2017;15(3):e170-e173. ©2017 Frontline Medical Communications. doi: <https://doi.org/10.12788/jcso.0343>

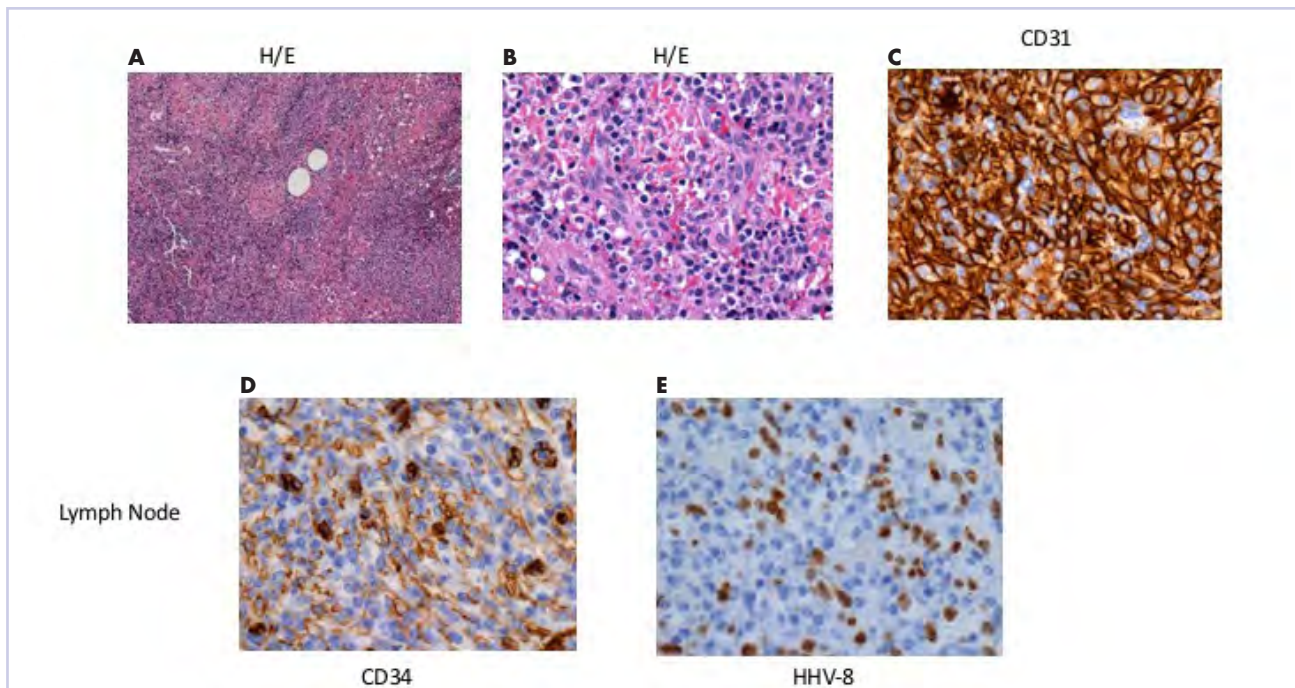


FIGURE 1 Results of left axillary lymph node biopsy (scale bar, 40 μ m). **A**, The node architecture is partially effaced with interwoven fascicles of spindle, oval- to round- shaped atypical cells, vascular slits and erythrocytes, predominantly located in interfollicular areas, sinusoids, and with extension into perinodal adipose tissue. Some residual follicles are present. The preserved B-cell follicles are positive for CD20. **B**, Increased magnification of the picture A demonstrating atypical cells. CD10 and BCL-6 are positive in scattered cells. **C**, The atypical cells are positive for CD31. **D**, The atypical cells are positive for CD34. **E**, The atypical cells are positive for latency-associated nuclear antigen human herpes virus-8 (granular nuclear staining).

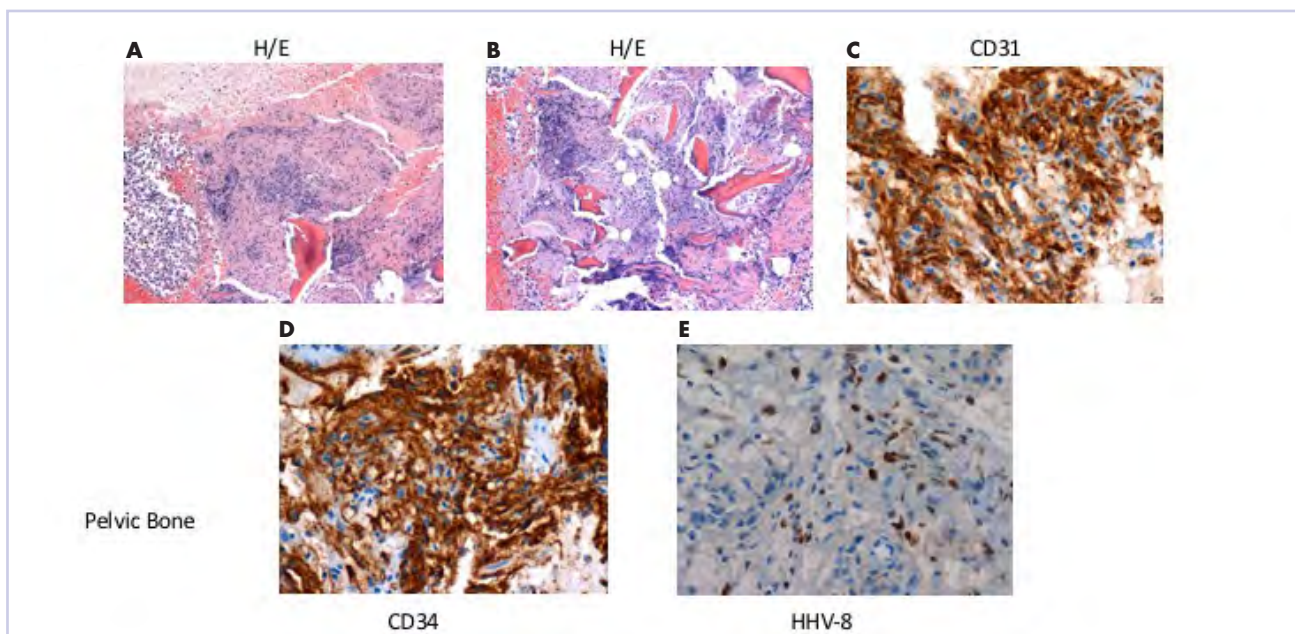


FIGURE 2 Results of the pelvic bone biopsy (scale bar, 40 μ m). **A**, A focus of proliferation of ill-defined fascicles of oval spindle cells separated by slit-like spaces containing erythrocytes. The stroma shows infiltration of lymphoid proliferation with numerous plasma cells and immunoblasts. **B**, Increased magnification of the picture A demonstrating atypical cells. **C**, The atypical cells are positive for CD31. **D**, The atypical cells are positive for CD34. **E**, The atypical cells are positive for latency-associated nuclear antigen human herpes virus-8 (granular nuclear staining).

overall risk of developing Kaposi sarcoma in AIDS patients was 20,000 times greater than it was in the general population, and 300 times greater than in other immunosuppressed patients.⁵ This suggests an increase in incidence, in direct relation, with a decrease in the CD4 count.

Kaposi sarcoma can present with a range of clinical features, from negligible cutaneous lesions to a hastily progressing neoplasm. Involvement in the musculoskeletal system is infrequent, but encountered increasingly in the AIDS-related subtype. Moreover, it is recurrently observed in the African population.⁶ In one of the largest reviews to date exploring Kaposi sarcoma involving the musculoskeletal system, Caponetti and colleagues observed the greatest osseous involvement distinctly in patients with CD4 and T-cell counts below 100 cells/mm³.⁶

Kaposi sarcoma musculoskeletal involvement, specifically bone, is atypical. If it does occur, it usually manifests as a result of contiguous invasion from an adjacent nonos-

seous lesion. Caponetti and colleagues that isolated osseous Kaposi sarcoma lesions (with no overlying skin lesion) were found to be more likely to be associated with AIDS in the review by Caponetti and colleagues.⁶ As in our patient, it is also typically a manifestation of more widely disseminated disease.⁷

Most of the osseous lytic lesions in AIDS patients are located in the axial skeleton. Radiological features of musculoskeletal Kaposi sarcoma are variable. As observed by Caponetti and colleagues, Kaposi sarcoma lesions can appear as a periosteal reaction, cortical erosions, osteolysis, or osseous destruction, with irregular-shaped cortical erosions being most typical.⁶ Despite their osteolytic features, Kaposi sarcoma lesions are often not visualized by conventional radiography.⁶ The preferred imaging for identification of lytic bone changes is CT (Figure 3). Magnetic resonance imaging can also help distinguish marrow abnormalities as well as adjacent soft tissues masses. Radiologically, Kaposi sarcoma osseous lesions have parallel features to bacillary angiomatosis, tuberculosis, or lymphoma.⁸ Therefore, biopsy of the lesion is essential in establishing the diagnosis of Kaposi sarcoma.

The etiologic prompt for Kaposi sarcoma has not been fully elucidated. However, it has been hypothesized that HHV-8 infection may initiate the process. Guihot and colleagues showed that patients with Kaposi sarcoma have notably fewer HHV-8-specific T cells than patients who are asymptomatic HHV-8 carriers, regardless of CD4 T-cell count or HHV-8 load.⁸ As per Guihot's conclusions, this impairment may be culpable for the deranged proliferation of HHV-8-transformed cells and the ultimate manifestation of Kaposi sarcoma.⁹ An insufficient T-cell response to HHV-8 lytic antigens is associated with Kaposi sarcoma and continues to support the notion that such genes are important in Kaposi sarcoma oncogenesis.

In theory, there should be clinical improvement in Kaposi sarcoma when immunity is restored. Cancers caused by the Epstein-Barr virus and Kaposi sarcoma-associated herpes virus may eventually also be preventable with vaccines.¹⁰

There is rarely bone involvement without the foreshadowing of a poor prognosis. Erroneous patient care may inevitably arise from Kaposi sarcoma in uncharacteristic sites. A differential of Kaposi sarcoma should be included if a patient with AIDS presents with osteolytic lesions on imaging. Biopsying the lesion cements the diagnosis and eliminates the possibility of mimicry conditions such as bacillary angiomatosis, benign vascular lesions, and angiosarcoma. As of today, a HAART regimen remains the standard initial care for patients with Kaposi sarcoma.



FIGURE 3 Osteolytic vertebral lesions (sagittal view). Red arrows show the osteolytic lesions in the L2 (left) and in L2 and L5 (right) vertebrae.

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