

Pulmonary Hemorrhage as the Initial Presentation of AIDS-Related Kaposi Sarcoma

Yasmin Amir, MD; Ali Hadi, MD; Ahmed Hadi, MD

PRACTICE POINTS

- Visceral Kaposi sarcoma (KS) should be considered in patients with unexplained systemic symptoms in the setting of poorly controlled human immunodeficiency virus (HIV).
- If cutaneous KS is diagnosed in an HIV patient, a detailed history and physical examination should be undertaken to evaluate for signs of systemic disease.

To the Editor:

Kaposi sarcoma (KS) is an angioproliferative tumor of endothelial origin associated with human herpesvirus 8 infection. It is one of the most prevalent opportunistic infections associated with AIDS and is considered an AIDS-defining illness. In the general population, the incidence of KS is 1 in 100,000 worldwide.¹ At the onset of the human immunodeficiency virus (HIV) epidemic in the early 1980s, 25% of individuals with AIDS were found to have KS at the time of AIDS diagnosis. Beginning in the mid-1980s and early 1990s with the introduction of highly active antiretroviral therapy (HAART), the incidence of KS declined to 2% to 4%,² likely secondary to restoration of immune response.³

The clinical course of KS ranges from benign to severe, involving both cutaneous and visceral forms of disease. Cutaneous KS is the most common form of disease and typically characterizes the initial presentation. It is classically described as violaceous patches, papules, or plaques that can become confluent, forming larger tumors over time. Biopsy of cutaneous lesions may vary based on the clinical morphology. The patch stage

typically is characterized by abnormal proliferating vessels surrounding larger ectatic vessels.⁴ Vascular spaces are more jagged and lined by thin endothelial cells extending into the dermis, forming the classic promontory sign.⁵ In the plaque stage, the vascular infiltrate becomes more diffuse, involving the dermis and subcutis, and there is proliferation of spindle cells.⁴ In the nodular stage, spindle-shaped tumor cells form fascicles and vascular spaces become more dilated.^{4,5} Advanced lesions are further associated with hyaline globules staining positive with periodic acid–Schiff.⁴ Lymphocytes, plasma cells, and hemosiderin-laden macrophages are admixed within this pathologic architecture.^{4,5}

Visceral KS most commonly occurs in the oropharynx, respiratory tract, and gastrointestinal tract, and rarely is the initial presentation of disease. Classically, visceral KS is an aggressive, potentially life-threatening form of disease and has been found to have a much worse prognosis than cutaneous KS alone. Pulmonary involvement is the second most common site of extracutaneous KS and is known as the most severely life-threatening form of disease.¹ Interestingly, since the advent of HAART, the incidence of KS with involvement of the visceral organs has declined at a more dramatic rate than cutaneous KS alone.³ Therefore, although more aggressive in nature, KS with visceral features has become increasingly rare and should be largely preventable given advances in AIDS therapy. We present a case of advanced AIDS-related KS with pulmonary involvement that is rarely seen after the advent of HAART.

A 39-year-old man with HIV diagnosed 8 years prior presented with fever, chest pain, progressive dyspnea, and hemoptysis of 5 months' duration. At the time, he was nonadherent to medications and had poor

From the Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, New York.

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Correspondence: Ali Hadi, MD, 1425 Madison Ave, New York, NY 10029 (alihadi91@gmail.com).

follow-up with primary care physicians. At presentation he was tachycardic (149 beats per minute), tachypneic (26 breaths per minute), and his oxygen saturation was 80% on room air. Physical examination of the skin revealed asymptomatic violaceous penile lesions that the patient reported had been present for the last 8 months (Figure 1). Pertinent laboratory values included an HIV-1 viral load of 480,135 copies/mL (reference range, <20 copies/mL) and CD4 count of 14 cells/mm³ (reference range, 480–1700 cells/mm³). A chest radiograph was obtained and revealed bibasilar opacities compatible with a pleural and/or parenchymal process. Bronchoscopy was then performed and revealed bloody secretions throughout the tracheobronchial tree.

Histologic examination of biopsies of the penile lesions revealed spindle cell proliferation with hemorrhage (Figure 2A) that stained positively for HHV-8 (Figure 2B), consistent with KS. Biopsies taken during bronchoscopy similarly revealed spindle cells with hemorrhage (Figure 3). The patient was diagnosed with AIDS-related KS with visceral involvement of the lung parenchyma and tracheobronchial tree. The patient was then admitted to the medical intensive care unit and intubated. Therapy with HAART and paclitaxel was initiated. After 7 days of poor response to therapy, the family opted for terminal extubation and comfort care measures. The patient died hours later.

This case report describes the classic phenomenon of AIDS-related KS in a patient with a long-standing history of immunocompromise. Even in the era of HAART, this patient developed a severe form of visceral KS with involvement of the respiratory tract and lung parenchyma.



FIGURE 1. Violaceous crusted plaque on the penis consistent with Kaposi sarcoma.

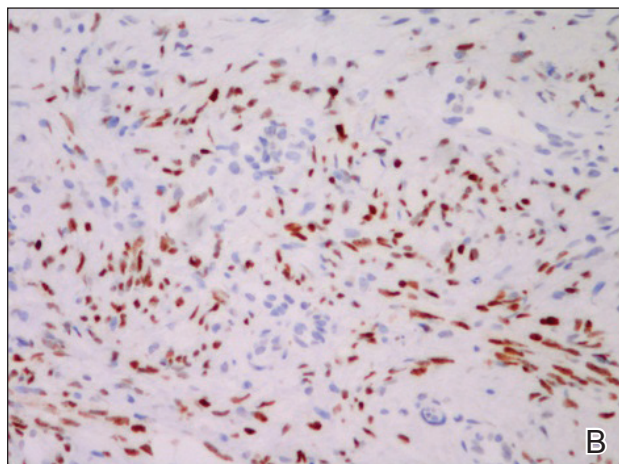
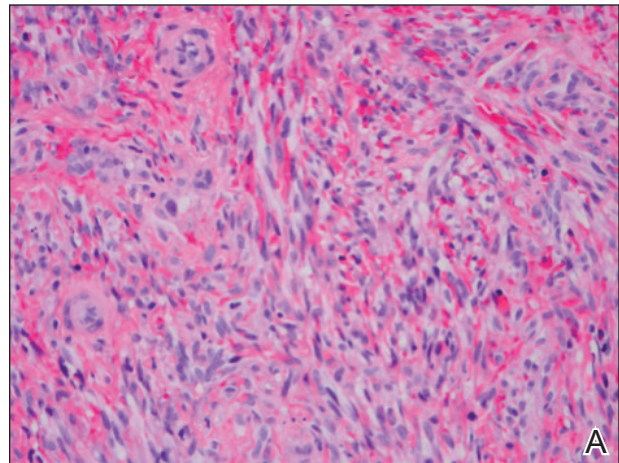


FIGURE 2. A, Histopathology of a penile lesion showed spindle cell proliferation with hemorrhage (H&E, original magnification $\times 40$). B, Histopathology stained positive for human herpesvirus 8 (original magnification $\times 40$).

Since the advent of HAART for the treatment of HIV/AIDS, the incidence of KS, both visceral and cutaneous forms, has dramatically declined; the risk for visceral KS declined by more than 50% but less than 30% for cutaneous KS, supporting the observation that although visceral involvement has classically been noted as the more aggressive and life-threatening form of disease, HAART appears to have a stronger effect on visceral disease than cutaneous disease.³ Although the overall impact of AIDS-defining illnesses has substantially improved over the years, those with AIDS infection remain at risk for opportunistic illness.²

It has been shown that HAART therapy leads to response in more than 50% of cases of KS.⁵ The administration of HAART in KS patients is associated with improved survival and an 80% reduced risk of death, even when started after KS is diagnosed.⁶ In a comparison of the differences in clinical manifestations of KS between patients who were already receiving HAART at the time of KS diagnosis to those who were not on HAART, it was

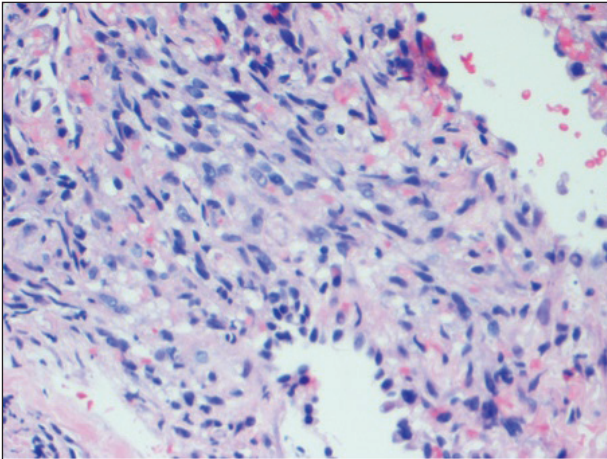


FIGURE 3. Histopathology of the bronchopulmonary tree during bronchoscopy showed evidence of spindle cell proliferation and hemorrhage (H&E, original magnification $\times 40$).

shown that patients already on therapy presented with less aggressive clinical features. A smaller percentage of patients who were already on HAART at KS diagnosis presented with visceral disease compared to those who were not on therapy.⁷

It is evident that treatment of AIDS patients with HAART is not only first-line therapy for the disease but also the best preventative measure against development of KS. Management of KS also centers around the initiation of HAART if the patient is not already maintained on the proper therapy.⁸ In addition to HAART, treatment options for visceral KS include a variety of chemotherapeutic agents, including but not limited to the use of single-agent adriamycin, vinblastine, paclitaxel, and thalidomide, or combination therapies.

Although notable advances have been made in the management of AIDS patients, this case highlights the

need for clinicians to be aware of the risk for KS in the context of immunocompromise. Specifically, patients with advanced AIDS who are not adherent to HAART or who have a poor response to therapy have an amplified risk for developing KS in general as well as an increased risk for developing more severe visceral KS. Maintenance of patients with HAART is shown to greatly reduce the risk for both cutaneous and visceral KS; therefore, patient adherence with therapy is of utmost importance in preventing the occurrence of this deadly disease and its complications. Appropriate follow-up should be made, ensuring that these patients at high risk are adherent to therapy and have proper access to medical care to allow for prevention and early identification of potential complications.

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