



Case Report

Pulmonary Kaposi's sarcoma as the initial presentation of human immunodeficiency virus infection



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ABSTRACT

Kaposi's sarcoma (KS) usually presents in HIV-infected patients with cutaneous lesions that may advance to extensive visceral disease. There have been only a few documented cases in which the initial presentation of Kaposi's sarcoma involved the bronchopulmonary system. We describe a newly diagnosed patient who presented with pulmonary KS as his initial presentation of the disease. Our report is intended to increase clinicians' awareness that pulmonary Kaposi's sarcoma should be considered in HIV-infected patients who present with respiratory symptoms, even if they do not manifest the typical mucocutaneous manifestations of KS or have low CD4 counts. Early diagnosis and therapy are essential in improving outcomes as this condition carries a high mortality.

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Introduction

HIV-related Kaposi's sarcoma (KS) is a low grade vascular tumor associated with human herpesvirus 8 (HHV-8), usually seen in patients with low CD4 cell counts. Kaposi's sarcoma (KS) presents with mucocutaneous disease in 80–90% of cases, but may advance to extensive visceral disease [1]. In rare instances, early presentation may manifest with only respiratory signs and symptoms. We describe a patient with bronchopulmonary KS as the initial presentation of HIV infection.

Case presentation

A 29-year-old man with no significant past medical or sexual history other than having sex with men presented to the emergency department with a three-month history of increasing lower extremity edema. The patient was noted to have a warm, erythematous area on his right tibia with slight serous drainage consistent with a cellulitis or early abscess. Cultures of the lesion grew methicillin-susceptible *Staphylococcus aureus*. His HIV

antibody test was positive; CD4 count was 325 cells/mm³ and plasma HIV RNA viral load was 518,645 copies/ml. The patient was treated with a 10-day course of oral trimethoprim-sulfamethoxazole and cephalexin. He returned one month later with complaints of shortness of breath, dry cough, and swelling of his lower extremities, scrotum and penis. On examination, he was febrile and had diffuse adenopathy with palpable anterior and posterior cervical, submental, supraclavicular and axillary lymph nodes and extensive edema involving the bilateral lower extremities. No other mucosal or skin findings were present. Diffuse interstitial infiltrates and basilar alveolar opacities were present on chest radiographs. Computed tomography (CT) scan of the chest, abdomen and pelvis demonstrated diffuse anasarca and ill-defined nodular opacities in both lung bases (Fig. 1).

Antiretroviral therapy (ART) with darunavir, ritonavir and raltegravir was initiated. He was treated empirically with intravenous trimethoprim-sulfamethoxazole for possible pneumocystis pneumonia and azithromycin and ceftriaxone for possible community acquired pneumonia. The following day his respiratory status deteriorated requiring transfer to the intensive care unit. He underwent bronchoscopy with transbronchial biopsy of the right lower lobe and left lower lobe. No gross endobronchial lesions were noted. The bronchial biopsy showed areas of interstitial spindle cell proliferation extending into alveolar septae (Figs. 2 and 3). Immunoperoxidase staining for human herpes

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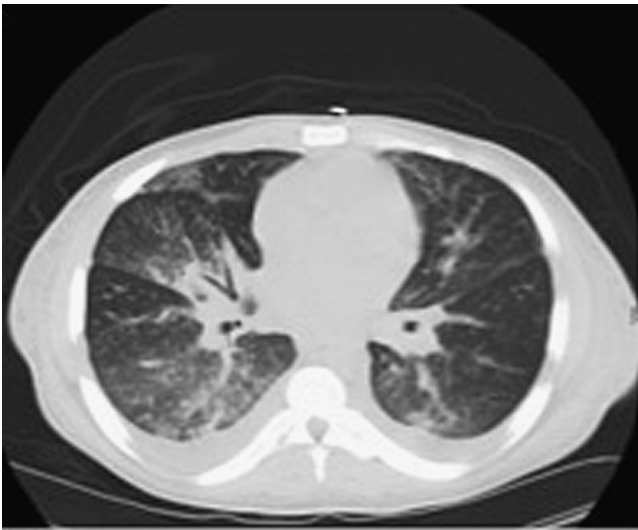


Fig. 1. Computed tomography scan of the chest. CT of the chest showing anasarca, pulmonary edema, small bilateral pleural effusions, and ill-defined nodular opacities in both lung bases.

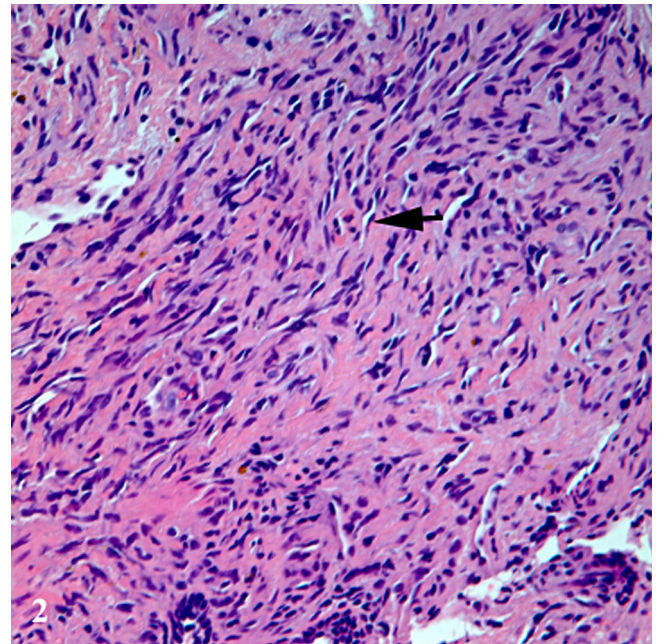


Fig. 3. Intermediate power micrograph showing an area of spindle cell proliferation seen in Fig. 2. The arrow points to a cleft like space lined by spindle cells (H&E stain, 100× magnification).

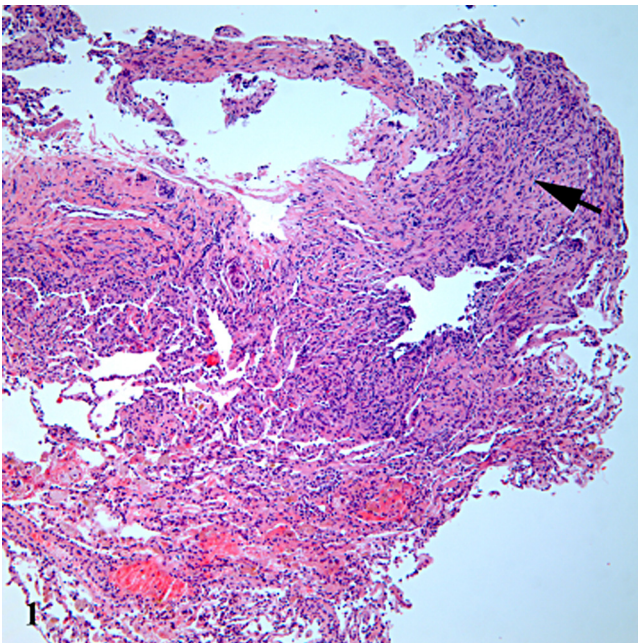


Fig. 2. Histopathology. Scanning power micrograph of the bronchial biopsy showing the pulmonary parenchyma with proliferation of spindle cells (arrow) forming cleft like spaces, widening the interstitium and extending to the alveolar septae (H&E stain, 40× magnification).

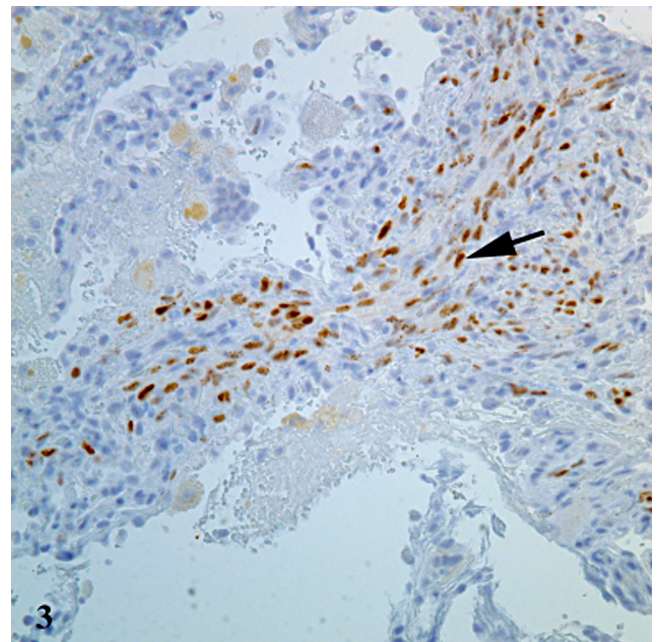


Fig. 4. Intermediate power photomicrograph of the bronchial biopsy stained by the immunoperoxidase method for human herpes virus-8 (HHV8) in an area of spindle cell proliferation. The brown stained nuclei (arrow) represent a positive reaction diagnostic of involvement by Kaposi's sarcoma (HHV-8 immunoperoxidase stain, 100× magnification).

virus-8 (HHV8) showed positive nuclear staining in the proliferating spindle cells, confirming the diagnosis of pulmonary Kaposi's sarcoma (Fig. 4). The patient was evaluated by our oncology service but was considered too ill to tolerate radiation or chemotherapy for treatment of KS. He was continued on ART, but developed progressive symptoms and expired two weeks after diagnosis.

Discussion

Pulmonary KS has been reported to occur in 6–32% of HIV-infected patients with cutaneous disease, with ages ranging from 22 to 71 years; less than 5% present with pulmonary KS as the

initial manifestation [13]. KS is more common in men who have sex with men, but cases have been reported in women as well. HIV-infected patients with pulmonary KS may be asymptomatic or present with shortness of breath, fever, cough, chest pain, or hemoptysis. Pulmonary KS can involve the lung parenchyma, pleural spaces, airways and lymph nodes [5]. Initial manifestations include erythematous, violaceous cutaneous lesions (macular, papular or nodular) involving the face, oral mucosa, and upper

trunk, with increasing involvement of visceral organs as the disease progresses [7]. CD4 counts are usually <200 cells/mm [3], but more recent observation has shown an increased incidence of KS at CD4 \geq 350 [4]. Patients with parenchymal lung involvement may present with dyspnea, hypoxemia, or dry cough that develops over weeks. In some cases, hemoptysis, fever, malaise and respiratory failure may occur [13]. Pleural effusions can be seen in up to two-thirds of patients with parenchymal KS and may be the sole initial manifestation of the disease. Rapid progression of pulmonary KS may occur in the setting of glucocorticoid use for other conditions in HIV-infected patients [5,13].

Diagnosis of pulmonary KS is based on physical examination findings, CT features, and characteristic endobronchial lesions [1]. Findings suggestive of KS on chest CT include hilar densities along peribronchovascular pathways, and a nodular pattern along with pleural effusions [8]. The diagnosis is confirmed by typical pathologic features such as inflammation, angiogenesis, spindle cell proliferation and PCR or HHV-8 immunoassay on tissue biopsy [7]. Seroprevalence of HHV-8 is 80–95% in patients with classic KS, with HHV-8 detection via bronchoalveolar lavage in more than 80% of patients with pulmonary KS [11]. Infection of endothelial cells by HHV8 leads to expression of viral protein products, which creates an angiogenic-inflammatory state. KS results from proliferation of cells in response to this inflammatory state and various angiogenic cytokines [6]. Development of KS is strongly associated with defects in cellular immunity. Decreasing CD4 counts have shown to be associated with increasing risk of AIDS associated KS [2].

Characteristic endobronchial lesions have a macular red or purple appearance, and may be located at the airway bifurcations. Diagnosis of pulmonary KS may be made presumptively if these characteristic lesions are present along with radiologic findings, and infection has been excluded [5]. If characteristic endobronchial lesions are present, biopsy of these lesions is generally not recommended as this may lead to pulmonary hemorrhage [12]. However, lung biopsy may be needed to make a definitive diagnosis in cases when the clinical and radiological picture is not typical [5]. Diagnosis is essential as pulmonary KS may mimic infectious causes and treatment of these conditions differs. Our patient did not have the characteristic endobronchial lesions and bronchial biopsy established the diagnosis.

Treatment includes antiretroviral therapy with chemotherapy reserved for patients with symptomatic pulmonary disease or those with disease progression despite antiretroviral therapy [3]. Some patients with pulmonary KS have been treated with ART alone and sustained an adequate response to treatment, while others require chemotherapy [5]. Patients who have symptomatic pulmonary involvement or evidence of disease progression despite ART may benefit from chemotherapy. First-line chemotherapy agents for the treatment of KS include the anthracyclines – liposomal doxorubicin and liposomal danorubicin [9]. Stebbing and colleagues proposed a prognostic index for acquired immunodeficiency syndrome (AIDS) associated KS, which includes four factors: age, the occurrence of KS at or after AIDS onset, presence of comorbid conditions, and immune status as marked by the CD4 count [14]. These widely used factors were incorporated into a prognostic score calculation in a large study of 5873 patients. The authors suggest that those with a high risk (score >12), should be treated with ART and chemotherapy together, while those with a low risk (score <5) may be given ART alone, with chemotherapy considered if progression of disease occurs. However in some cases, the systemic chemotherapy itself may be associated with a higher morbidity. In severe cases, patients may be considered for entry into clinical studies with newer agents [14]. Our patient had poor prognostic factors and was not given chemotherapy due to high risk for associated morbidity.

In patients with endobronchial obstruction as a result of pulmonary KS, therapy should be aimed at maintaining an adequate airway and oxygenation. This may require endoscopic laser resection, stent placement or radiation therapy [5,7]. Even with the advent of ART and chemotherapy, pulmonary KS remains an ominous diagnosis with a median survival of only 1.6 years. In one large study of 1140 patients, five-year survival for patients with pulmonary KS was 49% as compared to 82% for those with classic KS [3,13].

Aboulafi reported a frequency of 0–15% in patients with pulmonary KS without mucocutaneous involvement, but rarely did pulmonary KS present initially [1]. As this case illustrates, pulmonary KS should be considered in patients with or at risk for HIV infection who present with respiratory symptoms, even if the typical mucocutaneous manifestations of KS or low CD4 cell counts are absent. Patients with pulmonary KS may present with shortness of breath, cough, chest pain, or less commonly, hemoptysis. In certain cases, asymptomatic patients may have abnormalities on CT scan characteristic of pulmonary KS such as hilar densities along peribronchovascular pathways, and a septal or nodular pattern with pleural effusions. The diagnosis of HIV related pulmonary KS is often clinical: based on mucocutaneous disease, suggestive findings on CT scan, and characteristic endobronchial lesions. A detailed evaluation should be performed to exclude other infectious causes or tumors. Our patient presented with shortness of breath, but did not have these CT findings or endobronchial lesions; lung biopsy was required to make the definitive diagnosis.

Pulmonary KS should also be considered in the differential when HIV-infected patients develop rapidly progressive respiratory symptoms after the initiation of glucocorticoid therapy. Treatment with combination antiretroviral therapy is recommended for all patients. For those with symptomatic pulmonary involvement or evidence of disease progression despite ART, chemotherapy should be considered. Early diagnosis and therapy are essential in improving outcomes in this potentially deadly disease.

Conflict of interest

The authors declare no conflict of interest.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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