Case report

Primary pulmonary Kaposi Sarcoma in a newly diagnosed cisgender heterosexual HIV positive patient presenting before cutaneous manifestations

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Introduction

AIDS-related KS is a well described and recognized disease in which visceral involvement is rare. It is mainly found in men who have sex with men (MSM) or bisexual men infected with the human herpes virus 8 (HHV-8) [1]. KS in the lungs is usually seen in the setting of extensive mucocutaneous disease and is rarely a primary event. Antiretroviral therapy (ART) and chemotherapy are the mainstays of treatment for widespread KS [2]. After initiation of ART, HHV-8 levels in plasma and new tumor formation declines due to increase in immune response. Consequently, effective ART use has led to decreased incidence of KS in the United States [2].

Case report

A 24-year-old African American male with three week history of newly diagnosed HIV infection, presented to the emergency department (ED) with 1 month history of pleuritic chest pain, shortness of breath and nonproductive cough. He also experienced a 15 pound weight loss over the past 3 months with decrease in appetite. He was only sexually active with women. The patient had missed his first scheduled follow up visit and so he had not been initiated on ART.

Initial physical exam in the ED, showed the following: blood pressure of 129/64 mmHg, heart rate of 117 beats/min, temperature of 98.1°F, respiratory rate of 17 breaths/min and oxygen saturation of 100% while on room air. He was alert and oriented and not in distress. He was noted to have non-tender right sided cervical lymphadenopathy and bilateral rhonchi at lung bases. There was no skin breakdown or rash seen on inspection. Laboratory results were significant for WBC 3200/mm³ with 13% lymphocytes, hemoglobin 11.6 g/dL, LDH 272 U/L, creatinine 1.9 mg/dL, CD4 count 54/mm³, and HIV viral load 334,991 copies/mL. Chest radiograph (CR) showed coarse bilateral lower lung interstitial infiltrates and mild perihilar infiltrates (Fig. 1).

He was admitted to the hospital for suspected HIV related pulmonary infection and empirically started on trimethoprim/ sulfamethoxazole and azithromycin. Workup was negative including evaluation for Mycobacterium tuberculosis, Legionella pneumonia, Histoplasma capsulatum, Cryptococcus neoforms, and viral respiratory panel including influenza virus. On day 3 of hospital admission, physical exam revealed a new papular dark violaceous skin rash under his left eye, and lesions on his left shoulder, bilateral arms and torso. The papules were suspicious for KS and a left shoulder skin biopsy was performed. The biopsy showed a

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ABBREVIATIONS

AIDS-related Kaposi sarcoma (KS) is a vascular malignancy that usually presents with mucocutaneous lesions. Bronchopulmonary involvement as an initial manifestation is a rare phenomenon. This case describes a young male presenting with pulmonary symptoms mimicking HIV-related opportunistic infection who was eventually diagnosed with primary pulmonary KS. The aim of this report is to emphasize that KS should be recognized as a differential diagnosis in AIDS patients presenting with pulmonary symptoms. Making the diagnosis may be a difficult task, at times, requiring invasive procedures such as lung biopsy.

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vascular tumor positive for HHV-8 immunostain confirming the diagnosis of KS. Meanwhile, a bronchoalveolar lavage (BAL) was done and silver stain was negative for *Pneumocystis jirovecii* pneumonia (PJP). Nine days after admission, his creatinine levels progressively worsened from 1.86 on initial presentation to 2.70. It was determined that trimethoprim/sulfamethoxazole was contributing to his acute kidney injury and he was switched to atovaquone for PJP prophylaxis.

High resolution chest CT (Fig. 2) was performed which revealed diffuse irregular opacities of varying appearance with linear and nodular features, mixed confluent and nodular soft tissue and interlobular septal thickening. Bronchoscopy with BAL was repeated. No bronchial lesions were visualized and, again, the pathology and cultures were negative. During the course of his hospital stay, patient continued to develop fevers as high as 102 degrees Fahrenheit with multiple episodes of diarrhea, tachypnea, tachycardia, and hypoxemia. However, blood cultures and *Clostridium difficile* toxin were negative. His lung auscultatory findings worsened and diffuse bilateral crackles and rhonchi were audible. CXR showed worsening pleural effusions bilaterally.

Video assisted thoracoscopic surgery (VATS) was done which showed multiple diffuse hemorrhagic lesions in the right upper, middle, and lower lung lobes with a suspicion for KS. The right middle lobe lung biopsy revealed multifocal perivascular atypical spindle cell proliferation staining strongly positive for HHV-8 Latency Associated Nuclear Antigen. (Fig. 3) He was diagnosed with AIDS related KS and was started on ART therapy. Patient was transferred to an outside hospital after 33 days of hospitalization for chemotherapy. He received 6 cycles of doxorubicin and his last cycle was 4 months after initial diagnosis. He was seen at an infectious disease outpatient clinic 3 months after diagnosis and was doing well with a CD4 count of 211/mm³ and a viral load of 431 copies/mL.

![Fig. 1. CXR PA and lateral view on initial presentation showing coarse bilateral interstitial and perihilar infiltrates.](image1)

![Fig. 2. High resolution CT scan showing diffuse irregular opacities with interlobular septal thickening.](image2)
Discussion

Among HIV positive patients, detection of HHV-8 antibody is an indication of KS. KS is 20 times more likely to occur in homosexual men than in heterosexual men. In the 1980s, 40% of homosexual American men diagnosed with AIDS were found to have KS at the time of initial diagnosis, which later dropped to 20% in the 1990s [1]. According to the CDC, this change has been reported due to the improved treatment with ART triple therapy leading to a 59% reduction in incidence.

Pulmonary KS is considered a rare finding in the absence of cutaneous manifestations [3]. The number of cases may be underreported due to the fact that pulmonary KS is not among the top differentials for pulmonary disease in AIDS patients. In HIV positive patients presenting with pulmonary symptoms, organisms such as Pneumocystis jiroveci, Histoplasma capsulatum, Mycobacterium tuberculosis, and Legionella pneumophila are considered the top culprits. Sometimes only after an invasive lung biopsy, is the diagnosis of KS definite, as seen with our patient. Many times this route is avoided due to risk of complications such as pneumothorax or hemorrhage. Therefore, majority cases of confirmed pulmonary KS have been reported postmortem in HIV positive patients with cutaneous manifestation [4].

The clinical presentation of pulmonary KS is indistinguishable from other respiratory infections. Majority of patients present with dyspnea and cough, while a few can have fever, night sweats, hemoptysis, or chest pain [1]. An article established three traits of pulmonary KS. Firstly, respiratory involvement frequently occurs after, rather than before the development of mucocutaneous lesions. Secondly, pulmonary involvement is usually detected more frequently at autopsy (50%) rather than clinically (33%). Lastly, a coexisting opportunistic infection is present in approximately two thirds of patients with known KS who present with new pulmonary findings [1]. Our patient did not present with classic cutaneous KS initially but developed the characteristic violaceous papules on his face and shoulders about a month after his respiratory symptoms began.

For the diagnosis of pulmonary KS, the chest radiograph frequently shows thickening along bronchovascular bundles in the perihilar region. A reticulonodular infiltrate can appear as the tumor grows [1]. These nodules can become irregular with further development of interstitial infiltrates, along with hilar and mediastinal lymphadenopathy. In 50% of the cases, a pleural effusion is present, as shown in our case.

Visualization of the lesions via bronchoscopy appears to be the most sensitive modality for diagnosis of pulmonary KS. However, 40–70% of the pulmonary KS cases are diagnosed via alternative techniques [5]. As in this case, there were no visible tracheobronchial lesions on bronchoscopy and ultimately VATS and lung biopsy had to be performed.

For widespread KS, treatment is required with both ART and chemotherapy. After ART is initiated, HHV-8 levels in plasma and new tumor formation declines due to increase in immune response. Consequently, effective ART use has led to decreased incidence of KS in the United States [3]. The most widely used regimen for the treatment of pulmonary KS has been adriamycin, bleomycin, and vindristine or vindesine (ABV) combination chemotherapy. It has been shown that with ABV, pulmonary symptoms resolved even before radiographic changes were seen. Unfortunately, such benefits are usually short lived, and even with combination therapy, time until relapse is usually brief. In one study with 30 AIDS patients on chemotherapy, 2 patients died and 24 of the remaining 28 had at least one episode of neutropenia. The median survival in patients was only 6.5 months [6]. Roughly half of patients died from progressive KS and respiratory failure. Neutropenia and infection were common complications.

Recently, the US Food and Drug Administration approved the use of liposomal daunorubicin and liposomal doxorubicin for treatment of AIDS-related KS. These drugs are effective and are generally associated with less alopecia, mucositis, and cardiotoxicity than their non liposomal anthracycline counterparts.

Patients on ART are found to have an indolent presentation, seen in a study showing 60% of the study patients on ART having 10 or less lesions and 21% having only one lesion [2]. In patients who are already on ART, there is also a decrease in visceral KS presentation.

Conclusion

Pulmonary Kaposi sarcoma is a very rare presentation of AIDS related KS and can represent a diagnostic challenge as seen in this
Pulmonary KS presents with nonspecific respiratory symptoms, therefore, it is often a diagnosis of exclusion. Patients with mucocutaneous presentation of KS, low CD4 count and high viral load are at higher risk for pulmonary involvement. Lung biopsy may be needed for final diagnosis.

Consent

Written consent was taken from the patient and is available upon request.

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Conflict of interest

None of the authors report any financial or personal conflicts of interest with this report.

Author statement

Sarah Khan, the primary author, contributed to Conceptualization, Roles/Writing of original draft and review and editing. Jolie Guevara contributed to Conceptualization and Writing including Review and editing. Ana Barbosa, Awista Ayuby, and Fred Bien-Aime contributed to Data Curation and Roles/Writing of original draft. Larissa Verda contributed to Writing/review and editing. Nancy Glick was directly involved in Investigation, project administration, supervision, and review and editing. Vikas Mehta contributed to Data curation, Investigation, and Visualization.

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