JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES
2019, VOL. 9, NO. 4, 354–357
https://doi.org/10.1080/20009666.2019.1640017

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CASE REPORT

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A rare case of pulmonary Kaposi sarcoma presented with respiratory failure

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ABSTRACT

Kaposi sarcoma (KS) is the most commonly diagnosed malignancy in HIV-infected patients. With new treatments, incidence and severity of KS have significantly decreased.

A 57-year-old African American male with medical history of AIDS presented with progressively worsening cough, shortness of breath, fever, night sweats, and 60 lb weight loss. On physical examination, he had diffused dark purple skin lesions and decreased air entry in the right lower lung fields. Chest x-ray and subsequent chest computed tomography (CT) showed moderate right lung pleural effusion with scattered bilateral diffuse infiltrates. The patient's absolute CD4 count was 27 cells/microliter. Thoracentesis was negative for infection or malignancy. He was started on chemotherapy paclitaxel along with HAART for extensive pulmonary KS. Since starting the treatment, his condition has significantly improved with near complete resolution of the pleural effusion, oral, and skin lesions.

In conclusion, the diagnosis of AIDS-related pulmonary KS is often clinical, typically based on the presence of mucocutaneous disease and compatible features on CT chest. The differential diagnosis of pulmonary KS is broad. A detailed evaluation should exclude an infectious etiology or other tumors. Chemotherapy along with HAART can be used for treatment of severe pulmonary KS.

ARTICLE HISTORY
Received 2 April 2019
Accepted 28 June 2019

KEYWORDS
AIDS; Kaposi sarcoma; Chemotherapy; HAART

1. Introduction

Kaposi sarcoma (KS) is a vascular tumor of the blood vessels and lymph nodes associated with the Human Herpesvirus 8 (HHV-8) also known as KS Herpesvirus (KSHV) [1–3]. KS usually develops in the patients with acquired immunodeficiency. It is one of the major complications of acquired immunodeficiency syndrome (AIDS) [4] and most often is seen in the patients with Low CD4 cell counts. Since introduction of antiretroviral therapy, there has been significant improvement in the clinical outcome of the patients with HIV infection. The use of highly active antiretroviral therapies (HAART) has led to a decline in the incidence of KS [4–7]. A prospective cohort study of HIV-infected individuals before and after introduction of HAART demonstrated decrease in incidence of KS from 30/1000 patient-years prior to 1995 to 0.03/1000 patient-year in 2001 [8].

KS usually presents with cutaneous lesions which progress slowly, but it can also present as an aggressive disease with significant morbidity and mortality [7,9]. In 80–90 percent of the cases, pulmonary involvement with KS occurs in the setting of extensive mucocutaneous disease [9,10]. However, the pulmonary involvement can be the initial manifestation of KS and occurs in 15 percent of the patients without mucocutaneous involvement [11,12].

2. Case

A 57-year-old African American male with medical history of AIDS presented with progressively worsening cough, shortness of breath, intermittent fever, and night sweats for about 10 months. He also reported 60-pound weight loss during that time. However, he was on a liquid diet because of difficulty of swallowing due to extensive oral lesions and odynophagia. The patient reported that he was off from HAART therapy for approximately one year but restarted treatment 14 months ago. He was on cobicistat, elvitegravir, emtricitabine, and tenofovir. However, he was noncompliant with his treatment. He had a biopsy of oral lesions done prior to the admission, showing KS.

Physical examination was significant for diffuse dark purple patches and plaques involving the face, back, arms, legs as well as hard palate and gums (Figures 1and 2). On chest examination, he had decreased air entry in the right lower lung fields.

Complete blood count was significant for normocytic anemia and thrombocytopenia. The patient's absolute CD4 count was 27 cells/microliter. Chest x-ray (Figure 3) and subsequent chest computed tomography (Figure 4), showed moderate right lung pleural effusion with scattered bilateral diffuse infiltrates and mild mediastinal and retroperitoneal lymphadenopathy.

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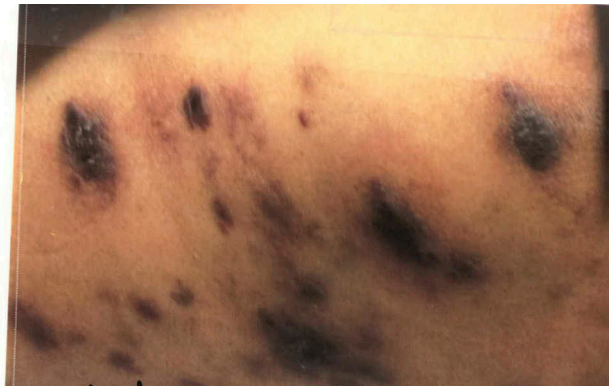

Figure 1. Diffuse KS skin lesions involving back.

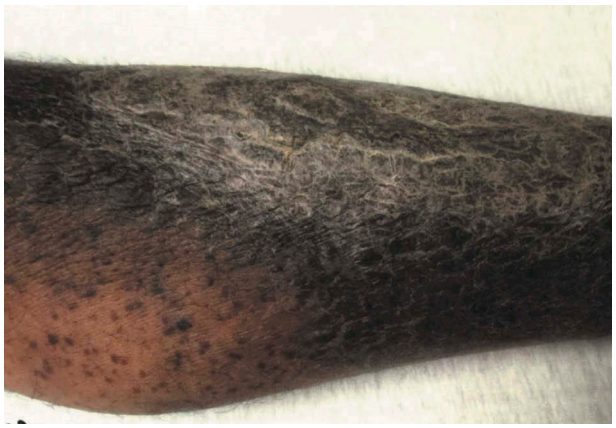

Figure 2. Diffuse KS skin lesions involving leg.

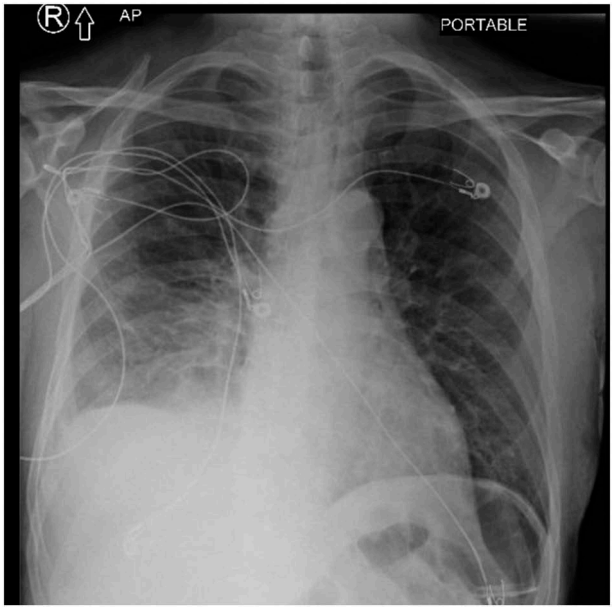

Figure 3. Chest x-ray shows moderate right effusion, hazy opacities at the right lung base and vague ground glass changes in the left lung base.

Immediately after the admission, the patient continued to deteriorate with worsening hypoxemia, requiring 15-liter oxygen with nonrebreather mask and transferred to the ICU for acute respiratory failure. He underwent thoracentesis which revealed hemorrhagic

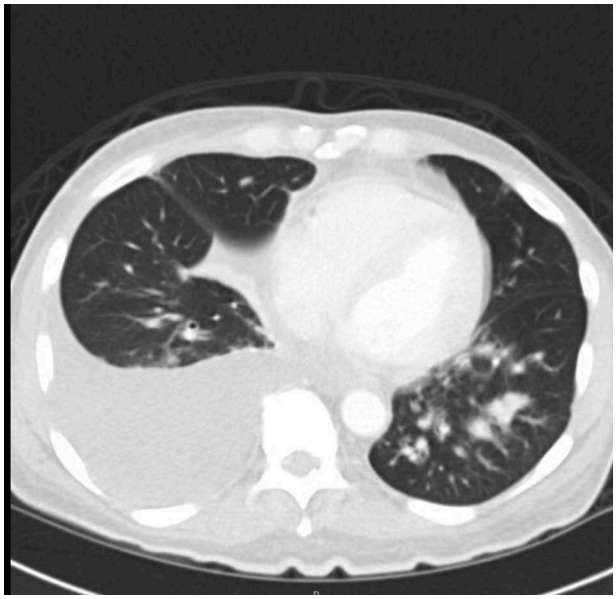

Figure 4. CT chest with contrast shows moderate size right pleural effusion with bilateral scattered infiltrates.

pleural fluid, negative for infection or malignancy. Infectious etiology has been excluded after blood culture and sputum culture were found to be negative for bacterial, viral, or fungal infections. Pulmonary tuberculosis, Coccidioidomycosis, pneumocystis jiroveci, and syphilis were also ruled out. Other malignancies which can involve lung and pleura in patient with AIDS (such as pulmonary lymphoma and lung cancer) were less likely as CT scan of chest, abdomen, and pelvic did not show any lymphadenopathy and pleural effusion cytology found to be negative for any malignant cells.

After exclusion of Infectious etiologies, and other malignancies, the patient was diagnosed with poor risk and extensive KS (T1I1S1). He was immediately started on chemotherapy with paclitaxel along with HAART. Dexamethasone 10 mg was also added at the time of chemotherapy administration for prevention of hypersensitivity reaction. Since receiving the chemotherapy, his condition has significantly improved with near complete resolution of the pleural effusion, oral and skin lesions. The patient was able to tolerate oral diet and has regained 30-pound weight. He completed total six cycle of chemotherapy with paclitaxel 190 mg with no significant side effects.

3. Discussion

Pulmonary KS usually occurs in critically immunosuppressed patients. It can involve the lung parenchyma, airways, pleura, or intrathoracic lymph nodes. Lung involvement in KS most commonly occurs in presence of extensive mucocutaneous disease, and very rarely can present as an isolated disease [6,9]. In 1998, AIDS Clinical Trials Group (ACTG) developed a staging system for KS, called TIS system

Table 1. Tumor-immune system-systemic illness (TIS) staging system and prognosis.

	Good Risk (0) (Any of the following)	Poor Risk (1) (Any of the following)
Tumor (T)	Only located in the skin and/or lymph nodes and/or minimal oral disease (Flat lesions confined to the palate or roof of the mouth)	Tumor-associated edema (fluid buildup) or ulceration (break in the surface of the skin) Extensive oral Kaposi sarcoma Gastrointestinal Kaposi sarcoma Kaposi sarcoma in other organs in the body
Immune system (I)	CD4 cell count is 200 or more cells per cubic millimeter	CD4 cell count is less than 200 cells per cubic millimeter
Systemic illness (S)	No systemic illness presents No 'B' symptoms, which include unexplained fever, night sweats, greater than 10% involuntary weight loss, or diarrhea for more than 2 weeks	History of systemic illness and/or thrush One or more 'B' symptoms are present Other HIV-related illness is present, for example, neurological disease or lymphoma

(Table 1). The classification is based on three criteria: tumor extent (T), the status of patient's immune system, measured by CD4 cell count (I), and presence of systemic symptoms (S). Each factor is further grouped into good risk (0) or poor risk (1).

Pulmonary KS usually manifest clinically by dyspnea, hypoxemia and dry cough [13,14]. Pleuritic chest pain, hemoptysis, fever, respiratory failure, and upper airway obstruction can also occur. When fever presents, it cannot be distinguished from superimposed infection. In pulmonary KS, Physical examination of the chest is usually normal, but nonspecific signs such as crackles, wheezing, and stridor may be present. KS lesions can range from isolated tracheal lesions to diffuse tracheobronchial involvement causing narrowing and airways obstruction [6]. It may cause radiographic infiltrates and respiratory symptoms that mimic a variety of other infectious and neoplastic processes.

Although, the patients with mucocutaneous KS have a higher likelihood of lung involvement with KS, there are no unique manifestations that can distinguish KS from other pathologic processes in the lungs. A detailed evaluation should exclude infection or other etiologies. The evaluation of pulmonary symptoms in patients with HIV infection usually includes imaging and thoracentesis if a pleural effusion is present. Bronchoscopy and bronchoalveolar lavage (BAL) are often performed in HIV positive patients with pulmonary symptoms and abnormal chest X-ray or chest CT scan finding. The main purpose is to obtain BAL samples to evaluate for opportunistic infections or tumors other than KS.

In our case, the patient initially presented with fever, cough, and shortness of breath. He was started on broad spectrum antibiotics, due to concern for opportunistic infections. However, his clinical status continued to deteriorate on antibiotic treatment and raised the suspicious for noninfectious lungs pathologies. Although the final diagnosis of pulmonary KS is ideally done by demonstrating the typical violaceous mucosal lesions in the trachea or main bronchi at bronchoscopy [9], unfortunately, this was not feasible in our patient due to high oxygen requirement and concern for procedure-induced worsening hypoxia. Our patient was diagnosed with pulmonary KS after infectious etiologies and other malignancies have been ruled out.

Since introduction of multidrug antiretroviral regimens, based on a combination of RTIs and PIs in 1996, mortality and morbidity associated with HIV infection has declined significantly [15,16]. HAART also has been associated with partial or complete regression of lesions in KS patients [17,18]. Studies showed that tumors can regress in size and number in response to HAART, and therefore all patients with KS should receive combination antiretroviral therapy if no other contraindications exist [19]. Using HAART in patients with pulmonary KS has increased median survival time of the patients to 1.6 years compared to 4 months in those who has not received treatment [4].

Currently, several different therapeutic options are available for patients with KS. Decision on type of treatment usually depends on several factors such as the extent of disease, visceral organ involvement, and rate of tumor growth. Immune status and concurrent complications of HIV infection are also important factors. HAART with concomitant chemotherapy is indicated for visceral disease and/or rapidly progressive disease [7]. Paclitaxel and pegylated liposomal doxorubicin (PLD) are active cytotoxic agents recommended as first line therapy for HIV-related KS as per NCCN (National comprehensive cancer network) guidelines, with response rates of about 50%–60% [19]. A systemic review of randomized trials and observation studies in patient with advanced HIV-related KS found no evident differences between liposomal doxorubicin, liposomal daunorubicin, and paclitaxel, although the number of studies identified was low [20].

However, doxorubicin is a major CYP2D6, CYP3A4 and P-glycoprotein substrate. Clinically significant interactions have been reported when doxorubicin was administered with inhibitors of CYP2D6, CYP3A4 and/or P-glycoprotein (such as cobicistat in this case), resulting in increased concentration and clinical effect of doxorubicin. We avoided using Doxorubicin for this patient due to the concern for increased risk of adverse effect.

Doxorubicin use is also associated with palmar-plantar erythrodysesthesia (PPE), also called hand-foot syndrome, which is a relatively common dermatologic toxic reaction with cytotoxic chemotherapy drugs such as doxorubicin. Given the fact our patient already had extensive painful cutaneous KS lesions in bilateral hands, we decided not to pursue the treatment with doxorubicin and use paclitaxel instead.

He was immediately started on chemotherapy with paclitaxel along with HAART. He was able to complete six cycles of chemotherapy without any major side effects. Since starting on chemotherapy, he had significant improvement in clinical condition and respiratory symptoms, with near complete resolution of pleural effusion, oral, and skin lesions.

In conclusion, the differential diagnosis of pulmonary KS is broad and includes the full range of AIDS-associated infections and neoplasms that cause pulmonary symptoms. Pulmonary KS should be suspected in all HIV-infected patient who present with respiratory symptoms. There is no unique manifestation that can distinguish pulmonary KS from other infection or neoplastic pathology in lung. A high index of suspicion and a detailed evaluation to exclude an infectious etiology is required for diagnosis and treatment. Although bronchoscopy can be a high diagnostic yield, patients can be diagnosed with pulmonary KS with exclusion of other etiologies.

Disclosure statement

No potential conflict of interest was reported by the authors.

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