Pulmonary Kaposi Sarcoma with Osseous Metastases in an Human Immunodeficiency Virus (HIV) Patient: A Remarkable Response to Highly Active Antiretroviral Therapy

Ahmed Dirweesh, Muhammad Yasir Khan, Shaikh Fawad Hamiz, Nigahus Karabulut

Corresponding Author: Ahmed Dirweesh, e-mail: adirweesh@stfrancismedical.org

Conflict of interest: None declared

Patient: Male, 34
Final Diagnosis: Pulmonary Kaposi's sarcoma with bony metastases
Symptoms: Cough • weight loss
Medication:
Clinical Procedure:
Specialty: Infectious Diseases

Objective: Rare disease
Background: Kaposi sarcoma (KS) is known to involve the mucocutaneous tissues and the aero-digestive tracts. In acquired immune deficiency syndrome (AIDS) patients, KS has an aggressive course and carries poor prognosis. We present a case of pulmonary KS with osseous metastases as the first presentation of human immunodeficiency virus (HIV) infection in a young male. The lesions impressively decreased in size and numbers following initiation of highly active antiretroviral therapy (HAART).

Case Report: A 34-year-old heterosexual male presented with a one month history of cough and 15–20 pound weight loss within six months. Examination revealed oral thrush, decreased breath sounds and crackles on the right lower lung base. Imaging showed a large right perihilar mass with multiple lytic lesions involving thoracic and lumbar vertebrae, ribs, sternum, and clavicles. Blood and sputum cultures, smears for acid fast bacilli, and a QUANTIferon gold test were all negative. He tested positive for HIV and his CD4 count was 7 cells/uL. Bronchoscopy with biopsy was unrevealing. Pathology of the right hilar mass was diagnostic of KS. Following initiation of antiretroviral therapy his condition dramatically improved; repeat chest CT scan showed marked regression of the bony and pulmonary lesions.

Conclusions: The dual action of HAART on the recovery of the immune system and against human herpes virus 8 (HHV-8) may essentially cause regression of KS lesions.

MeSH Keywords: AIDS Serodiagnosis • Anti-HIV Agents • HIV • Sarcoma, Kaposi

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Background

Kaposi sarcoma (KS) is a highly vascular tumor first described by Moritz Kaposi in 1872 as multifocal angio-proliferative lesions, with fewer reported cases among women and heterosexuals [1,2]. It results from abnormal proliferation of endothelial cells that eventually develop into a true sarcoma. Four variants of KS have been identified. The classic one is more indolent, affects lower extremities, and rarely involves viscera. In the African variant, there are several clinical patterns and visceral involvement may or may not be seen [3]. Another form of KS has been described in immunosuppressed patients, especially after renal transplantation, and it is typically limited to the skin [4,5]. KS associated with acquired immune deficiency syndrome (AIDS) is recognized as a separate variant of KS because of its more aggressive behavior with visceral dissemination [6].

In the 1980s, the prevalence of KS began to increase dramatically. The affected population mostly involved young homosexual men, and had a far more aggressive course than the typical indolent behavior of KS. These cases would involve internal organs unlike KS seen and reported earlier that was limited to skin manifestations, and often KS occurred with rare opportunistic infections, such as Pneumocystis carinii, and frequently ended with death of the patient [6,7]. The newly identified syndrome was mislabeled initially as KS and opportunistic infections, but it was soon recognized that these rare infections indicated progressive immune deficiency which later became known as AIDS [8].

Patients with AIDS are 20,000 times more likely to have KS compared to the general population, and it is the most common neoplasm found in AIDS patients [9]. In some cohorts of homosexual men with AIDS, the lifetime risk of KS approaches 50% [10] and interestingly, it occurs more in patients who acquired human immunodeficiency virus (HIV) through sexually contact [9]. Peculiar demographic and geographical distribution of HIV-associated KS prompted speculations about the various infectious causes of KS. The causative role of human herpes virus 8 (HHV-8) was confirmed when longitudinal studies demonstrated the presence of HHV-8 DNA in KS lesions, regardless of their source or subtype [11,12].

We present a case of pulmonary KS with osseous involvement as the initial manifestation of HIV infection in a young heterosexual male. The patient’s condition responded dramatically to an isolated highly active antiretroviral therapy (HAART) regimen, and repeat imaging revealed profound regression of the disease and disappearance of most of the lesions.

Case Report

A 34-year-old Hispanic male without significant past medical history presented to our hospital with a one month history of cough; productive of whitish sputum. At presentation, he denied fever, chills, night sweats, chest pain, hemoptysis, back pain, recent travel or sick contacts. He reported that he had approximately a 15–20 pound weight loss during the last six months. He denied smoking, socially drank alcohol, and had unprotected sexual intercourse with multiple partners in the past.

On admission, his temperature was 97.9°F; heart rate was 85 beats per minute, respiratory rate was 16 breaths per minute, blood pressure was 107/66 mm Hg, and oxygen saturation was 100% on room air. Examination showed oral thrush, decreased breath sounds and crackles on the right lower lung base. No cutaneous lesions were reported and the rest of clinical examination was unremarkable. His complete blood count (CBC) showed hemoglobin of 9.7 g/dL, WBCs 2.3×10^9/L, and platelets of 164×10^9/L. His creatinine was 0.62 mg/dL, and blood urea nitrogen was 10 mg/dL. Radiograph of the chest showed extensive right and left perihilar opacity more on the right side, and computed tomography (CT) scan of the chest showed a right sided large perihilar mass (Figure 1) with multiple thoracic...

Figure 1. (A, B) Axial chest CT scan showing a large right perihilar mass (arrow).
and lumbar vertebrae, ribs, and sternal tiny lytic lesions consistent with bony metastasis (Figure 2).

Blood and sputum cultures were negative. Tuberculosis was ruled out by three consecutive negative sputum smears for acid fast bacilli and a negative QUANTIferon gold test. He tested positive for human immunodeficiency virus (HIV) and his CD4 counts came back at 7 cells/uL. He was started on prophylaxis with bactrim 80–160 mg daily and azithromycin 1200 mg weekly for opportunistic infections. Bronchoscopy with biopsy was performed but was unrevealing and he underwent a video assisted mediastinoscopy with biopsies of the right hilar mass. Pathology showed spindle cells positive for CD34, BCL2, vimentin, and HHV-8 with diffuse positivity for CD31 diagnostic of KS. He started treatment with HAART in the form of emtricitabine and tenofovir disoproxil fumarate 200/300 mg and dolutegravir 50 mg. The patient was actively involved in decisions regarding management options. He favored HAART isolated regimen without additional chemotherapy. His condition showed continuing clinical improvement; a repeat CT scan of the chest at three months showed profound regression of the disease with disappearance of most of the lesions (Figure 3).

Discussion

KS results from abnormal proliferation of endothelial cells that eventually develop into a true sarcoma. Four variants of KS have been identified. The classic form of KS is more indolent, affects lower extremities, and rarely involves viscera. In the African variant, there are several clinical patterns and visceral involvement may or may not be seen [3]. Another form of KS has been described in immunosuppressed patients, especially after renal transplantation and it is typically limited to skin and can rarely present with generalized lymphadenopathy [4–6]. KS associated with AIDS is recognized as a separate variant of KS because of its more aggressive behavior with visceral dissemination [7].

In the 1980s, the prevalence of KS began to increase dramatically. The affected population mostly involved young homosexual men with far more aggressive course than the typical indolent behavior of KS. These cases would involve internal organs, unlike KS seen and reported earlier that was limited to skin manifestations only; and often occurred with rare opportunistic infections such as Pneumocystis carinii and frequently ended with death of the patients [7,8]. The newly identified syndrome was mislabeled initially as KS and opportunistic infections but it was soon recognized that these rare infections instead indicated progressive immune deficiency, which later came to be known as AIDS [9].
Patients with AIDS are 20,000 times more likely to have KS compared to the general population and it is the most common neoplasm among AIDS patients [10]. In some cohorts of homosexual men with AIDS, the lifetime risk of KS approaches 50% [11] and interestingly, the incidence is higher in patients who acquired HIV through sexually contact [10]. Peculiar demographic and geographical distribution of HIV associated KS prompted speculations about the various infectious causes of KS; the causative role of HHV-8 was confirmed when longitudinal studies demonstrated the presence of HHV-8 DNA in KS lesions, regardless of their source or subtype [12,13].

KS typically presents with mucocutaneous lesions, mostly affecting lower extremities, face, trunk, genitalia, and oropharyngeal mucosa [14]. Hong and Lee in 2002 found that extracutaneous or visceral KS lesions were more common in HIV infected patients compared to HIV-negative patients [15]. KS has been reported in virtually all anatomical sites and its anatomical distribution has changed significantly with the advent of HIV. Soon after the onset of the AIDS epidemic, head and neck AIDS-related KS became one of the most common manifestations of AIDS [16]. The rarity of KS reports in uncommon regions, such as gonads, spinal cord, and peripheral nervous system, may be due to underreporting or asymptomatic lesions, and it is possible that many cases go unreported or unrecognized [17].

Although a few cases have been reported as isolated visceral manifestations of KS, it is very uncommon for visceral involvement to occur without skin manifestations [18,19]. Gastrointestinal tract, lungs, liver, and spleen are other visceral sites of involvement. Most patients with pulmonary KS already have cutaneous lesions at the time of diagnosis. Incidence of pulmonary KS is still not well known and it may be attributed to under diagnosis for reasons as discussed earlier [20]. Some clinical studies have shown a higher prevalence in individuals with AIDS who already had the cutaneous form of the disease (over 32%) compared to those without it (3–13%). Thus, it is relatively rare to have pulmonary KS without skin manifestations [21–23]. Bronchopulmonary KS was found upon autopsies in 47% of patients with AIDS who had the cutaneous form, which reveals a possible under diagnosis of pulmonary involvement [24].

KS of the lungs may be asymptomatic and discovered incidentally by radiologic imaging or bronchoscopy. Symptomatic pulmonary KS most often present with cough, dyspnea, and fever but symptoms may vary based on co-existence of other opportunistic infections. Chest radiograph can be normal but usually shows bronchial-wall thickening, nodules, Kerley B lines, and pleural effusions [25,26]. Granular opacities or cystic spaces on chest x-ray usually indicates concomitant Pneumocystis carinii infection [25]. CT scans are modestly superior to chest radiography in allowing identification of patients with and without thoracic disease and in the differential diagnosis of pulmonary complications of patients with AIDS [26].

Musculoskeletal system involvement by KS is rare occurrence [17]. AIDs-related KS mainly involves the axial skeleton and/or maxillofacial bones [27,28]. Osseous KS lesions are commonly osteolytic, and CT scan and MRI are superior to plain radiographs for the detection of bony lesions [29,30].

The current approach to the management of KS associated with AIDS usually involves use of HAART, with or without treatment directed against KS. In one study that included 13 patients who were treated with HAART, none had progression of their lesions after a median follow-up of 10 weeks [31]. Another study showed regression in the size of KS lesions with HAART and a decline in viral load of HHV-8 [32]. Our patient has shown clinical improvement with regression of the perihilar mass on repeat imaging with the HAART therapy alone, which is consistent with the available literature on treatment of KS. The advent of HAART has led to a substantial reduction in morbidity and mortality in KS associated with AIDS [33]. Radiation can also be used when there is limited cutaneous involvement in HIV-positive patients with KS [34,35].

Generally, more widespread disease, or disease affecting internal organs, is treated with systemic therapy directed towards KS (including interferon alpha, liposomal anthracyclines, or paclitaxel).

In a systemic review of the Cochrane database, liposomal anthracyclines were found to have superior response rate without an increase in toxic side effects [35]. In another systemic review of the Cochrane database, authors concluded that in patients with T1 KS, there was significant reduction in disease progression when treated with HAART plus chemotherapy as opposed to HAART alone [36]. Liposomal anthracyclines have been generally accepted as first-line chemotherapeutic agents for severe progressive KS associated with AIDS but there are no guidelines as of yet from the World Health Organization (WHO) [37].

Conclusions

It is very uncommon for KS to involve visceral organs without associated skin manifestations. The influencing effect of HAART on the immune system and against human HHV-8 can result in dramatic regression of KS lesions.

Conflicts of interest

None.
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