Case Report

Adenotonsillar Kaposi Sarcoma with Severe Upper Airway Obstruction in Acquired Immunodeficiency Syndrome-Related Disseminated Disease – A Case Report and Literature Review

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Abstract

Reported cases of upper airway obstruction (UAO) due to obstructive adenotonsillar Kaposi sarcoma (KS) are rare in our environment. We report a 29-year-old human immunodeficiency virus (HIV)-positive female Nigerian who had defaulted treatment for 6 years but represented with disseminated KS and features of severe UAO that necessitated emergency tracheostomy and adenotonsillectomy. She had remarkable improvement in her breathing, feeding, and speech while being in a stable and satisfactory clinical state postoperatively until 3 days later. She suddenly deteriorated and died. Histology report of the adenoid and tonsillar tissues revealed features in keeping with KS (nodular stage). Lack of compliance with antiretroviral therapy and default from care could have facilitated the development of an aggressive KS and the rare presentation. Adherence to the management protocol of HIV infection would bring about early detection of KS, which can be promptly managed with a possible favorable outcome, thereby preventing or reducing dissemination.

Keywords: Disseminated Kaposi sarcoma, human immunodeficiency virus infection, obstructive adenotonsillar Kaposi sarcoma, upper airway obstruction

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Introduction

Among persons living with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS), Kaposi's sarcoma (KS) is the most common cancer.[1-4] It is a well-recognized AIDS-defining malignancy[5] and a major cause of morbidity and mortality in sub-Saharan Africa.[1,6] It is a rare, multifocal lesion that affects visceral organs and mucocutaneous sites,[2,5,7,8] including the lungs, liver, spleen, skin of the lower extremities, genitalia, trunk, face, eye, lymph nodes, oral cavity mucosa, and aerodigestive tract.[5,7,8] In the aerodigestive tract, while there have been reports that the oropharynx is a usual site of KS,[9,10] consequent airway obstruction is rare;[10] just as obstructive adenotonsillar involvement.[11] We present the case of a 29-year-old HIV-positive Nigerian female who abandoned orthodox care for about 6 years and later developed disseminated KS with severe upper airway obstruction (UAO) due to adenotonsillar involvement.

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Case Report

A 29 year-old single female presented with generalized nodular/papular body rashes of 3 months, cough of 6 weeks, low grade, intermittent fever, and anal swelling of 4 weeks. There was 4-week duration of rashes in the mouth, dysphagia, odynophagia, weight loss, difficulty in breathing, and muffled voice, which worsened in the past 2 weeks before presentation. Cough was initially productive of yellowish sputum, later became bloodstained; there was no history suggestive of neither asthma nor pulmonary tuberculosis (TB).

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The hyperpigmented facial swellings were initially small and painless until 2 weeks before presentation; anal swelling also became painful at about this period with associated rectal bleeding, no history of melena stool.

There was a history of risky sexual behavior (multiple sexual partners, with occasional unprotected sex), and she had been diagnosed with retroviral disease (RVD) about 6 years earlier. She started tenofovir-based antiretroviral (ARV) therapy which she had for only 2 months, then defaulted to orthodox care for "spiritualty-based" care.

Examinations revealed a chronically ill-looking young female, pale, anicteric, febrile – 38.1°C (at presentation), generalized hyperpigmented nodular/papular rashes [Figure 1a], generalized palpably enlarged, firm, mobile, nontender cervical lymph nodes, in all the levels of the neck, bilaterally, as well as axillary and inguinal, largest being about 4 cm in its widest diameter, severe respiratory distress, and mild bilateral pitting pedal edema. Pulse Rate was 100–116 beats per minute and blood pressure was 110/70–140/90 mmHg.

- Oral cavity: Oral thrush, nodular hyperpigmented lesions within the oral vestibule and floor
- Oropharynx: Huge, nodular, Grade IV ("Kissing") palatine tonsils, markedly occluding the oropharynx
- Chest: Severe respiratory distress, Respiratory Rate was 36 breath per minute, dull percussion note over the right mid/lower lung zones, coarse crepitations over the lung fields, and reduced air entry over the right mid/lower lung. SpO2 was 90%–92% in room air and 96%–98% on humidified intranasal oxygen
- Abdomen: Palpably enlarged liver about 10 cm below the right coastal margin (about 20 cm span).

Digital rectal examination revealed Grade III hemorrhoid at 11 o'clock and perianal ulceration.

CD4 count at the diagnosis of RVD was 616 cells/ml (6 years earlier). Packed cell volume (PCV), during index presentation, was 23%. She was transfused with three pints of whole blood. Posttransfusion PCV was 31%; WBC – 3.0 × 10^9/L (N/M/L – 56%/6%/38%); and platelet – 182 × 10^9/L. Serum electrolytes, urea, and creatinine were within normal limits. Sputum m/c/s revealed normal flora. Gene experts did not detect *Mycobacterium tuberculosis*. Index CD4 count was 33 cells/ml. A diagnosis of Disseminated KS in HIV/AIDS (Stage IV) with Severe UAO secondary to adenotonsillar KS was made.

The patient was placed on IV amoxicillin/clavulanic acid (augmentin), tablet azithromycin, fluconazole, septrin, omeprazole, gestid, oral nystatin, and ferrous sulphate/folic acid.

She had an emergency tracheostomy and adenotonsillectomy done [Figure 1b].

Findings at surgery revealed normal trachea, on the one hand, multinodular, hard adenoid vegetations (occluding about 75% of the nasopharynx), and huge, nodular, and firm palatine tonsils. The oral vestibule and posterior pharyngeal wall of the oropharynx and hypopharynx were not spared of the nodular lesions, although discrete. The estimated blood loss during the adenotonsillectomy was 100 ml.

She had a satisfactory postoperative recovery, achieving SPO_2 of 96%–99% in room air. Histologic diagnosis of adenotonsillar KS was confirmed.

She remained in a stable clinical condition while being worked up for chemotherapy and highly active antiretroviral therapy (HAART). However, on the 4th postoperative day, she suddenly deteriorated and subsequently died.

Discussion

Historically, KS predated HIV/AIDS[2,4,6,7,12] and is well-documented in individuals without HIV/AIDS.[6,10] It was first described by Hungarian Moritz Kaposi in 1872. He reported a relatively aggressive angiomatous neoplasm that was mainly found in elderly men of Italian, Jewish, and Mediterranean origin. His discovery was later known as classical KS.[2,7,12] The other forms are endemic (African), epidemic or AIDS associated, and immunosuppressive or transplant related.[4,6] A combination of factors have been implicated in the development of KS, including the role of HHV8, altered immunity (immunosuppression),[8,9,13] and inflammatory/angiogenic condition (s).[9] These factors are potential foundations for posttraumatic KS lesions through the Koebner phenomenon. Evidences of this phenomenon have been established in classical, AIDS-associated, and transplant-related KS.[9] Pantanowitz and Dezube[9] posit that trauma may be the inflammatory precursor for HHV8 to be mobilized to an injured site. Trauma to the oropharynx or any other part of the body by herbalists/unorthodox caregivers, to address pain or discomfort, is not unusual in our environment. However, our patient denied any history of such.

The estimated risk of KS in AIDS patients was over 300 times when compared with other immunosuppressed patients.[5] This suggests a higher level of altered immunity in HIV/AIDS with a high incidence of KS during the advanced stage of HIV/AIDS. Indeed, AIDS-associated and immunosuppressive-related KS are more aggressive than other forms.[5] Our patient's default from orthodox care for 6 years would have worsened her altered immunity.

AIDS-KS runs a variable course ranging from an indolent, slowly progressive pattern to a rapidly progressive, disseminated, and fatal disease.[5] The skin, oral mucosa, lymph nodes, and visceral organ are commonly involved,[5,14] with the head-and-neck region being more affected in AIDS-KS than the lower extremities and cutaneous lesions, which are more common in immunosuppression-related KS.[5] Oral KS, mostly affecting the hard palate, gingiva, and tongue, is associated with lower CD4 counts than cutaneous disease[5] and may be the first sign of HIV infection.[5,15] Ozbudak *et al*.[15] alluded to the rarity of tonsillar involvement in KS. Visceral KS may be asymptomatic or

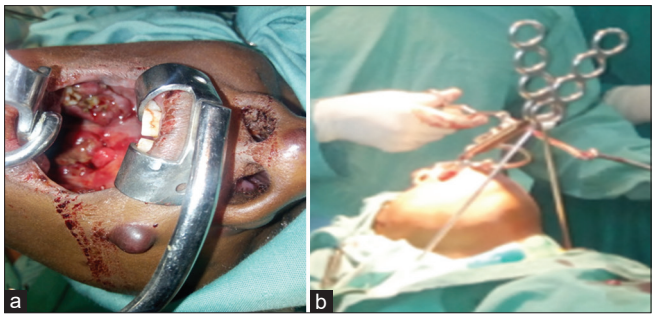

Figure 1: (a) Hyperpigmented/purplish nodular lesions on the tip of the nose and just to the left side of the upper lip while exposing the oral cavity/oropharynx. (Picture was taken using a 13-megapixel rear camera of an infinix hot 8 pro android phone). (b) Tonsillectomy was carried out after emergency tracheostomy had been done. (Picture was taken using a 13-megapixel rear camera of an infinix hot 8 pro android phone)

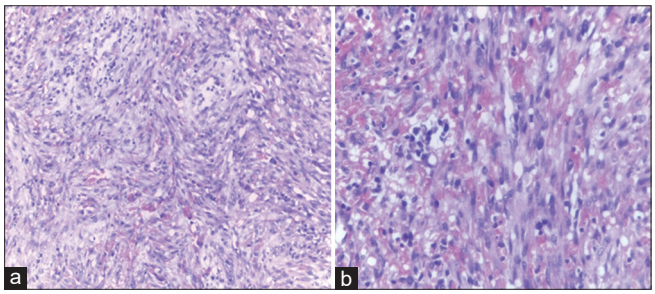

Figure 2: (a) H and E, ×400 demonstrates the adenoid vegetations showing slit-like spaces lined by plump spindle-shaped cells with intervening blood-filled spaces and extravasation of red blood cells. (b) H and E, ×400 demonstrates the palatine tonsil tissues showing slit-like spaces lined by plump spindle-shaped cells with intervening blood-filled spaces and extravasation of red blood cells

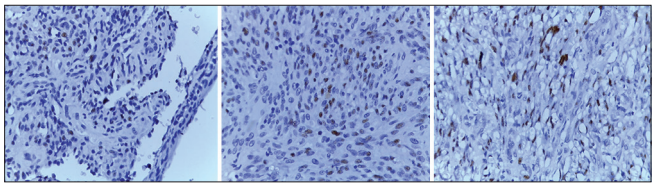

Figure 3: HHV8 immunostaining, ×400 demonstrates adenoid vegetations, and palatine tonsils showing diffuse and strong nuclear staining of the spindle cells and endothelium

rapidly fatal. More than 25% of AIDS-KS patients have visceral lesions most commonly involving the gastrointestinal tract, liver, spleen, and lungs.[5] While the gastrointestinal disease is often asymptomatic, pulmonary KS which mostly presents with dyspnea and cough (without fever unless concomitant infection is present) is rapidly fatal, especially without treatment.[5] The course of the disease in our patient depicts a disseminated form with representation in the lower extremities, skin (generally), oral cavity, oropharynx, and possibly gastrointestinal and pulmonary systems.

In sub-Saharan Africa, most individuals with HIV seropositivity and KS manifestation among AIDS patients are in the third and fourth decades of life. This is largely due to high-risk behavior.[16,17] Ahmed *et al*.[16] reported a median age of 32 years, and noted that the females were much younger than the males. They alluded to an early occurence of HIV infection or an aggressive disease in the females. They noted a greater burden of disease in females, with more cases of oral lesions that often interfered with feeding and speech but rarely affected the airways.[16] Our patient was a 29-year-old female diagnosed with HIV infection 6 years earlier. There was a history suggestive of risky sexual behavior, and the oropharyngeal features in her significantly interfered with her airway (as well as her feeding and speech), necessitating emergency tracheostomy and adenotonsillectomy. Choussy *et al*.[10] alluded to two cases of UAO in AIDS-related KS that had emergency tracheostomy but died shortly after from primary hemorrhage. In our patient, there was no remarkable bleeding following the tracheostomy, unlike the adenotonsillectomy, and she was satisfactorily stable for 3 days.

The confirmatory diagnosis of KS is through histopathological assessment of a tissue specimen and immunohistochemical staining.[4,14] KS is characterized by abnormal proliferation of lymphatics. Lesions may occur in three forms: patch, plaque, and nodule. Nodular lesions are more common in immunosuppression-related and AIDS-KS and are marked by the proliferation of slit-like vascular channels, extravasated erythrocytes, and spindle cells.[5] Bacillary angiomatosis also causes vascular proliferative lesions as seen in KS,[5,14] but the presence of pleomorphic bacilli on Warthin-Starry silver stain helps distinguish bacillary angiomatosis, whereas the identification of HHV8 DNA may help distinguish KS from other vascular lesions.[5,14] Our patient had a nodular form of KS, associated with HHV8, with morphologic and immunohistochemistry staining patterns consistent with those of KS [Figures 2 and 3].

Following the adoption of effective ARV therapy in the care of HIV/AIDS, the incidence of KS reduced.[3,5] Total remission has been reported in 20%–80% of patients and better outcomes seen in the HIV therapy compliant ones who had limited-stage disease[14] (confined to the skin, lymph nodes, or minimal oral disease; CD4 >150/mL).[18] Patients with advanced-stage KS (tumor-associated edema/ulceration, extensive oral disease, and visceral disease [nonnodal]; CD4 <150/mL) mostly present with an aggressive disease that rapidly affects vital organs.[15] While our patient had a CD4 count of 616 cells/ml at the diagnosis of HIV infection, the count was 33 cells/ml at the diagnosis of KS. Such conditions require cytotoxic therapy, in addition to the ARVs, for effective KS regression[17,18] through immunologic cytotoxic cell-mediated response targeted at HHV8.[18] Cytotoxic agents relevant in the systemic treatment of KS include liposomal anthracyclines (doxorubicin and daunorubicin), interferon-alpha, Vinca alkaloids (vincristine and vinblastine), bleomycin, etoposide, and paclitaxel.[4,5,14,15]

Pittore *et al*.[19] reported a 42-year-old male with an isolated right tonsillar KS who had tonsillectomy and HAART with complete eradication of the tumors. Abdullahi and Adeiza[20]

reported a 35-year-old woman who defaulted to orthodox care for about 2 years and subsequently presented with disseminated KS and smear-positive pulmonary TB. She was managed with anti-TB medications and HAART, with complete regression of all the KS lesions without the need for KS-specific therapy, despite the disseminated disease. This may suggest that HAART clearly has an immune restoration role in the management of AIDS-related KS, irrespective of the systemic involvement. Indeed HAART is an established cornerstone in the treatment of AIDS-KS, regardless of the stage of the disease.[5,14] Our patient defaulted for a longer period, had a worse level of dissemination, and did not have the opportunity to be treated with HAART.

It is worthy to note that a possibility of disease progression after starting ARVs (*de novo* KS) exists in a few of the HIV-infected patients through paradoxical immune reconstitution inflammatory syndrome (IRIS).[4,18] With the progression of the disease after HAART and/or cytotoxics had been instituted, targeted therapy on specific pathways in KS pathogenesis (including angiogenesis, HHV8 replication and life cycle, and cytokine regulation) is being considered the modality of choice.[19] Tuttle *et al*.[4] reported a 29-year-old Brazilian male with disseminated KS with tonsillar and pulmonary involvement in the setting of paradoxical IRIS. The Brazilian had a computed tomography scan of the chest which indicated pulmonary KS. Our patient could not afford a similar investigation, but the findings on clinical examination of her chest suggested the likelihood of pulmonary involvement. This possible pulmonary involvement could have accounted for the sudden turn of events that led to the death of the patient; following the relief of the UAO, she became stable with satisfactory oxygen saturation for about 3 days, and she was being prepared for HAART and cytotoxic agents. However, these treatments were aborted by her sudden death. In advanced-stage KS, high tumor burden, poor immune status as reflected by low CD4 count, and the presence of systemic illnesses are predictors of slim survival.[5,18,19] Indeed, the prognosis was poor in our patient.

The lack of compliance with ARV therapy and default from care could have worsened the altered immunity in our patient and upgraded the stage of her disease, thereby facilitating the development of an aggressively disseminated KS, with a rare presentation of UAO due to severely obstructive adenotonsillar involvement. The possible dissemination to visceral organs, especially the lungs, could have paved the way for the sudden deterioration that led to her death.

To this end, adherence to the management protocol of HIV infection is instructive in the early detection of KS and its prompt management, with the possibility of favorable outcomes, thereby preventing or reducing dissemination.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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