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Fatal Disseminated Kaposi's Sarcoma in Two Patients with Human Immunodeficiency Virus (HIV) Infection

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Case series

Patient: Male, 25 • Male, 30
Final Diagnosis: Kaposi sarcoma
Symptoms: Oral lesions
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Unusual clinical course





Background: Kaposi's sarcoma (KS) is a common condition in patients with human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS). In these patients, the occurrence of KS is reduced by treatment with highly active antiretroviral therapy (HAART). Fatal and disseminated KS is presented in two patients with HIV/AIDS.

Case Reports: A 25-year-old man and a 30-year-old man with HIV/AIDS presented with KS affecting the skin, oral cavity, gastrointestinal tract, liver, lungs, kidneys, adrenal glands, and bone. Both patients had a rapidly deteriorating clinical course associated with a low CD4 count and developed respiratory failure and death.

Conclusions: Fatal disseminated KS is associated with severe immunosuppression due to with a low CD4 count. The presentation of these two cases highlights the potentially aggressive clinical course of KS in patients with HIV/AIDS and reinforces the need for early diagnosis and rapid treatment with HAART.

MeSH Keywords: Antiretroviral Therapy, Highly Active • HIV • Sarcoma, Kaposi

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/910004>

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Background

Kaposi's sarcoma (KS) is an aggressive vascular neoplasm that was first described by Moritz Kaposi in 1872 as a multifocal skin tumor consisting of hyperpigmented and nodular lesions [1–3]. In 1980, in the United States of America (USA), the first 50 cases of KS were reported in homosexual men who were positive for infection with human immunodeficiency virus (HIV) infection and who had acquired immunodeficiency syndrome (AIDS) [4,5]. Kaposi's sarcoma was considered to be pathognomonic for HIV/AIDS [4,5]. Chang et al. isolated human herpes virus 8 (HHV8) in more than 90% of tissues obtained from patients with KS and HIV/AIDS, supporting the role of HHV8 as the etiological agent of Kaposi's sarcoma [6].

An earlier study that analyzed a large US cohort of HIV-positive patients showed that the incidence of KS was very high in the first six months following the initiation of highly active antiretroviral therapy (HAART), with an incidence of 1,342/100,000 person-years [7–9]. However, the incidence of KS decreased substantially after the initial six months of HAART treatment and the stabilized at a rate of about 164/100,000 person-years [7–9].

KS is a malignancy of viral etiology with a clinical course that varies from cutaneous lesions to disseminated disease with multi-organ involvement. Four clinical variants of KS have been described, including classical KS, endemic KS, iatrogenic KS, and epidemic KS. Iatrogenic and epidemic variants of KS develop in the setting of immune suppression and may present with oral, skin, and visceral lesions, more commonly including lesions in the in the gastrointestinal tract and lungs, and more rarely involving the liver, spleen, bone, bone marrow, adrenal glands, heart, central nervous system, and kidneys [10].

The staging of HIV/AIDS-related KS determines prognosis. KS can be divided into low-risk and high-risk disease, based on three main clinical criteria, which include the patient's immune status, the tumor burden, and the presence of systemic disease. Patients with low-risk KS have lesions that are confined to the skin and lymph nodes, a CD4 count >200 cells/mm³, and an absence of a history of opportunistic infections. Patients with high-risk KS have extensive cutaneous lesions, oral or visceral disease, a CD4 count <150 cells/mm³, systemic disease, and opportunistic infections. Patients with AIDS-related KS with CD4 cell counts <100 cells/mm³ have the worst prognosis [11,12]. First-line treatment of visceral KS in patients with HIV/AIDS is highly active antiretroviral therapy (HAART), usually with a combination of liposomal doxorubicin, bleomycin, vincristine, or etoposide [13].

Two cases of fatal and disseminated KS are presented with tumor involvement of the liver, lungs, oral cavity, kidneys, adrenal glands, and bone, which highlight the potentially aggressive clinical course of KS in patients with HIV/AIDS.

Case Report

Case 1

A 25-year-old man attended the outpatient clinic complaining of painful lesions in the oral cavity for the previous six months, associated with a dry cough, evening fever, and weight loss of 21 kg. He also noted the appearance of dark-colored lesions that were not painful or pruritic, which had spread throughout the body.

Physical examination showed papules, nodules, and violaceous (purple) skin lesions measuring between 3–10 mm, located on the trunk, upper limbs, face, and neck (Figure 1A). There were also violaceous nodular lesions involving the hard palate and oral mucosa (Figure 1B). His liver was palpable, 3 cm from the right costal border, and the abdomen was tender on palpation in the epigastrium and right hypochondrium. The cervical, submandibular, and retro-auricular lymph nodes were enlarged. Serology tests for antibodies to hepatitis B, hepatitis C, and syphilis were negative.

Due to his declining physical condition, which included vomiting and increasing dyspnea, he was admitted to hospital. A diagnosis of human immunodeficiency virus infection and acquired immunodeficiency syndrome (HIV/AIDS) was made, which was confirmed with a positive HIV test. The patient was diagnosed to be in an advanced stage of HIV/AIDS and treatment with highly active antiretroviral therapy (HAART) was commenced, which included lamivudine, tenofovir, and efavirenz. Before HAART began, a hemogram showed moderate pancytopenia, with a CD4 count of 15 cells/mm³ and a viral load of 1,515,835 copies/mL. Screening for the BK polyomavirus and the use of the GeneXpert polymerase chain reaction (PCR) for tuberculosis were negative. The initial HAART regimen was replaced with tenofovir, lamivudine, and dolutegravir.

Computed tomography (CT) imaging of the chest showed bilateral pleural effusions, bilateral lung consolidation, mediastinal lymphadenopathy, and irregular nodular lesions in the upper right lobe, suggestive of Kaposi's sarcoma (KS). An upper gastrointestinal tract endoscopy showed nodular lesions in the gastric incisura and the duodenum, and red areas in the gastric antrum, esophagus, stomach, and duodenum (Figure 1C). Colonoscopy to the terminal ileum showed nodular lesions in the colon, which were also consistent with a diagnosis of KS (Figure 1D). Abdominal ultrasound showed parenchymal changes in the liver and mild ascites.

A biopsy of one of the skin lesions confirmed the histopathological diagnosis of KS. The patient was referred to the oncology department of the local hospital, where he developed progressive dyspnea, pancytopenia, and hemothorax, with a



Figure 1. Case 1. The appearance of the lesions of Kaposi's sarcoma (KS) in the skin, and mucosa of the small bowel and large bowel. (A) Violaceous lesions of Kaposi's sarcoma (KS) in the skin of the face, neck, and upper limbs measuring between 3–10 mm in diameter. (B) Violaceous and nodular lesions of KS involving the hard palate and oral mucosa. (C) Lesions of KS in the esophagus, stomach, and duodenum. (D) Flat maculopapular lesions of KS in the terminal ileum.

decrease in the CD4 count to <11 cells/mm³ and a viral load of 1,630,855 copies/mL. His condition continued to deteriorate and he died due to acute respiratory failure, less than three months following his diagnosis of HIV/AIDS.

Case 2

A 30-year-old man attended the outpatient department with a complaint of pain in the oral cavity associated with lesions involving the left side of his face. He had undergone a decline in his general health, weight loss of 13 kg in the previous seven months, and pain and edema of the right side of the face,

resulting in facial asymmetry (Figure 2). He also complained of a headache, hyperemesis, sporadic hematochezia, dyspnea, a productive cough with hemoptysis, dysuria, and urinary hesitancy with balanoposthitis. He did not have dysphagia and was able to eat. Physical examination showed that he was lucid, oriented in space, disoriented in time, afebrile, and hydrated. He was not cyanotic or icteric, but he was hypoxic.

The patient was admitted to hospital. Screening for the BK polyomavirus and the use of the GeneXpert PCR for tuberculosis were negative. Serology tests for hepatitis B, hepatitis C, syphilis, human T cell leukemia virus (HTLV) 1, HTLV 2, and



Figure 2. Case 2. The appearance of the lesions of Kaposi's sarcoma (KS) in the skin of the face, before and after chemotherapy with paclitaxel. (A) Extensive lesions of Kaposi's sarcoma (KS) involving the middle and lower one-third of the left side of the face at diagnosis. (B) Regression of the lesions following chemotherapy with paclitaxel.

CMV were negative. A rapid test for HIV was positive. His CD4 count was 53 cells/mm³ with a viral load 1,214,731 copies/mL. A biopsy of one of the skin lesions showed immature spindle cells, which were confirmed to be endothelial cells by positive immunostaining with antibodies to CD31 and CD34 using immunohistochemistry, which supported a diagnosis of KS. HAART was commenced with tenofovir, lamivudine, and dolutegravir.

A CT scan of the neck showed a large infiltrative lesion with local invasion into the right side of the face, involving the maxilla, right maxillary sinus, the hard and soft palate, the uvula, and extending into to the right nasal fossa, nasopharynx and part of the oropharynx, compatible with KS (Figure 3A). A contrast-enhanced CT scan of the chest showed an expansive subpleural tumor at the right pulmonary apex, measuring approximately 3.7×2.9 cm, and there were multiple nodular lesions in both lungs (Figure 3B), supraclavicular lymphadenopathy but no pneumothorax. A CT scan of the upper abdomen and pelvis showed infiltrative tumor masses in the liver, adrenals, right kidney (Figure 3C) and the pre-sacral region and

retroperitoneum, and bone metastases in the right sacroiliac region, consistent with metastatic KS.

The patient developed worsening dyspnea due to mechanical obstruction of the upper airways, which required a tracheostomy and parenteral nutrition. The CD4 count had increased to 151 cells/mm³ and the viral load had decreased to 1,714 copies/mL, due to adherence to antiretroviral therapy during hospitalization. Chemotherapy with paclitaxel 100 mg was given for 21 days. However, the patient developed a pulmonary infection and died from septic shock in the intensive care unit (ICU).

Discussion

Kaposi's sarcoma (KS) is a multifocal neoplasm that usually presents initially with skin involvement. Visceral involvement can be metastatic or late-stage disease and is present in approximately 25% of human immunodeficiency virus (HIV)-positive

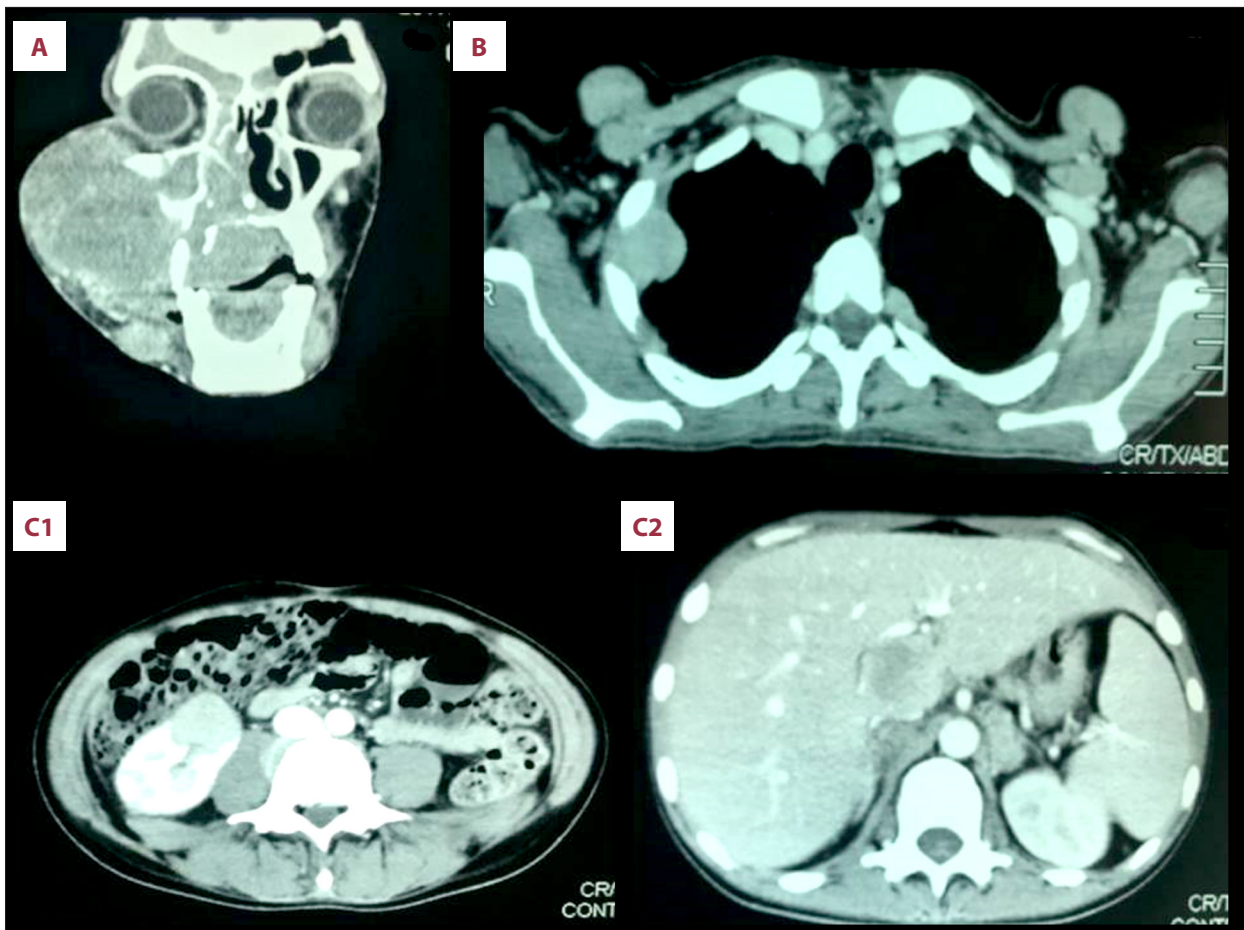


Figure 3. Case 2. Computed tomography (CT) images of the lesions of Kaposi's sarcoma (KS) in the skull, maxilla, hard palate, nasal cavities, chest, and abdominal and pelvic organs. **(A)** Computed tomography (CT) of the skull shows soft tissue involvement by tumor near the lower right margin, resulting in erosion of the bone of the maxilla and hard palate, with infiltration of the homolateral orbital and nasal cavity. **(B)** CT of the chest showing subpleural tumor located at the right pulmonary apex, measuring approximately 3.7×2.9 cm. **(C1, C2)** CT of the upper abdomen and pelvis showing tumor nodules in the liver, adrenals, right kidney, pre-sacral region, and retroperitoneum, and destructive bone lesions in the right and sacral iliac bone, compatible with Kaposi's sarcoma (KS).

patients with KS [10]. The advent of highly active antiretroviral therapy (HAART) has resulted in a marked reduction of the incidence of KS in HIV-positive patients [8]. However, cases of disseminated and fulminant KS in HIV-positive patients who have not been diagnosed with HIV and KS at an early stage and who have not been treated with or adherent to antiretroviral therapy still occur, as demonstrated by the two cases in this report.

Lesions of KS affect the skin of the trunk and face, and the oral mucosa, progressing to purple (violaceous), non-pruritic plaques and nodules. The size of the lesions in KS can vary from millimeters to centimeters in diameter [2]. Ioachim et al. studied 86 cases of disseminated KS, of which 17 cases had no lesions of the skin or oral mucosa, but showed that commonly affected sites included the palate and oropharynx, with

purple tumors that could be associated with oral and gingival bleeding [10].

Patients with pulmonary KS usually also have cutaneous lesions. However, between 5–23% of patients with pulmonary symptoms do not have skin lesions. The most common pulmonary symptoms are progressive dyspnea, cough, and fever, in addition to hemoptysis, pleural effusion and respiratory failure in more advanced cases of KS [14,15]. Dirweesh et al. reported that the presentation of pulmonary KS with bone metastases as the first presentation of HIV patients was an uncommon presentation in KS without the involvement of visceral organs or associated skin lesions [16].

KS involvement of the gastrointestinal tract may be asymptomatic or present mild symptoms such as nausea, abdominal

pain, or vomiting. Intestinal KS can be diagnosed at any stage of HIV infection and is most commonly reported in severe immunosuppression, especially in HIV patients with an elevated viral load. Upper gastrointestinal endoscopy can show lesions that can vary in appearance, being erythematous, maculopapular, nodular, or polypoid [17,18]. Liver involvement in KS is often associated with hepatomegaly and abdominal pain and computed tomography (CT) or abdominal ultrasonography may show the presence of KS tumor in the liver capsule, hilum, portal vein, or invasion of the liver parenchyma [19].

Involvement of the adrenal gland is rare in KS, and most lesions of the adrenal gland are diagnosed incidentally after abdominal CT. Ramsingh et al. described a case of visceral KS in which the adrenal gland was partially replaced by a tumor mass composed of spindle cells, which were positive for CD34, CD31, and human herpes virus 8 (HHV8) using immunohistochemistry, confirming KS of the adrenal gland in a patient with HIV infection and acquired immunodeficiency syndrome (HIV/AIDS) [20]. Renal KS can occur in association with immunosuppression following renal transplantation but is uncommon in patients with HIV-associated KS, and when it occurs, it might reflect the degree of tumor dissemination and be an indicator of poor prognosis.

In the first of the two cases reported, purple (violaceous) lesions were detected on the skin and in the oral cavity, esophagus, stomach, duodenum, colon, liver, lymph nodes and lungs, which led to progressive clinical deterioration due to dissemination of the tumor, followed by hemothorax and acute respiratory failure. Due to the degree of immunosuppression (CD4 cell count to <11 cells/mm³), it was not possible to initiate an effective therapeutic protocol and the patient died.

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In the second of the two cases reported, the patient had a large facial tumor, hepatic and pulmonary nodules, an intracranial mass with edema, and involvement of bone, renal, and adrenal gland tissue by KS. Because the patients had a CD4 cell count of 151 cells/mm³, a chemotherapeutic protocol was initiated. However, the patient developed progression of the disease, with pulmonary infection and died from septic shock.

An uncommon presentation of visceral KS in two HIV-positive patients is presented in this report, with the dissemination of KS due to late diagnosis of HIV/AIDS and late treatment with HAART.

Conclusions

The presentation of fatal disseminated Kaposi's sarcoma (KS) in two patients with human immunodeficiency virus (HIV) infection highlight the possibility of a return of aggressive cases with visceral involvement by KS, similar to the first cases of acquired immunodeficiency syndrome (AIDS) described in the early 1980s. This is a matter of concern that might be explained by a reduction in awareness of the importance of HIV testing, lack of early diagnosis and treatment, all of which, as these two cases demonstrate, can result in high mortality rates. The availability of HIV screening might also be related to the geographic and regional differences in the fulminant evolution of KS, availability of immunological and molecular testing, both for the presence of HIV, human herpes virus 8 (HHV8), and tests for opportunistic infections, as well as the cost of HAART and chemotherapy.

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