中文題目：人類免疫缺乏病毒陽性患者的瀰漫性非皮膚卡波西氏肉瘤：高效抗逆轉錄病毒療法時代中的罕見案例

英文題目：Disseminated non-cutaneous Kaposi's sarcoma in a HIV-positive patient: a rare entity in the era of highly active antiretroviral therapy

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## Abstract

Kaposi's sarcoma (KS) is a vascular tumor associated with infection with human herpesvirus 8 (HHV-8) and is considered to be one of the acquired immunodeficiency syndrome (AIDS)-defining cancers [1]. Herein, we report a case of a human-immunodeficiency virus (HIV)-positive patient with disseminated non-cutaneous KS involving oral cavity, liver, and lungs, which is very rare in the era of highly active anti-retroviral therapy (HAART).

## Case report

A 28-year-old man presented to our emergent department with a 1-week of intermittent fever, cough, progressive dyspnea, and abdominal pain over right upper quadrant with generally yellowish appearance. He has been diagnosed as HIV/AIDS 4 years ago but he was not compliant to anti-retroviral therapy (ART), and he has been treated for *Pneumocystis jirovecii* pneumonia 3 months before this presentation. At the triage, he was afebrile (36.9°C), with heart rate 111 beats per minute, and blood pressure was 82/47 mmHg and the pulse oximetry showed 79% in the ambient air. On physical examination, it was notable for pale conjunctiva, icteric sclera, jaundice appearance, bilateral coarse crackles, decreased breathing sound in right lower lung field, right upper quadrant tenderness without rebounding pain or muscle guarding, and bilateral lower limb pitting edema. Meanwhile, there was an ulcerated and violaceous lesion at the hard palate (Figure 1). The laboratory data on arrival was remarkable for normocytic anemia (9.4 g/dL), thrombocytopenia (40000/μL), new-onset cholestatic conjugated hyperbilirubinemia (alkaline phosphatase, 738 IU/mL; total bilirubin, 4.4 mg/dL; conjugated bilirubin, 3.7 mg/dL; aspartate transaminase, 69 IU/mL; alanine transaminase, 13 IU/mL), hypoalbuminemia (1.7 g/dL), and hyperlactatemia (3.5 mmol/L). His CD4 lymphocyte count was 5/$mm^3$ and plasma HIV viral load was 80400 copies/mL. The arterial blood gas was pH 7.41 and PaO2 97 mmHg under a non-rebreathing mask. The chest radiograph showed bilateral interstitial opacities with multiple heterogeneous nodules and right pleural effusion. He was started on broad-spectrum antimicrobial agents. The contrast-enhanced computed tomography scan of the abdomen (Fig. 2) demonstrated bilateral hepatic and lung nodules, bilateral pleural effusion,

ascites, dilated bilateral intrahepatic ducts, and multiple enlarged lymph nodes in right cardio-phrenic angle, para-aortic, aortocaval and hepatic hilar region. Right thoracentesis further demonstrated bloody, and exudative pleural effusion, which was negative for malignancy. The conjugated hyperbilirubinemia got worse (total bilirubin rose to 10.5 mg/dL on hospital day 4). The respiratory distress progressed despite empiric antibiotics and then he was intubated. Biopsy of the oral lesion, liver, and transbronchial lung biopsy were performed and there were no microbiological evidences of bacterial, mycobacterial, viral or fungal infections. The pathology of the oral lesion (Fig. 3a and 3b) confirmed the diagnosis of KS, and the pathology of liver biopsy (Fig 3c.) and transbronchial lung biopsy (Fig 3d.) were all compatible with KS. The diagnosis of non-cutaneous disseminated KS involving the lungs, liver and oral cavity was then made. He was initiated with efavirenz/emtricitabine/tenofovir disoproxil on day 6. However, his condition got deteriorated rapidly with much elevated bilirubin level (>15 mg/dL). The patient and his family decided not to receive aggressive chemotherapy. He succumbed to the illness on hospital day 17.

## Discussion

In the era of HAART, the incidence of epidemic KS decreased significantly. At 5 years after AIDS onset, the cumulative incidence of KS in the USA has declined from 14.3% to 1.8% [2]. Though studies have reported significantly higher risk to develop KS among ART-treated patients with CD4+ T lymphocyte counts below 200 cells/$mm^3$, non-cutaneous KS is rare [3]. The most frequently involved sites of non-cutaneous KS are oral cavity, GI tract and lung. Stebbing et al [4] reported a cohort of 5932 HIV-infected patients in the HAART era, and 319 (5.4%) were identified with KS. Only 11 patients (3.4% of the KS patients and 0.2% of the total) was diagnosed with non-cutaneous KS. When it came to diagnose of non-cutaneous KS, it is difficult to differentiate common opportunistic infections from KS with organ involvement. The bronchoscopy-assisted bronchoalveolar lavage with or without lung biopsy or even tissue biopsy at lesions are essential to identify the infectious agents, such as bacteria, *P. jirovecii*, *Myocobaterium*, fungus or ever other co-infected virus and even possible neoplasm. In this case, KS with liver and lung involvement is uncommon and often undiagnosed antemortem. Even before the era of HAART, a case series reviewed 86 HIV-infected individuals and the only 7% of the cases were histologically proven KS in the liver [5]. Regarding treatment, HAART is recommended for all patients with AIDS-related KS and additional systemic chemotherapy might be indicated especially in the setting of rapid disease progression, visceral involvement, extensive lymphedema or extensive cutaneous KS unresponsive to local treatment. Pegylated liposomal doxorubicin or liposomal daunorubicin is the first-line choice of chemotherapy [6]. In conclusion, it's imperative to maintain drug adherence to restore CD4+ T

lymphocyte and to reduce the risk for AIDS-related KS. This case also underlines the importance of tissue proof for diagnoses of variable AIDS-defining illnesses in HIV-infected patients with very low CD4+ lymphocyte count.

## References


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Figure 1. Violaceous ulcerated oral mass at the hard palate

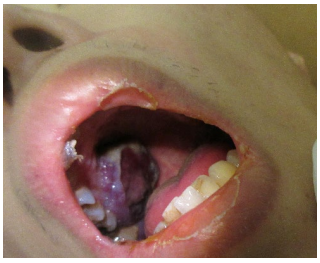


Figure 2.: Multiple hypodense hepatic mass and lung nodules

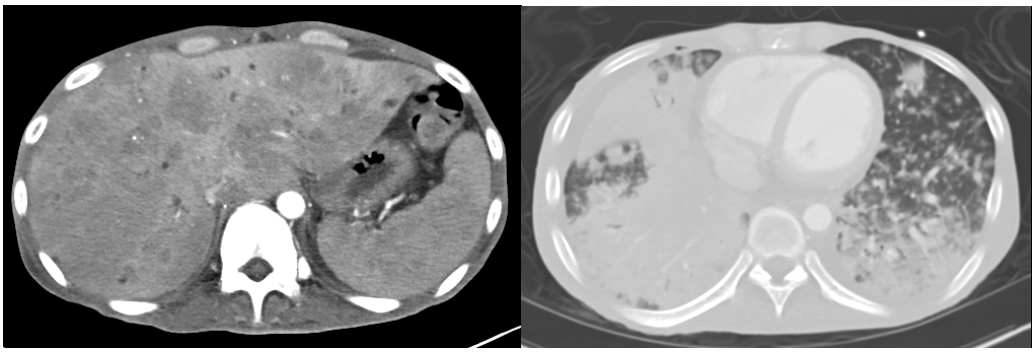
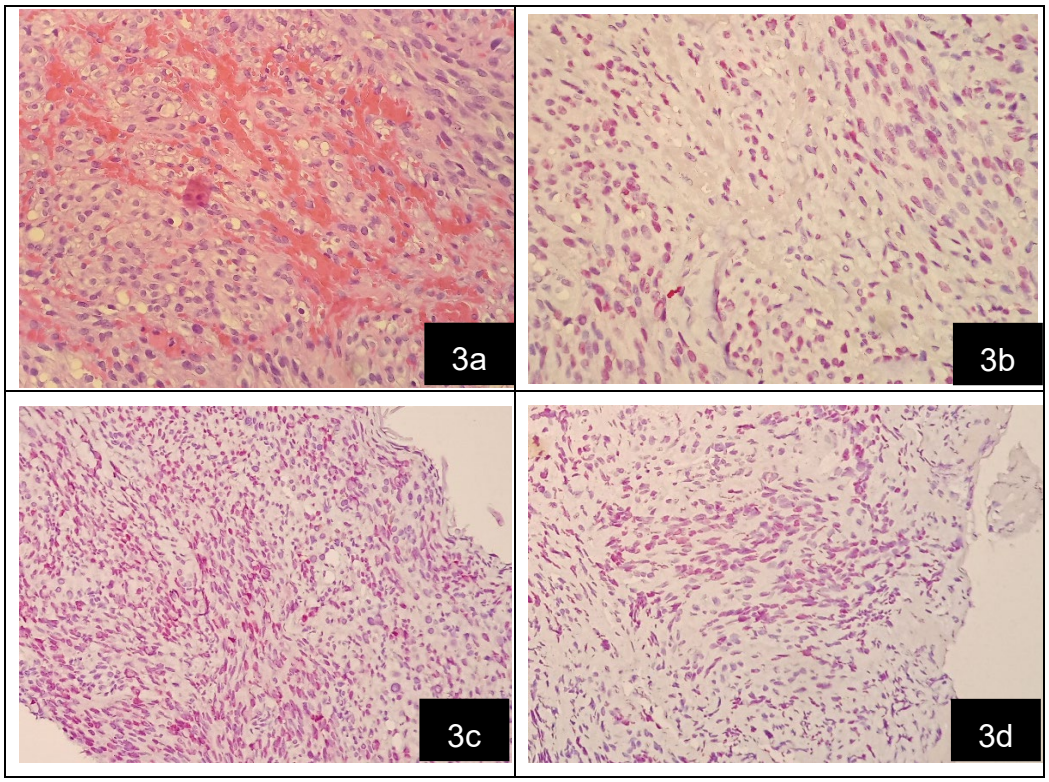


Figure 3




3a: Proliferation of endothelial cells with anastomosing vascular spaces in the dermis (oral lesion) (H&E stain, 400X)

3b: Tumor cells are positive for HHV-8 immunohistochemical (IHC) staining (oral lesion) (400X)

3c: Liver parenchyma infiltrated by oval to spindle-shaped tumor cells, which are positive for HHV-8 (100X)

3d: Proliferation of spindle-shaped cells in the subepithelial area with positive IHC staining for HHV-8 (lung) (100X)