Case in Point

Swollen Tongue in an Immune-Compromised Host

Charu Agrawal, BS; Chetan Jinadatha, MD, MPH; and Gagan Prakash, MD

A 25-year-old man with HIV presented with a worsening oral thrush and difficulty swallowing. The patient was initiated on a combination antiretroviral therapy and chemotherapy and, based on his clinical response, was diagnosed with Kaposi sarcoma.

A 25-year-old man presented to the clinic with a worsening oral thrush and difficulty swallowing for the past 3 weeks (Figure 1). He had been treated with fluconazole and penicillin with no benefit. In addition, he reported having a chronic dry cough. Past medical history was significant for human immunodeficiency virus (HIV) infection, and he was not on antiretroviral therapy (ART). The patient's HIV infection was diagnosed 2 years prior to his clinic presentation. He had travelled to Asia while in military service but has been living in Texas for the past 2 years. He has had multiple male sexual partners. Absolute CD4 count on presentation was 11 cells/μL, and his HIV viral load was > 450,000 copies/mL. A computerized tomography (CT) scan of the chest is shown (Figure 2). Microbiologic studies of the sputum (including acid fast bacilli) and bronchial washings were negative. Cytology of the bronchial wash was negative for malignancy. The patient underwent a biopsy of the tongue (Figure 3).

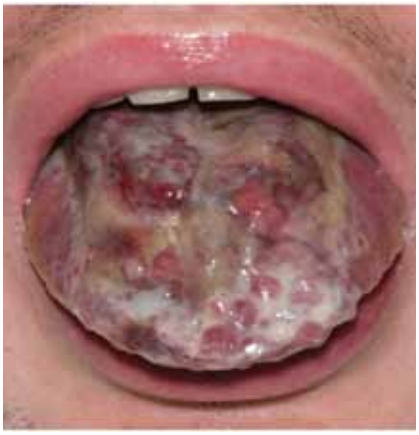


Figure 1. Tongue Lesion on Presentation.

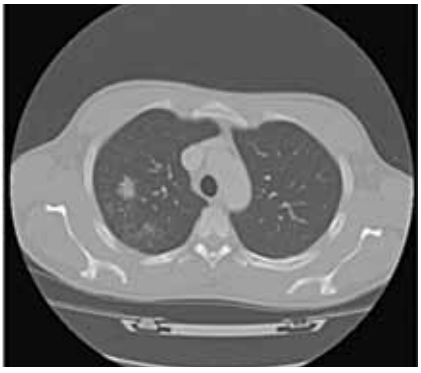


Figure 2. Computerized Tomography Scan of the Chest Showing the Infiltrate in the Right Upper Lobe.

DIAGNOSIS

The patient was diagnosed with Kaposi sarcoma (KS) based on the biopsy of the tongue. The patient was started on ART with a combination of emtricitabine/tenofovir and lopinavir/ritonavir. In addition, he received therapy with trimethoprim/sulfamethoxazole for prophylaxis of *Pneumocystis jiroveci* pneumonia and azithromycin for *Mycobacterium avium-intracellulare*. He underwent chemotherapy with liposomal doxorubicin for the KS. Given a lack of improvement of the pulmonary lesion on antibiotic therapy and the dramatic resolution with the initiation of ART and chemotherapy, a diagnosis of pulmonary KS was presumed based on the patient's clinical response (Figure 4).

DISCUSSION

Kaposi sarcoma is a rare tumor caused by KS–associated herpesvirus (KSHV), also known as human herpesvirus 8 (HHV-8), a γ2 herpesvirus from the rhadinovirus genus.[1] Ka-

Ms. Agrawal is a medical student at the Texas A&M Health Science Center, College of Medicine; and **Dr. Jinadatha** is the chief of the infectious diseases section and **Dr. Prakash** is a staff pulmonologist, both at the Central Texas Veterans Health Care System, all in Temple, Texas.

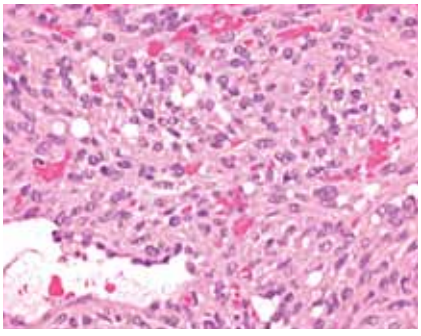


Figure 3. Immunohistochemical Stain of the Specimen From the Tongue Biopsy.

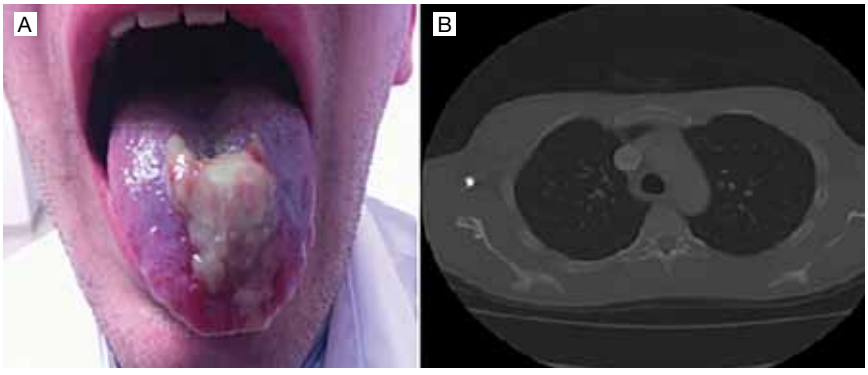


Figure 4. Improvement in the Tongue Lesion as Well as the Right Upper Lobe Lung Lesion With Initiation of Antiretrovirals and Chemotherapy.

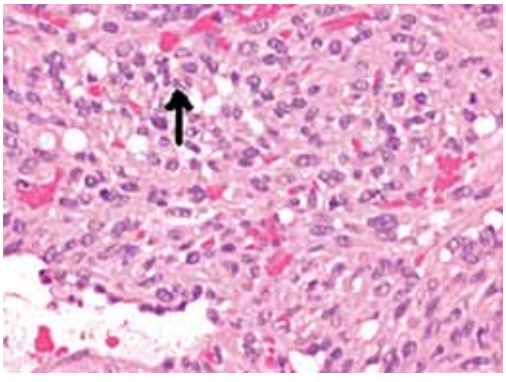
posi sarcoma was initially described by Moritz Kaposi in 1872 in 5 dermatologic patients with idiopathic multipigmented skin lesions.[2] Later in 1981, KS was described by the Centers for Disease Control and Prevention in more than 50 young homosexual men.[3] Kaposi sarcoma was found to be associated with profound deficiency in cell-mediated immunity and other concurrent life-threatening opportunistic infections. Kaposi sarcoma subsequently was described as an acquired immune deficiency syndrome-(AIDS-)defining illness with sexual transmission being the most common mode of acquisition.[3,4] Kaposi sarcoma presents with cutaneous lesions with or without internal organ involvement. The cutaneous lesions may be solitary, localized, or disseminated. It can involve the oral cavity, lymph nodes, and viscera (eg, the lungs and the gastrointestinal tract).[4]

There are 4 clinical variants of KS. Classic KS is relatively indolent, common in elderly patients of Mediterranean descent, particularly of Eastern European Jewish descent. It affects men more often than women in a 15:1 ratio. Small bluish nodules and plaques occur bilaterally on the feet, legs, or on the hands. The prognosis is fairly good with the average patient survival of 8 to 13 years on low-level chemotherapy.[4,5] African or endemic KS predominantly affects young men. There may be localized or generalized lymphadenopathy. The disease follows a fulminant course with visceral involvement.[5] Transplant-associated KS is usually seen in patients who have undergone a renal transplant, manifesting 1 to 2 years after transplantation. The tumor commonly regresses when the immunosuppressive therapy is stopped.[4,5] Epidemic/AIDS-related KS is an aggressive disease in patients with AIDS, particularly common in homosexual subgroups.[4-6] Affected patients are usually young adults or early middle-aged men. It initially presents as a maculopapular eruption on the skin or mucosa. This eruption disseminates widely and often involves the viscera and the lymph node. It has a strong predilection for the palatal and the gingival mucosa. The prognosis is related to the improvement in the patient's immune status with initiation of ART and possible treatment directed against KS.[4-6]

Polymerase chain reaction (PCR) for HHV-8 is positive in only about 50% of the peripheral blood cells.[7] However, both the less sensitive PCR and the Southern blot hybridization assay can detect HHV-8 in all lesions of KS. Serologic assays (HHV-8-specific antibodies) have higher sensitivities and may be more useful than PCR in screening for previous exposure to HHV-8.[7,8] Definite diagnosis is made by biopsy and microscopic examination, which shows the presence of spindle cells (Figure 5). The detection of the KS-herpesvirus protein latency-associated nuclear antigen (LANA-1) in tumor cells confirms the diagnosis.[4]

Wide ranges of treatment options are available for KS. Patients with

Figure 5. Immunohistochemical Stain for Human Herpesvirus 8 (HHV-8). (Arrow shows nuclear positivity in spindle cells, which is considered a hallmark trait of Kaposi sarcoma).



AIDS-associated KS should receive ART. Effective antiretroviral regimens are associated with a reduction in the incidence of AIDS-related KS and regression in the size and number of existing lesions. Several antiviral agents, including ganciclovir, foscarnet, and cidofovir, have been shown to inhibit KS-herpesviral replication in vitro.[1,4]

Patients with limited local disease may benefit from a variety of therapies, including intralesional chemotherapy (vinblastine), topical ointments (alitretinoin gel), cryotherapy, laser therapy, photodynamic therapy, and, infrequently, excisional surgery.[1,4] Radiation therapy is effective and often represents the best local treatment for palliation of pain, bleeding, or edema.[1,4] Patients with rapidly progressing extensive cutaneous or visceral disease should get systemic therapy.[4] Systemic treatments have traditionally involved cytotoxic chemotherapy. Although numerous chemotherapeutic agents have been shown to be effective, only 3 have Food and Drug Administration approval: liposomal anthracyclines, pegylated liposomal doxorubicin and liposomal daunorubicin, and the taxane, paclitaxel.[9]

CONCLUSION

In summary, KS is the most frequently diagnosed AIDS-associated malignancy in the U.S. Initiation of antiretrovirals with or without KS-specific chemotherapeutic agents is the treatment of choice. Prognosis depends on the response to antiretrovirals and the extent of the disease with a median survival of weeks to months. ●

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Author disclosures

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REFERENCES

1. Martellotta F, Berretta M, Vecchet E, Schioppa O, Zanet E, Tirelli U. AIDS-related Kaposi's sarcoma: State of the art and therapeutic strategies. *Curr HIV Res.* 2009;7(6):634-638.
2. Kaposi M. Idiopathic multiple pigmented sarcoma of the skin. *CA Cancer J Clin.* 1982;32(6):342-347.
3. Centers for Disease Control (CDC). Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men—New York City and California. *MMWR Morb Mortal Wkly Rep.* 1981;30(25):305-308.
4. Antman K, Chang Y. Kaposi's sarcoma. *N Engl J Med.* 2000;342(14):1027-1038.
5. Laurent C, Meggetto F, Brousset P. Human herpesvirus 8 infections in patients with immunodeficiencies. *Hum Pathol.* 2008;39(7):983-993.
6. Lodi S, Guiguet M, Costagliola D, Fisher M, de Luca A, Porter K; CASCADE Collaboration. Kapsoi sarcoma incidence and survival among HIV-infected homosexual men after HIV seroconversion. *J Natl Cancer Inst.* 2010;102(11):784-792.
7. Whitby D, Howard MR, Tenant-Flowers M, et al. Detection of Kaposi sarcoma associated herpesvirus in peripheral blood of HIV-infected individuals and progression to Kaposi's sarcoma. *Lancet.* 1995;346(8978):799-802.
8. Moore PS, Kingsley LA, Holmberg SD, et al. Kaposi's sarcoma-associated herpesvirus infection prior to onset of Kaposi's sarcoma. *AIDS.* 1996;10(2):175-180.
9. Sullivan RJ, Pantanowitz L, Casper C, Stebbing J, Dezube BJ. HIV/AIDS: Epidemiology, pathophysiology, and treatment of Kaposi sarcoma-associated herpesvirus disease: Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease. *Clin Infect Dis.* 2008;47(9):1209-1215.