

Oral Kaposi's Sarcoma In HIV Positive Patients. A Case Report and A Review of Literature

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Abstract

Introduction: Kaposi Sarcoma (KS) is a soft tissue malignancy that has been categorized into 4 subtypes, however, in the United States, it has frequently been noted in patients with HIV/AIDS and has thus become known as an AIDS-defining illness. When KS is found in the oral cavity, it is usually seen on the hard palate. Oral KS (OKS) is most commonly seen in patients with HIV/AIDS with CD4 counts below 200, and the disease is rarely reported outside of this patient population. HIV patients may be more likely to have KS with the decline of their immune function.

Report of case: We report the case of a 31 year old African American male with a 2 year history of HIV who presented to the Otolaryngology clinic with a painful tongue lesion. His CD4 count never fell below 200, which makes this case an outlier among the epidemiology of KS. This case is unique in two different ways. The dorsum of the tongue is one of the least common manifestations of OKS and secondly OKS is usually associated with CD4 counts <200 per microliter, and this patient's CD4 count stayed above 200 cells per microliter throughout his evaluation and treatment. The tongue lesion was causing dysphagia and odynophagia that was significant enough to cause him to seek medical care.

Discussion: Despite the relatively adequate resources for HAART therapy among the American indigent population, some patients still decline this highly efficacious treatment and succumb to its now rare complications. Physicians must actively investigate suspicious oral lesions in HIV patients, particularly when there is a question about the compliance of HAART therapy or other concerning features. The oral cavity may be the initial manifestation site for HIV associated KS thus any suspicious lesion in sexually active patients should lead to testing for HIV.

Keywords: HIV/AIDS; AIDS; HIV; Kaposi; Sarcoma; Immunossupression; HAART

Introduction

Kaposi sarcoma (KS) is a soft-tissue malignancy arising from the proliferation of spindle cells with vascular endothelial cell origin. The disease most frequently affects mucocutaneous tissues as well as the visceral aerodigestive tract. Lesions can arise anywhere along the digestive tract from the oral cavity to the perianal region. Human herpesvirus 8 (HHV-8) is a crucial factor in disease pathogenesis, however the exact mechanism of disease pathogenesis has not been elucidated [1]. KS has four main epidemiologic variants according to the inciting factor of disease: (1) Classic, or sporadic; (2) Endemic (African); (3) Epidemic (AIDS-related); and (4) Iatrogenic (post-transplant). Also, there have been reports of epidemic oral Kaposi Sarcoma (OKS) in the context of immune reconstitution inflammatory syndrome (IRIS). IRIS-associated OKS may present or worsen when the immune system regains function and begins to attack KS antigens.

KS is one of the first recognized opportunistic diseases in human immunodeficiency virus (HIV) infection. Although patients may develop KS at any stage of infection, it is more prevalent in patients with a lower CD4 count [2]. The incidence of KS started to drop significantly after the mid-1990s, with the introduction of Highly Active Antiretroviral Therapy (HAART), which partially restores immune system function, and has remained relatively stable since 2000 [3]. The incidence of KS has decreased in the United States (US) and Europe with the introduction of HAART, but in Africa it remains the most common type of cancer in HIV-infected immunocompromised individuals.

In the US, infection with HIV remains considered the greatest risk factor for KS. Approximately 1/3 of patients have oropharyngeal manifestations of disease, and the most common subsite involved

within the oral cavity is the palate [1,4]. Among the patients with OKS, very few have lesions involving the dorsal tongue [1]. The purpose of this paper is to (1) report a case of an HIV patient with an unusual presentation of dorsal tongue KS and (2) to provide an update on the current recommendations for the diagnosis and treatment of KS with a focus on the oral cavity.

Case Report

The patient, a 31-year old African American male, was initially diagnosed with HIV infection when he presented to the emergency department with myalgias and asthma exacerbation in February of 2010. He reported a significant tobacco abuse history as well as a history of cocaine abuse in the past. At that time, his viral load was over 500,000 copies per milliliter (ml) and absolute CD4 T helper cell lymphocyte (CD4) count of 281 cells per microliter. During that hospital admission, the patient was found to have a cavitary lesion of the left lung that was treated as pneumonia. On subsequent computerized tomography (CT) scan, persistence of the lesions led to further diagnostic testing. This was significant for *Mycobacteria Kansaii* for which he completed treatment with clindamycin, isoniazid, rifabutin, ciprofloxacin and ethambutol in

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August of 2011. He had persistent mycobacterium avium-intracellulare (MAC) post antibiotic treatment. His CD4 count in April of 2011 was 926 cells per microliter and HIV viral load was 56,510 copies per ml. The patient had been non-adherent with HAART therapy during the initial course of his HIV infection and had refused HAART therapy several times. It was unclear as to if patient ever had been started on HAART therapy.

In September of 2013, he presented to the Otolaryngology-Head and Neck Surgery clinic complaining of a painful midline tongue lesion. The lesion had been present for a few weeks. He denied otalgia and tongue numbness. He did report dysphagia and odynophagia. He also stated that he had recently initiated HAART therapy although this could not be confirmed with available medical records. On physical exam, the patient was noted to be thin but not cachectic. A nodular erythematous and friable lesion was present on the midline of the tongue extending from the circumvallate papilla to the midline dorsal surface. It was approximately 3 by 4 centimeters. Differential diagnosis for the lesion included lymphoma, Kaposi sarcoma, mycobacterial infection, squamous cell carcinoma, bacillary angiomatosis or pyogenic granuloma. The patient underwent biopsy of the tongue lesion initially in September of 2013 which revealed hyperplastic squamous mucosa overlying dense patchy lymphoid infiltrate. There was no evidence of mycobacteria nor histiocytic aggregates (Figure 1). Further investigation into the patient's history revealed that he had a history of non-adherence with medical therapy. At his follow up in April of 2014, the patient had a CD4 count of 450 with viral load of 55,330 copies per ml.

After his initial biopsy, the patient had persistent pain and a new



Figure 1: Gross photograph of oral lesion showing violaceous friable midline tongue lesion extending beyond circumvallate papilla.

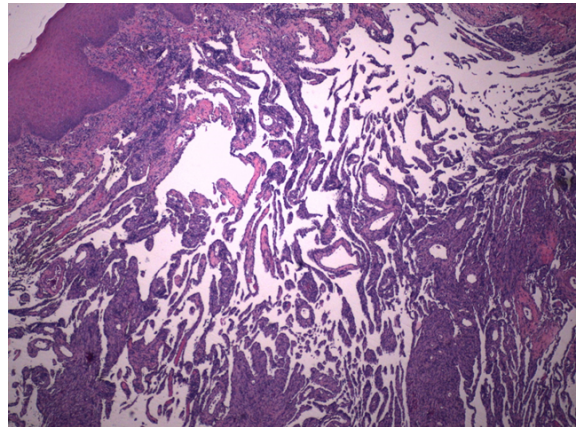


Figure 2: Lymphangioma-like area in the Kaposi sarcoma.

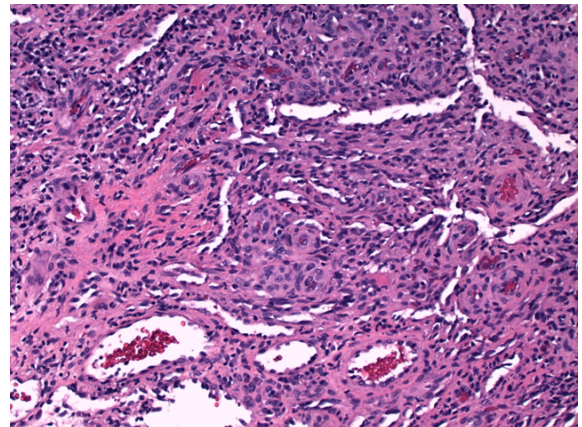


Figure 3: Dilated irregular vascular channels surround a preexisting vessels with a corresponding promontory sign.

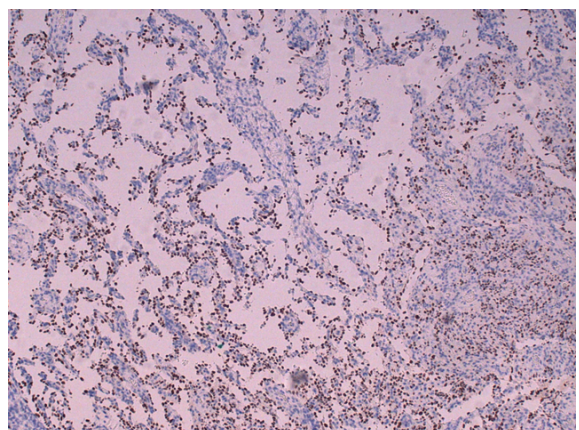


Figure 4: Positive HHV-8 nuclear staining of the oral lesion.

tongue lesion developed in the lateral tongue surface. As a result, he was taken again for biopsy of this lesion in June of 2014. Pathology revealed findings consistent with KS (Figures 2-4). The patient was referred for treatment with radiation, however, he has failed to keep his appointment, and was lost to follow up.

Discussion

Frequently KS can be the first sign of an occult HIV infection presenting in an indolent fashion without a lot of clinical symptoms [5,6]. The color of the lesions can range from dark pink, red, purple or brown. Overall, epidemiological studies report a greater incidence of KS in males compared to females, with the ratio depending on the subtype of KS [1]. In general, the most frequent site of involvement is the skin followed by the aerodigestive tract. The gastrointestinal system can be affected by multicentric lesions observed from oral cavity, oropharynx and esophagus to the perianal area, including organs like pancreas, liver and other organs like, lungs and tests. It is estimated that almost half of patients with AIDS and KS may present with associated visceral lesions [7].

Of the four variants, the epidemic form most commonly involves the oral cavity [2]. About 22% of HIV patients with KS have oral involvement as the initial manifestation. In up to 71% of patients there are oral KS along with dermal and visceral lesions. In a South African epidemiological study, Khammissa et al. showed that the gingiva was the most common site of oral involvement (30%), with the dorsum of the tongue being the least common (5%) [2].

This case contributes to the literature because of two unique components of this presentation of OKS. Our patient presented with KS in an unusual location within the oral cavity (dorsum of tongue) as well as manifesting disease with a CD4 count over 200 per microliter. OKS is usually associated with CD4 counts less than 200 per microliter. OKS is often the first manifestation of AIDS and thus is not as frequently seen in patients with higher CD4 counts.

In a series of 134 patients published in 1988 (before the advent of HAART) about one quarter of that population had the oral cavity as the initial site of manifestation. The most frequent intraoral site was the hard palate, soft palate, gingival and dorsal tongue involved in this order of frequency [8]. Therefore, it is important to keep KS in the differential diagnosis for new oral masses in patients with HIV, as well as, immunosuppressed patients undergoing cancer treatment.

There is a unique relationship between neoplastic transformation of KS and immune function. Recent epidemiologic studies suggested an association between all types of KS and the infectious etiology by the oncogenic human herpes virus type 8 (HHV-8), also known as Kaposi's sarcoma herpes virus (KSHV) and a high concentration of KSHV laboratory markers KS patients [9]. The interplay of T lymphocytes, HIV virus and herpes virus in contributing to the pathogenesis of KS remains to be defined. Some studies have shown that discontinuation of immunosuppressive therapy can improve the iatrogenic form of KS [1]. The focus of treatment among HIV patients with KS should be initiation and maintenance of HAART therapy. Proper compliance of HAART therapy may result in a less severe form of the disease or even possibly regression [10]. It is likely that initiation of HAART therapy can both improve immune system function and reduce HIV-1 viral load.

KS is by far more commonly found in immunosuppressed status and normally improves after HAART initiation or when halting iatrogenic immunosuppression. The use of HAART in these cases, contribute significantly not only for the restoration immune system elevating CD4+ number, but also for reduction of the viral load normally resulting in a significant clinical response to the tumor size. KS has recently been reported in HIV-negative men having sex with men. A retrospective study in 2008 showed a group of 28 men who were all HIV-negative, which shows that KS can rarely present in the absence of significant immunosuppression [11].

The treatment of epidemic KS (HIV-related) includes initiation of HAART therapy as well as multiple other treatment modalities. Surgical resection, radiation therapy, systemic chemotherapy [interferon alpha (IFN- α)], intra-lesional chemotherapeutic agents (bleomycin, vincristine, vinblastine), sclerotherapy, cryotherapy, laser, immune modulators and multiple other experimental treatments with a variable grade of response. Treatment goals include pain control, and reestablishment of oral function which ultimately results in quality of life improvement for these patients [1].

The burden of this tumor can be significant for many patients as it may cause a reduction in quality of life, feature tumor-associated edema, oropharyngeal dysphagia and may include a burden of poor esthetics as well. Hopefully the diligent implementation of HAART therapy could reduce the incidence and tumor complications associated with oral KS. Also, it is important that we question patients with associated risks about possible mucocutaneous findings, which may allow physicians to make this diagnosis sooner than later and reduce overall disease burden. We must educate our patients on the importance of HAART therapy and potential oropharyngeal manifestations of KS.

It is important to maintain a broad differential diagnosis for oral lesions, which may include: lymphoma (non-Hodgkin plasmablastic lymphoma), squamous cell carcinoma, melanoma, hemangioma, bacillary angiomatosis (*Bartonella henselae*), pyogenic granuloma [12,13]. This has been demonstrated through the current case with the initial nondiagnostic pathology.

Conclusion

The oral cavity may be the only or first site of KS, and therefore, becomes important in the diagnosis. Exams of the oral cavity should be done regularly in immunosuppressed patients, since a variable number of lesions can manifest initially in this site. Physicians must maintain a broad differential diagnosis which may include: lymphoma, squamous cell carcinoma, melanoma, hemangioma, and pyogenic granuloma. Mainly, in HIV patients with low CD4 counts, physicians should keep a low threshold for biopsy once an identified lesion does not respond to treatment. This diagnosis may not be considered initially in the post HAART era. It is important to maintain a high clinical suspicion and even if patients have normal CD4 counts, the immune system may not function in a normal fashion in the setting of active HIV.

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