

A PEER-REVIEWED ARTICLE

Kaposi sarcoma is the most common cancer diagnosed in HIV-infected persons

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Before the era of HIV/AIDS, Kaposi sarcoma (KS) was a rare neoplasm diagnosed primarily in elderly men of Eastern European and Mediterranean origin.¹ It can also occur in persons from Central Africa and occasionally in solid organ transplant recipients.^{2,3} Today KS is recognized as the most common cancer diagnosed in HIV-infected persons, with an incidence of >20,000 times that of the general population.⁴ It is most common in HIV-infected homosexual or bisexual men, and only rarely reported in intravenous drug users or other HIV risk groups.⁵

The incidence of KS has decreased significantly since the early years of the HIV/AIDS epidemic. In New York City, the disease was seen as early as the 1980s, prior to the availability of highly active antiretroviral therapy (HAART). KS was the initial AIDS-defining illness in about 50% of gay men in New York City in 1981-83, but this had decreased to 30% by 1984-1987.⁶ An even more dramatic reduction in incidence has occurred in the HAART era. Data from San Francisco document a peak incidence of KS of 31.3-33.3 per 100,000 white men for the period 1987-1991, with a marked decline to 2.8 for the year 1998.⁷ Multiple other studies have shown a similar decline in incidence coinciding with the widespread use of HAART.^{8,9}

Pathogenesis

KS is strongly associated with infection with human herpesvirus 8 (HHV-8), also known as the KS-associated herpes virus.¹⁰ HHV-8 has been found not only in AIDS-related KS but in all of the epidemiologic forms of KS.¹¹ Histologically, KS is characterized by the proliferation of spindle-shaped cells, leukocyte infiltration, and abnormal proliferation of small vessels. KS spindle cells are thought to be derived from lymphatic endothelium.¹² HHV-8 is found primarily in a latent form within KS cells.

The pathogenesis of KS is complex. It has been proposed that HIV and HHV-8 act in a synergistic fashion, through the production of factors such as inflammatory cytokines and the HIV *tat* gene product, to induce differentiation of KS progenitor cells into KS spindle cells. Defective cellular immunity related to HIV disease allows further development of the cancer.^{13,14}

Clinical manifestations/diagnosis

The presentation of AIDS-related KS is variable, ranging from small skin lesions in an asymptomatic patient to invasive disease with deep tissue and/or visceral organ involvement.¹⁵ Some patients may have minimal disease with very slow progression, while others may have rapidly progressive disease that causes significant morbidity and mortality, especially in the presence of poorly-treated HIV infection. KS may occur at higher CD4 counts but is more commonly diagnosed as CD4 counts decline to lower levels.

The skin is the most common site of the initial lesions of KS. Skin lesions range from small, painless nodules to macules. They may be single or multiple, and multiple lesions may coalesce to form larger, plaque-like lesions. Typical coloration of the lesions is due to their vascular nature and may be reddish, violet or brown. The skin lesions may be anywhere but most commonly occur on the face and lower extremities, and obstruction of the lymphatics may cause edema of these areas.

Extracutaneous KS is common, particularly in the gastrointestinal (GI) tract and the lungs. Visible lesions of the oral cavity, usually on the palate or gingiva, are not infrequent and if seen by dental providers may lead to the diagnosis of underlying HIV infection. GI lesions are often asymptomatic but may ultimately cause nausea, pain, bleeding, or obstruction.¹⁶ Pulmonary involvement is generally a late complication and usually results in symptoms such as cough and dyspnea. Typical chest x-ray findings include nodular or alveolar infiltrates and pleural effusion.¹⁷

Frequent examination of the skin and oral cavity are essential for the diagnosis of KS. Suspicious lesions should be biopsied to confirm the diagnosis and to differentiate KS from other conditions such as bacillary angiomatosis. Once the diagnosis has been made, oncologists experienced in the treatment of KS recommend a complete examination of the skin and oral cavity as part of a staging process.^{18,19} Endoscopic exam of the GI tract is recommended only if symptoms are present. Bronchoscopy should be part of the diagnostic evaluation if pulmonary disease is suspected but visualized lesions should not be biopsied due to bleeding risk.

Treatment

The treatment of patients with AIDS-related KS should be individualized. The primary goals of treatment are lesion regression and palliation of symptoms. In addition to the presence of symptoms and disease extent, the decision to initiate treatment should also be based on cosmetic issues and the social stigma associated with KS.

Anti-HIV drug therapy is an essential part of the treatment of AIDS-related KS. Suppressive HAART may induce an anti-KS response, and in the presence of limited, asymptomatic disease, HAART alone may be sufficient.²⁰ In patients with more advanced disease, HAART may lengthen the time of treatment response to KS-specific local or systemic therapy. HAART is thus recommended for virtually all patients with AIDS-related KS.

Local therapy is often recommended for patients with limited, slowly progressive disease for whom HAART alone does not provide an acceptable response. Approaches using local therapy include radiation therapy for isolated lesions of the skin or oral cavity, intralesional chemotherapy, cryotherapy, or laser therapy.

Anti-KS chemotherapy plus HAART is recommended for patients with more advanced disease causing significant impairment and for patients with pulmonary disease. A variety of agents have been used with some efficacy. These include doxorubicin, paclitaxel, vinorelbine and interferon- α . Chemotherapy may be associated with considerable toxicity. A detailed discussion of the treatment of KS is beyond the scope of this article and is reviewed in more detail elsewhere.^{18,19} Overall, the prognosis for patients diagnosed with KS has significantly improved since the advent of the modern era of anti-HIV drug therapy. ❖

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