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Kaposi's sarcoma in an HIV-positive person successfully treated with paclitaxel

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Abstract: Epidemic Kaposi's sarcoma is one of the malignant neoplasms, which can develop in HIV-infected patients. Although the prevalence of HIV infection is reported to be high in Asian countries, Kaposi's sarcoma is rarely reported. We report a case of Kaposi's sarcoma involving the skin and oral mucosa along with extensive bilateral lymphedema of lower extremities, treated successfully with paclitaxel and antiretrovirals.

Full text: Introduction

Kaposi's sarcoma (KS) is an angioproliferative disease characterized by proliferation of spindle-shaped cells. Epidemic KS is one of the AIDS-defining conditions, which now a days is rarely reported. There is no complete cure for KS but highly active antiretroviral therapy (HAART), topical and systemic therapies are useful in reducing the disease-associated morbidity and mortality.

Case Report

A-40-year-old, unmarried, HIV-seropositive man presented with asymptomatic dark-colored flat and elevated lesions over both the legs and difficulty in walking due to swelling over both the legs of six months duration. He was on treatment for abdominal tuberculosis for four months.

Lesions first started on the feet as flat, dark-colored lesions. After a few months, papules appeared on both legs, which gradually increased in size. This was followed by swelling over both the feet and legs. Simultaneously, new patches developed on both the hands and forearms. He had no episode of hemoptysis, hematemesis or melena.

Examination revealed bilateral nonpitting edema involving both feet extending up to lower two-thirds part of legs along with multiple skin-colored, translucent papules and plaques [Figure 1]. There were multiple erythematous to dark brown patches and plaques over the thighs [Figure 2], dorsal and palmer surface of hands. A single erythematous patch was noted on the soft palate. There was no hepatosplenomegaly and neither significant lymphadenopathy.

His laboratory investigations for complete blood cell count (CBC), liver and renal function tests were normal. Serology for HbsAg and VDRL was negative. X-ray chest showed fibrosis involving the right upper lobe. Systemic involvement due to KS was ruled out with the help of chest and abdominal CT scan. His CD4 count was 179 cells/mm 3.

Skin biopsy from a papule over the leg showed spindle cell proliferation in the dermis along with formation of cleft-like spaces. Extravasation of RBCs, infiltrate consisting of lymphocytes and plasma cell was seen in the dermis. Immunohistochemical markers for factor VIII and podoplanin were positive. DNA PCR for HHV-8 performed on paraffin-embedded skin specimen was positive. Thus, the diagnosis of KS was confirmed.

His antituberculosis treatment was continued and prophylaxis with cotrimoxazole-DS was started. Antiretroviral regimen (lamivudine, stavudine and efavirenz) was initiated. Considering his tumor burden and bilateral lymphedema, he was started on chemotherapy, which included injection paclitaxel (90 mg/m 2 of body surface area IV over 3h, 3 times/month). During this chemotherapy, his CBC was monitored regularly. He tolerated chemotherapy well without any side effects.

On completion of six cycles of chemotherapy, improvement was seen in the form of reduction in size of the skin lesions and disappearance of oral lesion [Figure 3]. Lymphedema reduced significantly, so he was able to walk normally and resumed his job.

Discussion

Four different epidemiological forms of KS have been described. [1] HIV-related KS is known as epidemic KS. During the earlier days of HIV epidemic, KS was seen as an early phenomenon but as the epidemic matured it is seen as late manifestation of HIV infection. [2] This may be due to increased awareness about HIV infection, early diagnosis and introduction of HAART.

KS may be seen any time during the course of HIV infection. The rate of progression varies from patient to patient and may not be related to the level of immunosuppression. Cutaneous involvement is the most common presentation (>90%). Systemic involvement is not uncommon. Other than the skin, oral mucosa, lungs (20 %), gastrointestinal tract (40%) and lymph nodes are the sites commonly involved. Skin biopsy and immunohistochemical investigations are crucial to confirm the diagnosis of KS. Endoscopy to rule out gastrointestinal tract involvement and CT scanning or bronchoscopy to rule out pulmonary involvement are necessary.

Prognosis of patients with epidemic KS depends not only on the extent of KS but also on other factors such as the level of immunocompromization, opportunistic infections and antiretroviral treatment. [3] As seen in other HIV-infected without KS, mortality in patients with KS is contributed mostly by other opportunistic infections. In some cases, lesions remain indolent and treatment may not be required.

AIDS clinical trial group (ACTG) has predicted the prognosis of patients with KS according to extent of tumor (T), immune status (I) and severity of systemic illness (S). [4] Good prognosis is expected when CD4 count> 150/mm 3 , only cutaneous involvement and no "B" symptoms.

In HIV-infected patients, KS is one of the indications to start antiretroviral treatment. HAART has significantly changed the morbidity and mortality associated with KS and also has reduced its incidence. [5] Both PI- and NNRTI-based antiretroviral regimens are equally effective. [6]

Local treatment modalities (intralesional vinblastine, cryotherapy, laser and radiation) are useful if skin or mucosal lesions are few and there is no systemic involvement. Indications for systemic treatment for KS are (1) visceral involvement, (2) extensive KS- associated lymphedema, (3) extensive and rapidly progressive cutaneous KS and (4) failure to respond to local treatment.

US FDA has approved liposomal anthracyclines (doxorubicin and daunorubicin) as the first-line agents to treat KS. [7] Paclitaxel has also been approved but due to its toxicity profile it is preferred as a second-line agent. Other systemic treatment modalities include interferon-alfa and combination chemotherapies with adriamycin, bleomycin plus vincristine or vinblastine.

Paclitaxel is a taxane, which promotes irreversible polymerization of microtubules. Paclitaxel has been used for aggressive classic KS, [8] advanced epidemic KS and for the cases of epidemic KS, which failed to respond to liposomal anthracyclines or combination chemotherapy with adriamycin, bleomycin and vincristine. [9]

Various dosage and schedules have been attempted. Higher dosage (135-175mg/m 2) every 3 weeks [10] or low dose (100mg/m 2) every 2 weeks [9] or weekly [10] are successfully used. Also, a weekly dose of 70mg/m 2 was found to be effective. [11] These studies observed significant improvements in the total quality of life and improvement in KS-related symptoms with acceptable toxicity. The low-dose regimens have relatively less adverse effects and are better tolerated.

Common adverse effects reported include neutropenia, alopecia and hypersensitivity reactions. [9],[12] Uncommon side effects observed included late fevers, late rash and eosinophilia. Premedication with systemic corticosteroid and antihistamines may be necessary 6 h before paclitaxel infusion to avoid hypersensitivity reactions. Sensory peripheral neuropathy can occur. Treatment with stavudine, didanosine or isoniazid may exacerbate neuropathy. Complete blood cell count needs to be monitored regularly during paclitaxel therapy.

KS cannot be cured completely. The abovementioned modalities help to reduce the symptoms, tumor burden and prevent progression of the disease. Prophylaxis and treatment of other opportunistic infections is necessary as uncontrolled infections may stimulate KS progression probably due to production of angiogenic cytokines.

In resource-limited countries such as India, where liposomal doxorubicin or daunarubicin is currently unavailable and not affordable, paclitaxel is a better option for treatment of KS than more toxic combination chemotherapies with bleomycin, vincristine and adriamycin.

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