# Clinical course of disseminated Kaposi sarcoma in a HIV and hepatitis B co-infected heterosexual male

Manoj Kumar Agarwala, Renu George, Thambu David Sudarsanam[1], Raju Titus Chacko[2], Meera Thomas[3], Sheila Nair[3]

Departments of Dermatology, [1]Medicine, [2]Medical Oncology and [3]Pathology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India

## ABSTRACT

AIDS associated Kaposi sarcoma (AIDS-KS) was first reported from India in 1993. Since then only 16 cases have been reported. Three of them had proven Human Herpesvirus 8 (HHV-8) infection. We report a case of disseminated KS in a heterosexual male from India with HIV, hepatitis B and HHV-8 infection. He was given six cycles of chemotherapy with liposomal doxorubicin over three months to which he showed a good response. The case highlights the clinical course and management of a HHV-8 positive disseminated KS in a patient co-infected with Hepatitis B and HIV.

**Key words:** Doxorubicin, HIV-hepatitis B virus co-infection, Kaposi sarcoma

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**Address for correspondence:**
Dr. Renu George, Department of Dermatology, Christian Medical College and Hospital, Vellore - 632 004, Tamil Nadu, India.
E-mail: renuegeorge@gmail.com

## INTRODUCTION

Kaposi sarcoma (KS) is a lymphoangioproliferative disease caused by human herpes virus 8 (HHV-8). Early KS seems to be a reactive process of polyclonal nature, which may remain so or progress to become a true sarcoma.[1] Acquired immune deficiency syndrome (AIDS)-KS may have an unpredictable clinical course varying from an incidental finding to a rapidly progressing cancer that can severely affect the quality of life. Treatment is with existing chemotherapy regimens, with dose depending on the extent and severity of the condition. It involves a substantial burden of toxicity. There have been only few reports of HHV-8 associated KS from India.[2-4] This has been attributed to the low prevalence of HHV-8 infection.[5] Here, we report the clinical profile and management of a case of KS associated with HIV-HBV co-infection from Manipur, India.

## CASE REPORT

A 38-year-old known HIV positive male from Manipur presented with complaints of purple colored skin lesions over the trunk and extremities since three years. The initial skin lesion appeared over the inner aspect of the thigh. Gradually, new lesions appeared. Spontaneous resolution was not seen, and there was no trauma-induced bleeding. He had a history of multiple unprotected heterosexual exposures; however, homosexuality was denied. He also gave a history of recurrent herpes genitalis. There was no history of blood transfusion or intravenous drug abuse.

The patient was first diagnosed with HIV infection in 2008 when he presented with fever, weight loss, and diarrhea. The CD4 count was 231 cells/ml with a viral load of 86 copies/ml. He was started on a combination of stavudine and lamivudine along with nevirapine. A year later, he tested positive for hepatitis B surface antigen (HBsAg) after which telbivudine was added to the existing regimen. A suspicion of KS was considered for which he received two cycles of paclitaxel in 2011. Six months later, he was referred to our center for further therapy as there was no improvement. General examination showed the patient to be cushingoid with cervical lymphadenopathy. Cutaneous examination revealed multiple discrete, nonulcerated, nontender violaceous nodules of size 2 cm × 2 cm, and plaques over the trunk and extremities [Figure 1]. Laboratory investigations revealed hemoglobin 13.8 g%; total white blood cell count 13,200/cu mm. Antibodies to HIV-1 were positive with CD4 cell count of

540 cells/ml (normal range: 559–1710). HBsAg was positive, and the viral load as detected by quantitative PCR was <10 IU/ml. The patient tested negative for HBeAg. PCR for HHV-8 from the peripheral blood sample was positive. Hepatitis C virus IgG antibodies were absent and VDRL test was nonreactive. Chest radiograph and computed tomography scan showed scattered postinflammatory changes in both lungs with no significant adenopathy. Sputum was negative for acid-fast bacilli. Ultrasonography revealed grade I to II fatty liver, whereas contrast-enhanced computed tomography scan of the abdomen did not reveal any abnormality.

Biopsy done from the skin lesion on left ankle was consistent with a diagnosis of KS [Figure 2]. Biopsy done from left supraclavicular lymph node and ulcerated nodules seen on gastroscopy also showed features of KS, thus confirming the metastasis. The patient also had esophageal candidiasis.

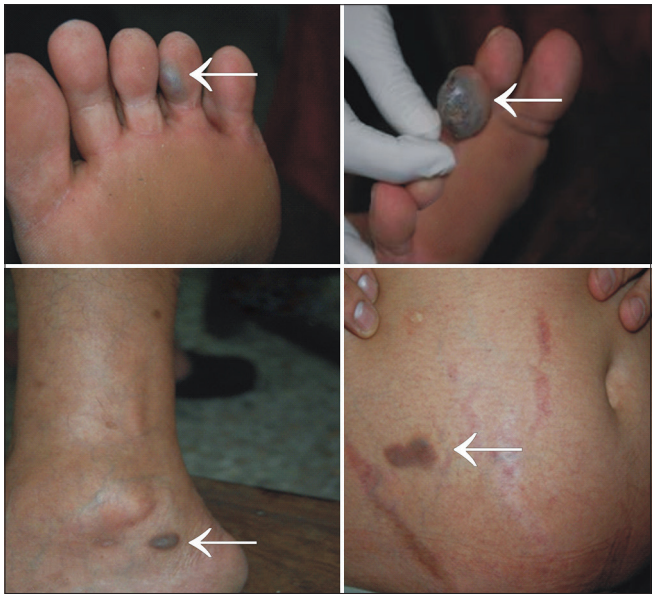

**Figure 1:** Discrete, non ulcerated, non tender violaceous nodules and plaques over the trunk and feet

Based on the above findings, he was staged as T1I0S1 as per the AIDS Clinical Trial Group staging system for KS[6] [Table 1]. After two years, the highly active antiretroviral therapy (HAART) was changed to lamivudine, tenofovir, and efavirenz when he presented to our centre. He was given six cycles of chemotherapy with liposomal doxorubicin over three months. He also received topical imiquimod for genital warts. At last follow-up six months later, he showed good response to therapy with regressing skin lesions and absence of new lesions. Repeat CT thorax, abdomen, and pelvis were normal.

## DISCUSSION

Acquired immune deficiency syndrome associated KS is infrequently reported from India. Only 16 cases have been reported till date, the first in 1993[7,8] [Table 2]. Documented HHV-8 infection of the skin has been previously reported in three cases from India.[2-4] This may be attributed to low prevalence of HHV-8. In a recent study, prevalence of HHV-8 infection in South India was estimated to be 4.7%.[9] PCR for HHV-8 from the peripheral blood sample was positive in our patient. Co-infection of HHV-8 and HIV-1 increases the probability of developing KS by 60%/year post-HIV infection.[10]

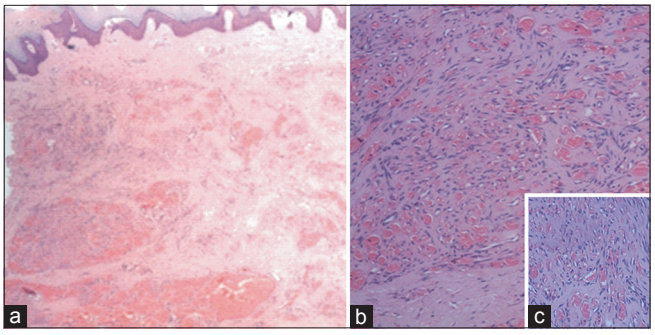


**Figure 2:** Skin with the dermis containing clusters of proliferated spindle shaped cells (a) lining slit like spaces (c) with numerous extravasated erythrocytes (b)

**Table 1: Revised ACTG staging classification for KS**

| | Good risk (all of the following) | Poor risk (any of the following) |
|---|---|---|
| Tumor, T | T0: Confined to skin and/or lymph nodes and/or minimal oral disease (nonnodular KS confined to palate) | T1: Tumor-associated edema or ulceration |
| | | Extensive oral KS |
| | | Gastrointestinal KS |
| | | KS in other nonnodal viscera |
| Immune system, I | I0: CD4 cell count >200/μL* | I1: CD4 cell count <200/μL |
| Systemic illness, S | S0: No history of OI or thrush# | S1: History of OI and/or thrush |
| | No "B" symptoms$^{\Delta}$ | "B" symptoms present |
| | Karnofsky performance status >70 | Karnofsky performance status <70 |
| | | Other HIV-related illness (e.g., neurologic disease, lymphoma) |

*A CD4 lymphocyte cut-off of 150 μL may be more discriminatory.[6] #OI is an opportunistic infection. $^{\Delta}$"B" symptoms are unexplained fever, night sweats, <10% involuntary weight loss, or diarrhea persisting >2 weeks. Adapted from: Krown, SE, Metroka, C, Wernz, JC. Kaposi's sarcoma in the AIDS: A proposal for uniform evaluation, response, and staging criteria. ACTG Oncology Committee. J Clin Oncol 1989; 7:1201. ACTG: AIDS Clinical Trials Group, KS: Kaposi sarcoma, AIDS: Acquired immune deficiency syndrome

**Table 2: AIDS-KS reported in Indian literature from 1993 to June 2013**

| Year and reported from | Age and sex | Occupation habit/history | Antibodies to HIV | CD4 count (cells/mm$^3$) | Site | Systemic involvement | Treatment done | Outcome |
|---|---|---|---|---|---|---|---|---|
| 1993, Mumbai | 35/female | CSW<br>Multiple UPSI, heterosexual | HIV-1<br>HIV-2 | 220 | Skin mucosa | Not involved | Vincristine, INF-α and radiotherapy | Not known |
| 1996, Chennai | 19/male | Unmarried<br>IVDU | HIV | Not known | Skin mucosa | Not involved | Not known | Not known |
| 1996, Mumbai | 50/male | Multiple UPSI and blood transfusion recipient | HIV | Not known | Skin | Not involved | Not known | Not known |
| 2001, Manipur | 22/male | IVDU | HIV | Not known | Skin | Not involved | Not known | Not known |
| 2001, Manipur | 30/female | Husband was IVDU | HIV | Not known | Skin | Not involved | Not known | Not known |
| 2002, Mumbai | 39/male | Multiple UPSI heterosexual | HIV-1 | 247 | Skin | Lungs | HAART, doxrubicin, bleomycin and vincristine | Died |
| 2004, Hyderabad | 35/male | Not known | HIV-1 | Not known | Skin | Lungs | HAART | Not known |
| 2005, Mumbai | 45/male | Driver and had multiple UPSI | Not known | 64 | Skin | Not involved | cART | Resolution of the lesion |
| 2007, Manipur | 35/male | IVDU | Not known | 402 | Skin mucosa | Not involved | Vincristine | Resolution of the lesion |
| 2008, Mumbai | 40/male Somalian | Multiple UPSI | HIV-1 | 8 | Skin mucosa | Not involved | HAART | No improvement and died due to TB |
| 2008 Vadodara | 30/male | Unmarried<br>Multiple UPSI, heterosexual | HIV | Not known | Skin | Not involved | Not given | Not known |
| 2008, Chennai | 30/male | Not mentioned | HIV | 10 | Skin | Not involved | HAART | Complete regression of lesion |
| 2009, Mumbai | 40/male | Unmarried | HIV | 179 | Skin mucosa | Not involved | cART and IV Paclitaxel | Reduction in size of the skin lesion and disappearance of oral lesion |
| 2009, Mumbai | 38/male | Denies exposure | HIV | 115 | Skin mucosa | Not involved | HAART | Not known |
| 2010, Gujarat | 26/male | Multiple UPSI heterosexual | HIV | 186 | Skin mucosa | Stomach and lymph node | Not known | Not known |
| 2012, Mangalore | 26/male | Laborer | HIV | 301 | Skin mucosa | | HAART | Not known |
| 2013, Vellore | 38/male | Business | HIV-1 | 231 | Skin mucosa | Stomach and lymph node | HAART and liposomal Doxorubicin | Partial response with resolution of the skin lesion |

HAART: Highly active antiretroviral therapy, cART: Combined antiretroviral therapy, IV: Intravenous, INF-α: Interferon-α, CSW: Commercial sex worker, IVDU: Intravenous drug use, UPSI: Unprotected sexual intercourse, KS: Kaposi sarcoma, AIDS: Acquired immune deficiency syndrome

Kaposi sarcoma has been described more commonly in homosexual men. KS however has not been reported extensively in India, which may be attributed to both the social stigma associated with homosexuality, as well as underreporting of cases. Our patient denied any homosexuality. Interestingly, half of the cases reported in Indian literature are from Mumbai and three from Manipur. Metastasis has been described in three previous cases from India, out of which one patient died and in the other two treatment outcomes are not known. Our patient had gastrointestinal involvement which is described in 40% of patients with AIDS-KS at presentation and suggests a poorer prognosis.[11] Further, HIV-HBV co-infection is associated with more severe liver disease and greater hepatotoxicity due to antiretroviral drugs. However, liver disease was not seen in our patient.

Acquired immune deficiency syndrome-KS is an aggressive disease often affecting the mouth, lungs, gastrointestinal tract or genitalia. HAART forms the mainstay of treatment in HIV-associated KS. Chemotherapy with pegylated liposomal doxorubicin being the recommended standard of care was administered for advanced KS in our patient. It is a superior formulation of conventional doxorubicin, with minimal toxicity and an enhanced pharmacokinetic profile. This case

highlights the clinical course and response to treatment with anthracyclines and HAART of an HHV-8 positive disseminated KS in a HIV positive patient with HBV co-infection.

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