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Original Research Article

Kaposi's sarcoma in North-East India: an under recognized burden

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ABSTRACT

Background: Kaposi's sarcoma (KS) is a rare AIDS-defining malignancy strongly associated with human herpesvirus 8 (HHV-8). Although KS is considered uncommon in India owing to its low HHV-8 seroprevalence, regions with high HIV prevalence, such as Northeast India, may exhibit a higher burden of KS. This study investigated the clinical characteristics and outcomes of KS cases in Nagaland, a region with a high HIV prevalence.
Methods: This retrospective observational study analyzed the demographics, clinical characteristics, and treatment outcomes of 16 KS cases diagnosed between 2011 and 2024 in Nagaland.
Results: The mean age of the patients was 45 years (±13.57) mean (±SD), and the male-to-female ratio was 1.7:1. Mucocutaneous lesions were the predominant presentation, while four patients exhibited pulmonary involvement. The median CD4 count at diagnosis was notably low at 54 cells/mm^3 (IQR 47-262.5)). Six patients had coexisting opportunistic infections, such as tuberculosis, and two patients had *Pneumocystis carinii* pneumonia. Four patients improved with antiretroviral treatment (ART) alone, while four received liposomal doxorubicin along with ART, showing varying outcomes. Three patients died, likely due to systemic involvement and comorbidities. One patient was HIV-naïve, suggesting classic KS.
Conclusions: This study provides initial evidence that may challenge the previously held notion of KS rarity in India by documenting a notable burden in Nagaland, India. Increased vigilance is warranted in areas with high HIV prevalence, and further research is needed to understand the epidemiology and optimize treatment strategies in this region.

Keywords: Kaposi sarcoma, Northeast India, Nagaland, Human herpesvirus 8

INTRODUCTION

Kaposi's sarcoma (KS) is a rare vascular tumor associated with human herpesvirus-8 (HHV-8) infection that primarily affects individuals with compromised immune systems, particularly those with HIV/AIDS.[1] Although KS is considered uncommon in India due to its low HHV-8 seroprevalence, emerging evidence suggests that regions with high HIV prevalence, such as Northeast India, may become hotspots for this malignancy.[2] Within this region, Nagaland has a high HIV prevalence; however, specific epidemiological data on KS are absent, representing a gap in understanding the regional burden. Our study addresses the paucity of regional epidemiological data and challenges existing assumptions regarding KS prevalence and demographics in India. Sixteen patients diagnosed with Kaposi's were examined, focusing on various aspects, including age, sex, clinical presentation, disease duration, antiretroviral therapy (ART) status, CD4 count, comorbidities, treatment modalities, and clinical outcomes. By examining these factors, this study offers insights into the characteristics and management of KS in this specific geographical context. This investigation is particularly significant as it documents the first reported series of Kaposi's cases in Nagaland, a state with a high

HIV prevalence, where cases have not been documented previously. These initial findings provide foundational insights to improve vigilance and clinical practice and lay the groundwork for future epidemiological studies of KS in regions previously considered low-prevalence areas, in addition to a better understanding of the disease.

METHODS

Study design

A retrospective observational analysis was conducted at the Department of Dermatology, Christian Institute of Health Sciences and Research, a secondary hospital in Northeast India. Sixteen patients with KS between 2011 and 2024, as recorded in the hospital information management system, were included in this study. The diagnosis was confirmed by histopathology. Immunohistochemistry (IHC) was performed wherever feasible. A total of 16 patients were included in the study.

Data characteristics

Demographics, clinical presentation, disease duration, antiretroviral therapy status, CD4 count, comorbidities, treatment modalities, and clinical outcomes were analyzed during the follow-up period.

Statistical analysis

Statistical analyses were performed using statistical package for the social sciences (SPSS) version 26. Descriptive statistics were used to summarize the data collected. Normality was assessed using the Shapiro-Wilk test. Normally distributed variables are presented as mean±SD, while non-normally distributed variables are reported as median (IQR). Categorical variables were expressed as frequency and percentage. Associations between the CD4 category and other categorical variables were assessed using the Chi-square test or Fisher's exact test, where applicable. Statistical significance was set at $p<0.05$.

RESULTS

A total of 16 patients were included in the study. The mean age of the patients was 45.00±13.57 years. The majority were male (n=10, 62.5%), while females accounted for (n=6, 37.5%), with a male-to-female ratio of 1.7:1. All KS cases in our study involved heterosexual men and women who were indigenous inhabitants of Nagaland. The median duration of illness was 6 months (IQR: 1–11 months).

The demographic and clinical characteristics are summarized in Table 1. Most patients had involvement of multiple sites, with lower limbs being the most commonly affected site (n=11, 68.7%), followed by the upper limbs (n=10, 62.5%), trunk (n=10, 62.5%), oral mucosa (n=7, 43.7%), face (n=2, 12.5%), and neck (n=1, 6.25%). Isolated oral mucosal involvement was observed in (n=2, 12.5%), while eye involvement was seen in (n=2, 12.5%). Lymphedema was present in (n=1, 6.25%).

Table 1: Demographic and clinical characteristics of patients (n=16).

Characteristic	N (%)/value
Gender	
Male	10 (62.5)
Female	6 (37.5)
Age (years), mean±SD	45.0±13.57
Duration of disease (months), median (IQR)	6 (1–11)
Number of skin lesions	
≤3	5 (31.25)
≥4	11 (68.75)
Site involved*	
Torso	10 (62.5)
Upper limb	10 (62.5)
Lower limb	11 (68.75)
Face	2 (12.5)
Neck	1 (6.25)
Oral mucosa	7 (43.75)
Eyes	2 (12.5)
Oral mucosa alone	2 (12.5)
Systemic involvement	
Lung	4 (25)
Gastrointestinal tract	2 (12.5)
Lymphedema	1 (6.25)
Co-morbidities*	
Anaemia	4 (25)
Pulmonary tuberculosis	4 (25)
TB lymphadenitis	2 (12.5)
Esophageal candidiasis	1 (6.25)
Sporotrichosis	1 (6.25)
Cutaneous penicilliosis	1 (6.25)
Pneumocystis pneumonia	2 (12.5)
Hepatitis C	1 (6.25)
Malignant melanoma	1 (6.25)
Asthma	1 (6.25)
Urinary tract infection	2 (12.5)

*Multiple responses possible for site involvement and co-morbidities

Disseminated disease was observed in (n=4, 25%). Opportunistic infections (OI) were present in (n=9, 56.3%), with pulmonary tuberculosis being the most common. Kaposi sarcoma developed following discontinuation of antiretroviral therapy in (n=4, 25%). Nearly all patients, except one (n=1, 6.25%), had HIV-associated Kaposi sarcoma.

The median CD4 count was notably low at 54 cell/mm^3 (IQR: 47-262.5) at the time of diagnosis. Severe immunosuppression (CD4 <100 cells/mm^3) was observed in 8 patients (50%), with a baseline CD4 cell count of less than 100 cell/ mm^3.

Summary statistics of continuous variables are presented in Table 2, showing a low median CD4 count and variable follow-up duration.

Table 2: Summary of continuous variables.

Variable	N	Value*	Mini-mum	Maxi-mum
Age (years)	16	45.0±13.57	29	78
Duration of illness (months)	15	6 (1–11)	0.5	36
CD4 count (cells/mm³)	13	54 (47–262.5)	22	397
Duration of follow-up (months)	10	11.50 (4.50–19.50)	1	30

*Values are presented as mean±standard deviation or median (interquartile range)

A statistically significant association was found between low CD4 count (<100 cells/mm³) and the presence of opportunistic infections ($p<0.05$), as shown in Table 3.

Table 3: Association between CD4 count and opportunistic infections (n=13).

CD4 count (cells/mm³)	OI present N (%)	OI absent N (%)	P value
<100	7 (87.5)	1 (12.5)	0.005
≥100	0 (0)	5 (100)	

Disease management and outcomes

Among the 16 patients, (n=10, 62.5%) received HAART alone, while (n=4, 25%) received HAART in combination with liposomal doxorubicin as first-line therapy. One patient (n=1, 6.25%) received a combination regimen of paclitaxel, carboplatin, and pazopanib.

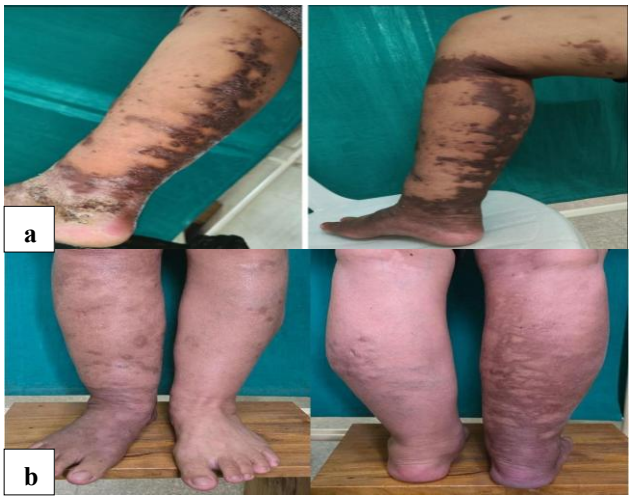

Figure 1: (a) Violaceous plaques with lymphedema at initial presentation, and (b) resolution of lesions following HAART and chemotherapy.

Treatment outcomes are summarized in Table 4. Among those who received chemotherapy, (n=3, 75%) showed significant clinical improvement, while one patient did not respond despite eight cycles of chemotherapy. Treatment default was observed in (n=3, 18.75%), and discontinuation of ART occurred in (n=1, 6.25%). Three patients (18.7%) with pulmonary involvement and OI died within a few months of diagnosis. The median follow-up duration was 11.50 months (IQR: 4.50–19.50), as shown in Table 2. Additionally, 31.25% (n=5) of patients were lost to follow-up.

Table 4: Treatment and outcomes of patients (n=16).

Variable	N (%)
Treatment received	
HAART alone	10 (62.5)
HAART + chemotherapy (Doxorubicin)	4 (25)
Other chemotherapy regimens	1 (6.25)
No treatment	1 (6.25)
Chemotherapy agents used	
Liposomal Doxorubicin	4 (25)
Paclitaxel-based regimens	1 (6.25)
Treatment outcomes	
Complete/near-complete resolution	5 (31.25)
Partial/mild improvement	3 (18.75)
No improvement	1 (6.25)
Death	3 (18.75)
Lost to follow-up	5 (31.25)

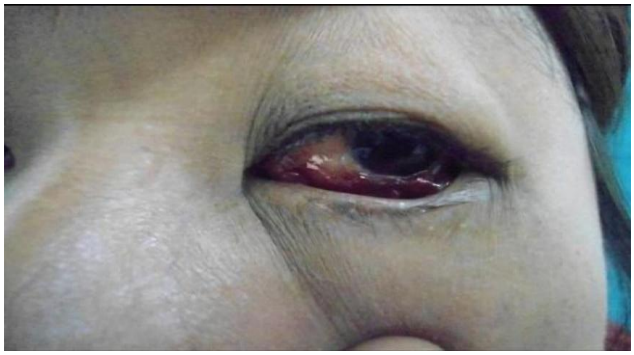

Figure 2: Nodule on eyelid conjunctiva.

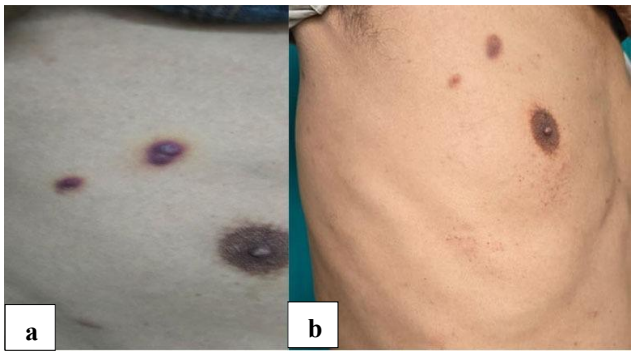

Figure 3 (a and b): Pre and post treatment image showing flattening of lesions with HAART.

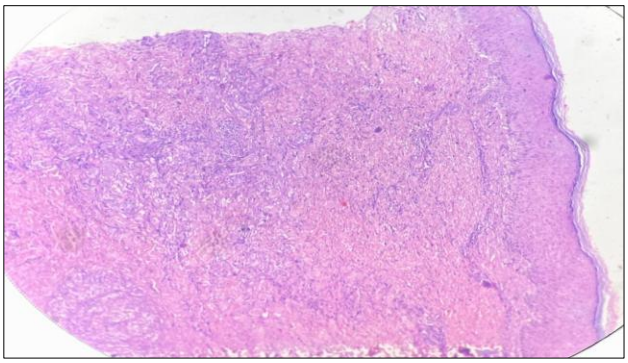

Figure 4: Skin biopsy showing ill-defined nodules with slit-like spaces containing erythrocytes in the dermis (H&E 10X).

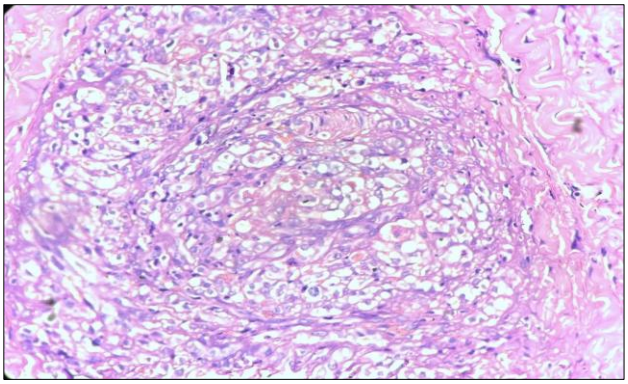

Figure 5: Nodules in the dermis showing ovoid to spindle-shaped endothelial cells admixed with lymphoplasmacytic cells and extravasated erythrocytes (H&E 40X).

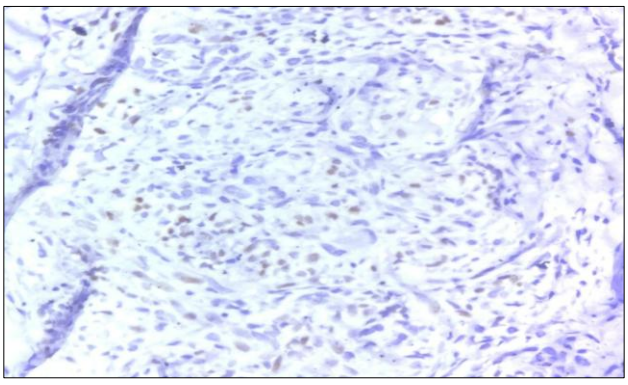

Figure 6: Nuclear expression of HHV8 in spindle and ovoid cells (immunohistochemistry HHV8 40x).

DISCUSSION

KS is a significant AIDS-defining illness and the most common malignancy in HIV-infected individuals. Historically, the incidence of KS in India has been low because of the low HHV-8 seroprevalence.[2] However, Northeast India, with its high HIV prevalence and proximity to East and Southeast Asian countries, could become an emerging hotspot. Additionally, the Northeast is known for distinct ethnicity and is close to East and Southeast Asian countries such as China, Thailand, Vietnam, and Cambodia, where HHV-8 is more common, posing a risk of virus acquisition.[3] Fewer than 30 cases of HIV associated KS have been documented in India.[4-6] Our study, to our knowledge, is the largest series of Kaposi's cases from Northeast India.

The mean age was 45 years (±13.57), and the duration of lesions ranged between 2 weeks and 3 years, with a median duration of 6 months (IQR 1-11 months). A significant observation was the sex distribution of the patients, which diverged from the pattern observed in the Indian literature. Bhatia et al noted a M: F ratio of 5.75:1.[4] In contrast, our study revealed a more balanced M: F ratio of 1.7:1, a noteworthy finding that challenges the prevailing notion that KS predominantly affects men and suggests that women may be equally susceptible to developing KS.

Cutaneous involvement is observed in >90% of cases. Systemic involvement can be observed, mainly affecting the gastrointestinal tract and lungs, with lung involvement having a poor prognosis. In our study, the extremities and trunk were primarily affected. Two patients had nodules on the eye (Figure 2). Pulmonary involvement was the most common systemic manifestation. One patient presented with lymphedema (Figure 1a), similar to a case documented by Prabhakaran et al.[6] Diagnosis was made based on histopathological examination (Figures 4 and 5) and immunohistochemistry (IHC) (Figure 6).

All previously documented cases in India involved heterosexual individuals except one case involving a homosexual man, reported by Bhatia et al.[4-6] Consistent with existing literature, all KS cases in our study involved heterosexual men and women. Munawwar et al found no significant difference in HHV-8 seroprevalence between heterosexual men and MSM in northern India, indicating that heterosexual men could potentially transmit HHV-8 to their partners.[7] They observed a 26% seroprevalence among HIV-infected individuals, while a study from South India reported <5%.[17] The immune status of most patients in our series was known after KS diagnosis, highlighting Kaposi Sarcoma as a potential indicator of HIV infection. Ngoruka et al observed that KS occurs at a CD4 count below 200 cells/mm^3, as was also observed in our study (56.25%).[8]

Patients with AIDS-associated KS are susceptible to OIs due to their compromised immune systems. Nine patients (56.3%) had OIs, of which six had tuberculosis (37.5%). Among patients with CD4 <100, 87.5% had an OI, whereas none of the patients with CD4 ≥100 had an OI. Fisher's Exact Test showed that this association was statistically significant (p=0.005) (Table 3). From this, we can infer that patients with markedly low CD4 counts are at a substantially higher risk of developing opportunistic infections. Besides HAART, antimicrobial prophylaxis is essential as unchecked infections may accelerate KS

progression, and comorbidities influence mortality. Arbune et al noted that tuberculosis serves as a negative prognostic factor for AIDS-related KS.[14] Two of the three deceased patients had tuberculosis, supporting the notion that advanced HIV infection with comorbidities can lead to poor outcomes.

Highly active antiretroviral treatment (HAART) remains fundamental for AIDS-related KS. Alongside HAART, liposomal anthracyclines, such as doxorubicin and paclitaxel are recommended for advanced disease.[9,10] Studies by Mosam et al and Gbabe et al showed that HAART with chemotherapy resulted in better outcomes than HAART alone.[11,12] In our study, 12 patients had localized disease and four had advanced disease. Four improved with HAART alone (Figure 3), and four received liposomal doxorubicin with varying outcomes (Table 4). Four patients who discontinued HAART developed KS, necessitating treatment resumption. This underscores the risk associated with discontinuation of treatment, which increases the likelihood of OI and disease progression, and highlights the critical importance of adherence to treatment and the need for counselling. Our findings align with those of Lupia et al and Arbune et al, linking poor adherence and a low CD4 count to KS development.[13,14]

One patient was HIV-naïve, indicating classic KS, with only two other documented cases in Northeast India.[15,16]

Limitations

CD4 data for some patients were incomplete because they could not be retrieved from the hospital information management system, which may have introduced bias in our assessment of the immune status at diagnosis and its correlation with clinical outcomes. Some patients were lost to follow-up; therefore, outcome data were missing in the subset, which introduces the potential for selection bias in our reported treatment outcomes. HHV-8 immuno-histochemistry could not be performed in all cases because of resource constraints. There was a lack of access to ancillary investigations, such as HHV-8 PCR, which hindered our ability to monitor the disease and assess the viral load. The single-centre study results may not be fully representative of broader KS epidemiology in Nagaland or Northeast India.

CONCLUSION

This case series provides valuable insights into the prevalence and characteristics of KS in Nagaland, a region in Northeast India with a significant HIV burden. Our findings reveal patterns in KS prevalence and demographics that diverge from previous assumptions for India, specifically indicating a more balanced sex distribution and confirming its occurrence in heterosexual individuals within this context. The study underscores the importance of early detection, consistent antiretroviral therapy, and comprehensive patient management to improve the outcomes of AIDS-associated KS. These cases emphasize the need for increased vigilance in areas with high HIV prevalence and suggest that Northeast India, particularly Nagaland, may represent an under-recognized burden for KS.

Further research (in the form of HHV-8 serotyping) is warranted to better understand the epidemiology, risk factors, and optimal treatment strategies for KS in this region, particularly given its unique ethnic composition and geographical proximity to areas with a higher HHV-8 prevalence.

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