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Kaposi's sarcoma in Malawi: a continued problem for HIV-positive and HIV-negative individuals

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Kaposi's sarcoma (KS) is the leading cancer in much of sub-Saharan Africa [1]. HIV has resulted in a dramatic increase in KS throughout the region, due to high overlapping prevalence of HIV and the etiologic agent of KS, Kaposi's sarcoma-associated herpesvirus (KSHV)[2]. KS is divided into four major categories: classical, iatrogenic, AIDS-related, and endemic. Endemic KS is the only KS subtype where a specific immune disturbance is not readily apparent [3]. In Malawi, KS is the leading cancer overall accounting for 34% of all malignancies recorded in the national cancer registry [4]. In a setting of high KS burden, we sought to describe contemporary burden and characteristics of KS in the HIV-positive and HIV-negative populations at a national teaching hospital in the capital, Lilongwe.

We analyzed KS cases from May 2014 until May 2016 in the Kamuzu Central Hospital Cancer Registry, which involves active registration of cancer cases across all hospital departments using standardized data collection forms. We identified 237 overall KS cases, of

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which 153 were confirmed HIV-positive and 21 confirmed HIV-negative. KS diagnoses were histologically confirmed in 39% (92/237) of cases overall, including 33% (50/153) of confirmed HIV-positive and 71% (15/21) of confirmed HIV-negative cases. We abstracted tumor location and subtype from all confirmed pathology reports.

As expected, KS patients were more commonly males regardless of HIV status (Table 1). Age distribution was significantly different based on HIV status ($p = 0.012$, Fisher's exact test, see Figure, Supplemental Digital Content 1; Graph of KS age distribution within HIV + and − by decade). HIV-positive cases primarily presented during young to mid-adulthood with 68% of cases occurring between 20 and 49 years of age. By contrast, HIV-negative cases were more evenly distributed among age groups. HIV-positive KS tended to present with disease at diverse anatomical sites, whereas HIV-negative KS appeared to primarily present in the lower extremities (60%). Similarly, lesion descriptions in pathology reports suggested greater lesion heterogeneity among HIV-positive patients, with predominantly plaque or nodular lesions among HIV-negative patients (73%). Finally, among patients for whom the primary treatment modality was recorded, 49% of HIV-positive patients and 33% of HIV-negative patients received chemotherapy. Of note, radiotherapy is not available in Malawi.

These findings suggest that despite high HIV prevalence in Malawi, HIV-negative endemic KS represents at least 9% of contemporary KS burden at a national teaching hospital, with possible differences in presenting characteristics between HIV-positive and HIV-negative patients. Despite major investments and research programs in the region focused on AIDS-related KS, endemic KS has received relatively little attention. At our center, endemic KS appeared to occur at both younger and older ages compared to HIV-positive KS. Lifelong KSHV infection in sub-Saharan Africa is often acquired in childhood through salivary and breast milk transmission, although KSHV may also be acquired in adulthood. Subsequent infection with HIV during adulthood abruptly alters host immune function allowing KS development, accounting for high KS burden in the HIV positive population between ages 20–49 years. In the absence of HIV, precipitating co-factors of endemic KS remain unclear and may be associated with volcanic soils, African natural products, and genetic predisposition [5–7].

As antiretroviral therapy (ART) scale-up continues in Malawi, which began in 2004 with ART coverage now reaching 67% of eligible HIV-positive patients [8], incidence of AIDS-associated KS is anticipated to decline. These trends, coupled with demographic shifts in sub-Saharan Africa with aging of populations overall, may result in higher proportions of KS in older individuals and relatively constant burden among children, regardless of HIV status. At our center, many of these patients had severe enough disease to require treatment with chemotherapy at a tertiary referral oncology clinic. This may become increasingly important, since treatment of older patients with cytotoxic therapy is challenging in resource-limited settings without appropriate supportive care infrastructure. Novel treatment paradigms, including greater application of non-cytotoxic therapies and local treatments for limited-stage disease, may therefore be needed. Finally, questions remain as to how endemic KS evolves from KSHV infection. Studies in the US and Malawi suggest the presence of at least two subtypes of KS on the basis of gene expression profiling [9, 10]. Understanding

precipitating and viral factors in HIV-negative populations may help guide therapy development and prevention efforts.

In conclusion, embedded efforts to better understand endemic KS are needed within larger regional initiatives focused on AIDS-related KS. If successful, such efforts have potential to guide prevention and treatment strategies which can better address overall KS burden in Malawi and comparable settings, as ART scale-up continues and populations continue to age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
KS Demographics at Kamuzu Central Hospital

Demographics were constructed from KS cases recorded from May 2014 until May 2016 in a hospital-based cancer registry at Kamuzu Central Hospital. Tumor location and subtype were gleaned from pathology reports from collected cases, when available.

	HIV− (N=21)		HIV+ (N=153)	
Age				
< = 19	5	24%	11	7%
20–49	7	33%	104	68%
> = 50	7	33%	20	13%
Unknown	2	10%	18	12%
Sex				
Male	16	76%	103	67%
Female	5	24%	50	33%
Tumor site				
Lower extremity	9	60%	17	34%
Trunk	2	13%	12	24%
Upper extremity	2	13%	2	4%
Head/Neck	0	0%	5	10%
Lymph Node	1	7%	12	24%
Other	1	7%	2	4%
Tumor Subtype				
Lymphadenomatous	1	7%	12	24%
Patch	0	0%	3	6%
Plaque	3	20%	8	16%
Nodular	8	53%	11	22%
Visceral	0	0%	2	4%
Unclear	3	20%	14	28%
Treatment Received				
Surgical Resection	1	5%	0	0%
Chemotherapy	7	33%	75	49%
Unknown	13	62%	78	51%