Severe Kaposi Sarcoma in an Urban Public Hospital

Shirin Elisha Kasturia,[1–3] Clifford Gunthel,[1] Cheng Zeng,[1] and Minh Ly Nguyen[1]

Abstract

The national incidence of epidemic Kaposi sarcoma (KS) has decreased dramatically since the availability of combined antiretroviral therapy. Despite national trends, we continue to see admissions for KS. Electronic medical records were queried to identify patients with HIV who were admitted with active KS between 2010 and 2013 and records were reviewed to determine patient characteristics and factors affecting survival. Data were collected from all hospital admissions until death or May 1, 2015. Kaplan–Meier survival analysis with log-rank tests were used to test for differences in survival and Cox proportional hazards models were used to assess the prognostic value of variables. Odds ratios were calculated to determine factors associated with death during hospital admissions. Forty-three patients were admitted 141 times, with 81 admissions specifically related to KS. The majority of patients were highly immunosuppressed when KS was diagnosed (median CD4 count: 11), and 68% had multiple organ involvement with KS. Comorbidities at diagnosis included hepatitis B (26%) and pneumocystis pneumonia (33%). Frequent reasons for admission included skin and soft tissue complaints (28.4%) and respiratory complaints (27.2%). The estimated median survival after KS diagnosis was 3.0 years. Lung involvement, liver involvement, poor performance status, and low CD4 T cell count (<50) were associated with lower survival. Lung infections were the only admission diagnoses significantly associated with an increased odds of death during admission (OR: 5.42, 95% CI: 1.04–28.24). KS in our population is associated with poor access to healthcare and management of HIV. Factors affecting survival, including CD4 count and pulmonary involvement of KS, are in accordance with previous studies. Pulmonary KS should therefore be considered early in AIDS patients presenting with respiratory complaints. Our study also demonstrated that respiratory infections are associated with significant morbidity in patients with KS.

Keywords: Kaposi sarcoma, HIV disparities, KSHV inflammatory cytokine syndrome (KICS)

Introduction

KAPOSI SARCOMA (KS) IS a highly vascular cancer of endothelial cell origin caused by human herpes virus 8 (HHV8), also known as KS-associated herpesvirus (KSHV).[1–3] One of the more aggressive clinical variants of KS is epidemic KS, or AIDS-associated KS.[4] KS in this clinical setting is often fatal without treatment, and survival times range from weeks to months.[4] Response rates to standard radiation and chemotherapy regimens are poorer for patients with epidemic KS compared with other KS variants.[4] Epidemic KS, however, responds well to combined antiretroviral therapy (cART).[4–9] Severe cases of AIDS-associated KS that are treated with systemic chemotherapy in addition to cART have resulted in clinical improvement and reduced disease progression, although mortality rates have not decreased in kind.[7,10,11]

After the introduction of cART in 1995, the incidence of KS decreased dramatically.[12–14] However, we continue to see cases of epidemic KS in the developed world despite availability of both cART and chemotherapy.[7,12,13,15–17] Typically, cases of epidemic KS present with low CD4 counts (<150 cells per mm3) and high viral loads (>4 log copies/ml). The disease usually begins to regress within several months after initiation of cART.[7,8,17] Several reports, however, suggest that there may be an increasing number of cases of HIV-associated KS persisting despite effective antiretroviral therapy, near normal CD4 counts, and undetectable viral loads.[2,18–22]

Other conditions associated with KSHV have also been identified in patients with HIV. Though rare, these include multicentric Castleman disease (KSHV MCD), primary effusion lymphoma, and KSHV-inflammatory cytokine syndrome (KICS).[3] KICS is a more recently described syndrome

[1]Emory University School of Medicine, Atlanta, Georgia.
[2]Rollins School of Public Health, Emory University, Atlanta, Georgia.
[3]Department of Emergency Medicine, University of California San Francisco, San Francisco, California.

that presents with the characteristic constellation of inflammatory symptoms seen in KSHV MCD and include fevers, fatigue, cachexia, edema, and lymphadenopathy. KICS, however, does not manifest the characteristic lymph node histopathology of KSHV-MCD.[23]

According to the National Cancer Institutes Surveillance, Epidemiology, and End Results Program (SEER), the highest national incidence of KS occurs in the South. In Atlanta, Georgia, an SIR of 1.75 cases per 100,000 people per year between 2009 and 2013 has been recorded, which contrasts with the national SIR of 0.5.[13] Grady Memorial Hospital (GMH) is a county hospital that serves the metropolitan Atlanta area. At GMH, and at its affiliated infectious disease clinic, we continue to diagnose and treat many cases of KS despite the availability of cART. We also continue to see severe KS that leads to hospital admission and even death. In this study, we sought to characterize the patients who were admitted to GMH with active KS, and examine what factors may be contributing to these admissions and to the survival of admitted patients. We hypothesize that concurrent infections or inflammatory states may exacerbate KS, resulting in worsening lesions and subsequent hospital admission. We also suspect that undiagnosed KICS and KSHV-MCD may be contributing to mortality in this population.

Materials and Methods

The study was approved by the Emory Institution Review Board (IRB12210) and the Grady Review Oversight Committee.

Study population

This study was conducted at GMH, a large public hospital serving metropolitan Atlanta. Patients admitted with active KS were identified by querying electronic medical records (EMR) for hospitalizations between October 2010 and October 2013 with a discharge diagnosis of KS. We excluded cases where active KS was not confirmed clinically or histologically in physician notes or pathology reports.

Data collection

Demographic information including sex, race/ethnicity, age, and risk-groups for HIV transmission was extracted from the EMR. Charts were reviewed for variables related to HIV/AIDS and KS, including diagnosis dates, CD4 T-cell counts, HIV $\log_{10}$ viral loads, locations of KS involvement, cART regimens, chemotherapy, Karnofsky performance status scores, and AIDS Clinical Trial Group (ACTG) staging at the time of KS diagnosis.[24] When multiple diagnosis dates were found in the records, the earliest date was used. On occasions when KS was listed among other diagnoses, the diagnosis date used was either when KS was biopsy-confirmed or alternative diagnoses were ruled out and only KS remained.

Karnofsky score, a measure of performance status, is documented in the EMR at time of hospital admission for all patients in this study. The Karnofsky score from the first hospital admission with KS was the performance status used in our analysis. This Karnofsky score used may not represent the exact score at diagnosis of KS, as some patients were diagnosed with KS in the outpatient setting where Karnofsky score is not always recorded. ACTG stage was extracted from clinical notes at the time of KS diagnosis; however, when the ACTG stage was not specifically documented, lab values and clinical notes were used to assign the stage.[24]

Subsequent hospital admissions after KS was diagnosed were also reviewed. We identified whether KS or another KSHV-associated condition was the reason for, contributed to, or prolonged the duration of admission. For admissions where KS was a diagnosis, we recorded the primary complaint, discharge diagnoses, and duration of admission. Other collected data included the following: whether the patient had other acute infections, received cART, had chemotherapy, spent time in the intensive care unit (ICU), was intubated, had sepsis, or died during admission. Notes and discharge documentation were further assessed for mention of KSHV-MCD, KS-immune reconstitution inflammatory syndrome (KS-IRIS), or KICS.

Patients were followed by chart review until the earliest date of death, last encounter, or May 1, 2015. When applicable the cause of death was obtained through clinical notes in the EMR or autopsy reports.

Statistical analysis

Kaplan–Meier survival analysis was used to estimate median length of survival for the cohort. Statistically significant differences in Kaplan–Meier survival curves of categorical predictors including ACTG staging, organ system of KS involvement, cART administration at KS diagnosis, presence of hepatitis B or C, and recent opportunistic infection, were assessed using log-rank method. Recent opportunistic infection was defined as having had at least one of the following: toxoplasmosis, cryptosporidiosis, mycobacterium tuberculosis, pneumocystis pneumonia, or cytomegalovirus over the course of follow-up.[25] Other opportunistic infections were not seen in our cohort. The continuous variables of age, Karnofsky score, $\log_{10}$ viral load, and CD4 T cell count were also assessed as categorical variables using the following categorizations: age (≤ 50 vs. >50 years),[17] Karnofsky score (≤ 70 vs. >70),[24] and $\log_{10}$ viral load (≤ 4 vs. >4 log copies/ml),[7] CD4 T-cell counts were assessed at cutoffs of ≤ 150, ≤ 100, and ≤ 50 cells/μl given the variable thresholds used to denote high risk in the literature.[7,16,17,24,26]

Bivariate Cox's proportional hazards models were used to assess the prognostic value of categorical variables that were statistically significant by log-rank test. When viral load was undetectable, the minimum detectable viral load was used. Multivariate analysis was also performed using these variables.

Odds ratios were calculated to determine whether death was more likely to occur during hospitalization directly related to KS. Odds ratios were also determined for each organ system that was listed as the primary complaint for the admission. As the CD4 count and viral loads were not checked in 4 out of the 12 cases of death during KS admissions, we did not calculate any associations between these variables.

Analyses were performed with SAS statistical software, version 9.4 (SAS Institute, Cary, North Carolina).

Results

The query of the GMH EMR for discharge diagnoses between October 2010 and October 2013 that included active KS revealed 43 individuals. All except one of the patients were male, and the majority, 35 (81%), were black (Table 1).

TABLE 1. GENERAL FEATURES AND HIV CHARACTERISTICS OF HIV-POSITIVE PATIENTS ADMITTED WITH NEW DIAGNOSES OF ACTIVE KS

	Number (%) or median (IQR)	
General characteristics		
Gender		
Male	42	(98)
Female	1	(2)
Race		
Black	35	(81)
White	5	(12)
Other	3	(7)
HIV transmission risk factors[a]		
MSM	26	(65)
Bisexual	4	(10)
Heterosexual	9	(23)
MSM, IVDU	1	(3)
Median age at KS diagnosis, years	37	(31, 45)
Median age at HIV diagnosis, years	30	(23, 39)
Median years between HIV and KS diagnosis	2	(0, 10)
HIV characteristics		
Taking CART at KS diagnosis	18	(42)
Median $\log_{10}$ viral load at KS diagnosis (log copies/ml)	4.3	(2.3, 5.3)
Median CD4 count at KS diagnosis (cells/mm^3)	11	(6, 97)
CD4 count >200	4	(9)
CD4 count <150	39	(91)
CD4 count <100	34	(79)
CD4 count <50	27	(63)

[a]Three individuals did not have a documented HIV transmission risk factor.

cART, combined antiretroviral therapy; KS, Kaposi sarcoma.

The most common risk factor for HIV transmission was men who have sex with men (MSM) ($n = 27$, 68%). The median ages at HIV and KS diagnoses respectively were 30 and 37 years, with a median time between two diagnoses of 2 years. Fourteen patients (33%) were diagnosed with KS within 1 year of HIV diagnosis, and four patients were diagnosed with HIV and KS concurrently. Less than half of the patients were on cART at the time of their diagnosis with KS. The median $\log_{10}$ viral load at KS diagnoses was 4.3 log copies/ml, ranging from undetectable to 6.8 log copies/ml. The majority of patients were severely immunosuppressed at the time of their KS diagnosis, with CD4 T cell counts of less than 50 and only 4 patients had a CD4 T cell count above 200 cells/ul (maximum of 374). Seven patients (16%) had Karnofsky scores of 70 or less at their first hospital admission with KS.

In terms of staging, all patients had at least one ACTG high-risk criteria during their first hospital admission for KS. Fourteen (33%) had a tumor stage of 1, 40 (93%) had an immune status of 1, and 32 (74%) had a systemic status of 1. The majority (74%) of patients had KS that involved the skin (Table 2). Many also had pulmonary or gastrointestinal

TABLE 2. CHARACTERISTICS OF KS IN HIV$^+$ PATIENTS ON FIRST HOSPITAL ADMISSION WITH ACTIVE KS

	n (%)
ACTG staging	
Tumor	
0	29 (67)
1	14 (33)
Immune	
0	3 (7)
1	40 (93)
System	
0	11 (26)
1	32 (74)
Location of KS	
Skin	32 (74)
Lung	18 (42)
GI	15 (35)
Lymphatic	12 (28)
Oral	9 (21)
Liver, spleen, or kidney	3 (7)
Bone	2 (5)
Number of organ systems involved	
1	14 (33)
2	14 (33)
3+	15 (35)

ACTG, AIDS clinical trial group.

(GI) involvement, 18 (42%) and 15 (35%) respectively. Fifteen (35%) had KS in three or more organ systems. Twenty-six (60%) had a recent or concurrent opportunistic infection when KS was first diagnosed, the most common of which was pneumocystis pneumonia (14, 33%) (Table 3). There was a high rate of sexually transmitted infections. Twelve patients (29%) had a reactive syphilis titer during at least one hospital admission. There was a high rate of viral hepatitis with 11 patients (26%) having positive tests for hepatitis B surface antigen (HBsAg) and 3 patients (7%) having positive polymerase chain reaction tests for hepatitis C virus. Although KSHV-MCD was considered in the differential diagnosis for six of the patients, it was confirmed in only one patient.

TABLE 3. INFECTIONS DIAGNOSED IN HIV$^+$ PATIENTS ON FIRST HOSPITAL ADMISSION FOR KS

	n (%)
Opportunistic infections	
Pneumocystis pneumonia	14 (33)
Toxoplasmosis	4 (9)
Mycobacterium tuberculosis	4 (9)
Cryptosporidium	2 (5)
Cytomegalovirus	2 (5)
Sexually transmitted infections	
Herpes simplex virus	9 (21)
Syphilis	12 (29)
Gonorrhea or chlamydia	4 (9)
Human papilloma virus with anal warts	5 (12)
Hepatitis B Virus (HBsAG$^+$)	11 (26)
Hepatitis C Virus (HCV PCR$^+$)	3 (7)

PCR, polymerase chain reaction.

TABLE 4. CHARACTERISTICS OF HOSPITAL ADMISSIONS FOR OR EXACERBATED BY KS (81 ADMISSIONS)

	Number (%) or median (IQR)	
Median number of admissions per patient	2	(1, 4)
Median duration of admission (days)	9	(5, 18)
HIV Related		
Median CD4 count at admission[a]	21	(7, 108)
Median $\log_{10}$ viral load at admission[b]	4.5	(2.3, 5.1)
CART received during admission[c]	61	(76.3)
Median length of time before ARV initiation (days)[d]	1	(0, 3)
Organ system of primary admission diagnosis		
Skin and soft tissue	23	(28.4)
Respiratory	22	(27.2)
Gastrointestinal	20	(24.7)
Neurological	4	(4.9)
Generalized symptoms[e]	14	(17.3)
Concurrent acute infection at time of admission		
Bacterial infection	40	(49.4)
Sepsis	28	(34.6)
Received chemotherapy	8	(9.9)
Admitted to ICU	15	(18.5)
Intubated	10	(12.4)
Death occurred during admission	12	(14.8)

[a]Seven admissions did not have a CD4 count near the admission date documented.
[b]Ten admissions did not have a viral load near the admission date documented.
[c]One early admission record did not contain whether or not CART was administered.
[d]Six admissions where CART was administered did not record specific start dates for treatment.
[e]Generalized symptoms included general malaise, fevers, hypotension, and failure to thrive.
ICU, intensive care unit.

Overall, the cohort had 141 hospital admissions with 81 (57.4%) related to KS (Table 4). Six of the admissions (7.4%), though not directly related to KS, were for neutropenic fever secondary to chemotherapy for KS. The following information pertains to admissions directly attributed to KS. The median number of admissions per patient was two with a median duration 9 days. The highest number of admissions for one patient was 10 and the longest admission

was 63 days. Chief complaints relating to skin and soft tissue such as cellulitis or super infection of KS-affected areas were the most common reasons for admission (28.4%). Respiratory complaints including dyspnea, cough, and hemoptysis were also common (27.2%), and these were generally caused or exacerbated by pulmonary KS.

Concern for KS-IRIS was mentioned in clinical notes for five admissions; however, formal diagnoses were never made. Fifty of the admissions (61.7%) involved an acute infection at presentation; the pathogen identified was bacterial in 40 of the 49 admissions where a pathogen was identified (81.6%). The most common bacterial pathogens included *Staphylococcus aureus* (31.7%), *Mycobacterium* spp. (12.2%), *Streptococcus* spp. (9.8%), *Clostridium difficile* (9.8%), and *Enterococcus* spp. (9.8%). The other 26.8% of pathogens included *Klebsiella*, *Pseudomonas*, *Shigella*, *Escheria coli*, *Acinetobacter anitratus*, and *Enterobacter cloacae*. Patients presented with or developed sepsis during 36 admissions (44.4%).

Although KICS was not diagnosed in any patients, there were five cases of sepsis where no pathogen was identified despite extensive testing, some of which may represent undiagnosed episodes of KICS. Fifteen hospital admissions for KS (18.5%) resulted in ICU admissions and patients were intubated during 10 admissions (12.3%). The oncology service was often consulted to assist with management and inpatient cytotoxic chemotherapy was administered during eight hospitalizations. CART was administered during 61 (76.3%) admissions. The median time between admissions and cART initiation was 1 day; however, the maximum amount of time was 45 days. In 39 (71%) of those administered cART, therapy was initiated less than 48 h after admission; administration was delayed in 16 (29%) hospitalizations. The most common reasons for delay included history of poor compliance, patient refusal, unstable clinical status, or concern for IRIS.

The Kaplan–Meier mean survival estimate after diagnosis with KS was 3.0 years (SE: 0.4). Three patients were lost to follow-up before the 6 months of follow-up. Of the remaining patients, 25 (63%) survived 6 months and 23 (58%) survived 1 year. Twenty-one (49%) died over the duration of follow-up. Of those who died, 15 (71%) died within 6 months of KS diagnosis and 17 (81%) died within 1 year of KS diagnosis. The cause of death was determined to be KS related, generally from respiratory complications, in 13 patients (62% of those who died). Twelve patients died during hospital admissions for KS and 11 of those who died had antecedent sepsis.

TABLE 5. ANALYSIS OF PREDICTORS OF KS MORTALITY BY COX PROPORTIONAL HAZARDS MODELS

	Bivariate model[a]				Multivariate model[b]	
Variable	Parameter estimate	SE	Hazard ratio	p	Hazard ratio	p
Lung involvement (ref = no)	0.90	0.46	2.45	.0494	1.05	.9217
Liver involvement (ref = no)	1.78	0.78	5.91	.0222	6.37	.0737
Karnofsky Score less than or equal to 70	1.14	0.47	3.11	.0159		
Karnofsky Score (continuous)	−0.08	0.03	0.92	.0029	0.94	.0475
CD4 T cell count under 100	1.22	0.63	3.39	.0539		
CD4 T cell count under 50	1.21	0.56	3.34	.0316	2.80	.1056
$\log_{10}$ viral load >4 log copies/ml	0.76	0.47	2.15	.1010	2.15	.2500
Age at KS diagnosis >50 years	−0.36	0.75	0.70	.6317	2.25	.3641

[a]Bivariate models of survival involve specified variable as predictor and survival duration as outcome.
[b]Multivariate model includes lung involvement, liver involvement, Karnofsky score, and CD4 < 50, log viral load >4 log copies/ml, age at KS diagnoses >50 years, as predictors and survival duration as outcome.

TABLE 6. ODDS RATIOS OF DEATH DURING ADMISSION TO THE HOSPITAL FOR ACTIVE KS BY ORGAN SYSTEM OF PRIMARY ADMISSION DIAGNOSIS

Type of primary admission diagnosis	n admissions (%[a])	n deaths (%[b])	Odds ratio	95% confidence interval
Skin and soft tissue	23 (28.4)	1 (1.2)	0.19	0.02–1.60
Skin/soft tissue infection	18 (22.2)	1 (1.2)	0.28	0.03–2.31
Respiratory	22 (27.2)	5 (6.2)	2.18	0.61–7.79
Lung infection	**7 (8.6)**	**3 (3.7)**	**5.42**	**1.04–28.24**
Gastrointestinal	20 (24.7)	4 (4.9)	1.66	0.44–6.23
Generalized symptoms	14 (17.3)	2 (2.5)	0.95	0.18–4.90
Acute infection on admission	50 (61.7)	9 (11.1)	2.05	0.51–8.24
Events during admission				
ICU transfer	15 (18.5)	10 (12.4)	64.00	10.90–375.77
Intubation	10 (12.4)	8 (9.9)	67.00	10.55–425.66
Sepsis	28 (24.6)	11 (13.6)	33.65	4.04–280.06

[a]Percentage of total admissions.
[b]Percentage of admissions for specified primary admissions diagnosis.
Boldface indicates primary admission diagnosis with statistically significant odds of death.

The following variables were not independently associated with mean survival in our cohort of AIDS patients admitted with KS: ACTG KS staging criteria, opportunistic infections, sexually transmitted infections, chemotherapy administration, age, viral load above 10,000 copies/ml, or cART administration. Of the organ systems involved, lung and liver involvement were associated with decreased survival by log-rank test ($p < .05$). Hazard ratios for death from subsequent bivariate cox regression are seen in Table 5. While the CD4 T cell count was not a significant predictor as a continuous variable, there was a statistically significant difference in probability of death when a CD4 T cell count of 50 cells/ul was used as cutoff (hazard ratio 3.34, $p = .03$). Karnofsky score was also a significant predictor when viewed as both a continuous variable ($p = .003$) or as a categorical variable with a score of less than or equal to 70 used as the cutoff for worse prognosis ($p = .02$). Karnofsky score less than or equal to 70 was the only variable that remained significant in multivariable analysis ($p < .03$).

When we looked at each hospital admission, there was no significant difference between the odds of death during hospitalizations where KS was one of the reasons for admission and hospitalizations where the admission was unrelated to KS (OR 3.30; 95% CI:0.89–12.28). If we used stratified logistic regression analysis to control for patient identity, the odds ratio calculated was lower and remained nonsignificant (OR 1.31; 95% CI: 0.22–7.8). There was a high risk of death during admissions for respiratory complaints ("dyspnea," "cough," "hemoptysis," etc.), GI complaints (i.e.: "diarrhea," "GI bleed," "abdominal pain," and "vomiting"), and whether the admission was for an acute infection; however, these associations were not significant (Table 6). When specifically analyzing lung infections (pneumonia or empyema), there was a significantly greater odds of death during admission (OR 5.42; 95% CI: 1.04–28.24). There were no cases of death during admissions for GI infections and thus an OR could not be calculated. There was no significant association of skin and soft tissue infection with death during admission (OR: 0.28; 95% CI: 0.03–2.31). Admissions that involved the ICU, sepsis, or intubation were very highly associated with death during admission (Table 6). There was no association between CD4 at admission and death during the subsequent hospitalization.

Discussion

Our study found that patients admitted to the hospital for epidemic KS were primarily black men, with MSM as the most common risk factor for HIV transmission. All but one of the patients were from the United States, and almost all were significantly immunosuppressed at the time of KS diagnosis (CD4 < 200). When we compare the characteristics of our study population to those with HIV in Georgia as a whole, the distribution of HIV risk factors is similar; however, we see a disproportionate overrepresentation of black American men in our cohort compared to the 55% seen statewide.[27] This likely represents the population served by our hospital, which is primarily lower-income, black American.

The majority of cases identified by our study presented with low CD4 counts (91% below 150) and high viral loads (56% with viral load above 10,000 copies/ml) and were not on cART (58%) when KS was first diagnosed. The severe immunosuppression and lack of cART use would explain the severity of KS manifestations in our cohort. As many as 26% of patients in our study also had active hepatitis B. Although hepatitis B is a sexually transmitted infection, it is also a vaccine preventable illness, and is another indicator of the lack of adequate primary and preventive care received by the patients identified in our study.

All our patients were in the "high-risk" category identified by the ACTG to determine prognosis for HIV$^+$ patients with KS. Thus, the staging did not provide further information with respect to survival. Our study was consistent with prior studies that have indicated that a lower threshold for CD4 count serves as a better predictor of survival.[28] Thus, in KS patients who already meet the ACTG high-risk staging category, CD4 counts, particularly those below a threshold of 50 cells per ul, may further help to assess prognosis. We also found that while the system category as a whole did not add to predicting survival, Karnofsky score, a measure of performance status, was a significant predictor of survival. The presence of recent or concurrent opportunistic infections was not significantly correlated with survival in our cohort. Historically, studies have demonstrated that opportunistic infections were associated with survival.[24,29,30] Much of this research was performed before cART was widely available, or did not control for it in

their studies. The presence of such intercurrent infections may be an indicator of immunological suppression, the more likely predictor. The effectiveness of immune reconstitution may therefore better serve as a predictor for survival in high-risk KS patients. The limited number of patients and loss to follow-up in our study limited our analysis of this factor.

When we looked at individual hospital admissions that were related to KS, the most frequent reason for admission was cellulitis. Many of these patients described either chronic lymphedema or itchy KS lesions, which may put them at risk for bacterial superinfection. Cases where no pathogen was identified could have represented symptoms of KS mistaken as cellulitis, as has been described by others.[31] Although these complaints were the most common reason for admission, they were not associated with increased odds of dying. On the other hand, both our survival analysis and the analysis of individual hospital admissions indicate that pulmonary involvement of KS and admissions for respiratory complaints, more specifically respiratory infections, are associated with a high risk of death. Pulmonary KS may increase the risk of acquiring lung infections, or lung infections and subsequent inflammatory responses may exacerbate pulmonary KS contributing to respiratory failure. The highly vascular nature of KS lesions may provide a portal for bacteremia or sepsis when they are associated with lung infections. In several cases in this study, pulmonary KS was not recognized until late into the hospital course (or even autopsy). Most of these patients received treatment for either presumed or confirmed pneumonia. A previous study of AIDS-related pulmonary KS found that the symptoms of KS could rarely be distinguished from that of superimposed infections, and 15.5% of cases did not have any mucocutaneous lesions.[32] Thus, it is essential to consider the possibility of pulmonary or disseminated KS in patients with AIDS who present with respiratory infections, particularly when they have known KS, and especially if the response to antibiotics is inadequate. The management of pulmonary KS is challenging. There is a risk of precipitating IRIS upon initiating cART. Chemotherapy can also cause further immunosuppression and increase the risk of further infections. In our experience, oncologists were often understandably reluctant to start chemotherapy in the inpatient setting as patients were critically ill and had poor performance status. In many of these patients, initiation of cART with careful monitoring for IRIS and empiric treatment of suspected infections may be the best therapeutic option. In some patients, there was a hesitancy to start cART if there was a history of poor medication adherence. Many of these patients required prolonged hospitalization, where their adherence could have been carefully monitored and encouraged.

There was only one case of documented KSHV-MCD in our study. Several patients had presented with diffuse lymphadenopathy and KSHV-MCD was considered but not pathologically confirmed. This may be because lymph node biopsies are invasive procedures and confirmation of KSHV-MCD is unlikely to change management in the acute setting. KICS was a rare diagnosis in this study. KICS has only been described recently and few physicians are aware of this clinical entity. Although no diagnoses of KICS were made, there were several patients who were admitted with high inflammatory states, and no infectious pathogen or other diagnosis was made. These admissions may have represented undiagnosed cases of KICS, although we cannot confirm this retrospectively. It is likely that we may see an increase in the incidence of KICS as more providers become familiar with this syndrome.

Our study was limited by several factors. The small sample size with a high rate of loss to follow-up limited our statistical analysis, and prevented us from fully assessing many potential predictors of survival. For example, high variability between cART regimens and changes to regimens during follow-up precluded them from being used as a factor for analysis in our small dataset. The cross-sectional design also prevents the determination of causality of any identified predictors. Additionally, using chart review to obtain our data limited the factors we were able to investigate. As an example, CRP was measured in only one individual. We attempted to categorize cART compliance; however, this information was not documented reliably, and as such was difficult to compare between patients. Finally, this study did not include all patients diagnosed and hospitalized with KS in our region. It only included patients admitted to one hospital for active, severe KS; thus, the results may not be generalizable to other hospitals with different patient populations.

Conclusion

The spectrum of KS manifestation seen in our study is not different from that seen in the 1980s at the peak of the HIV epidemic. While the HIV epidemic may have significantly slackened in much of the country, in metro Atlanta it is still expanding, with reported prevalence rates of 1,489 and 1,093 cases per 100,000 population in 2012 in Fulton and Dekalb counties respectively.[33] Not only is the prevalence of HIV in Atlanta higher than in the rest of the country, but these rates are rising, not declining. Atlanta was ranked fifth out of all metropolitan areas for highest rates of new HIV diagnoses in 2013.[34] The GA department of public health cited that 43% of patients with HIV in metro Atlanta in 2012 have an unmet need for primary care.[35] The lack of adequate HIV primary care in our population is not only manifested by the many cases of severe KS, but also by the low rates of cART utilization and high incidence of Hepatitis B in our study. There are still a significant proportion of new HIV cases that are diagnosed at an advanced stage, as demonstrated in the four patients who were diagnosed with KS at the same time as testing HIV seropositive. We must consider new methods for targeting and screening the at-risk populations in our community, particularly young black MSM. Barriers to accessing healthcare in this population should also be identified and addressed. Epidemic KS should not occur at such high rates in the era of widespread cART availability, especially in a developed nation.

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Author Disclosure Statement

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Address correspondence to:
Minh Ly Nguyen
Emory Center for AIDS Research Investigator
341 Ponce de Leon Avenue
Atlanta, GA 30308

E-mail: mnguye3@emory.edu