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Clinical presentation and treatment outcome of HIV associated Kaposi sarcoma in a tertiary health centre in Nigeria

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Abstract

Objective: Kaposi sarcoma (KS) is the most common tumour among AIDS patients and is considered as an AIDS defining illness. However, the introduction of HAART has led to a decline in the incidence of the disease among these patients. The objective of this study is to review the clinical presentation, treatment and outcome of HIV associated KS in a tertiary health facility in Nigeria. **Methods:** Records of all patients that were managed with HIV associated KS from January 2012 to December 2014 at Aminu Kano Teaching Hospital were reviewed and data obtained was analysed using a computer statistical software. **Results:** During the period under review, 3705 patients were recruited in the anti-retroviral treatment (ART) clinic out of which 24 were found to have HIV associated KS giving a period prevalence of 0.65%. The male to female ratio was 2.4:1. The mean age of the patients was 39.46 (±8.75) years. Six cases (25%) were diagnosed to have HIV as a result of KS. The remaining 75% were all on 1st line ARVs. Nine patients (37.5%) had treatment for Tuberculosis before they were diagnosed with KS. Based on the ACTG classification, 58.3% were poor risk group. Treatments given to the patients include HAART for 2 patients and 4 patients (16.7%) absconded. The remaining 18 patients had chemotherapy in the form of combination of intravenous Adriamycin, Bleomycin and Vincristine (ABV) with variable outcomes. Five patients failed ABV and had Paclitaxel given. At the end of the chemotherapy, 14 patients (58.3%) were in remission with 5 (20.8%) mortalities. There is no statistically significant difference between CD4 count before and after chemotherapy (P>0.05) **Conclusions:** Majority of our patients are classified poor risk. Paclitaxel can be used as second line treatment. Treatment of KS does not improve CD4 count in patients with HIV. There is need to clinically identify patients with KS early in ART centre in order to improve outcome.

Keywords: Presentation, Outcome, Kaposi sarcoma, HIV, Chemotherapy.

INTRODUCTION

Chronic Kaposi sarcoma (KS) is the most common tumour among Acquired Immune Deficiency Syndrome (AIDS) patients in Africa, affecting a high percentage of these individuals and is considered as an AIDS defining illness [1-5]. However, the introduction of Highly Active Anti-Retroviral Therapy (HAART) over the last two decades has led to a decline in the incidence of the disease among patients with AIDS [6-10]. The presentation can be as simple as a single patch to a disseminated disease involving multiple organs that may be life threatening [11]. The AIDS Clinical Trials Group (ACTG) classification uses tumor/immune system/systemic illness (TIS) grading method and group patients into good or poor risk [12]. The average age of KS manifestation among AIDS patients is 20 to 40 years and correspond with homosexual activity [13,14]. Reports from Africa have shown similar age of presentation with a male predominance [5,15-17]. A study from Sao Paulo found that 25% of HIV positive patients were diagnose as a result of the KS [18], while a local study from Zaria, Nigeria gave 7.1% [19]. Various modalities of management are available involving HAART, chemotherapy, radiotherapy, cryotherapy, immunotherapy, surgery and their combination [11,20,21]. Over time, antiretroviral resistance, intolerance or poor adherence to HAART has led to significant morbidity and mortality among AIDS patients with aggressive KS [22,23]. Patients with advanced symptomatic KS have shown no significant improvement when treated with HAART alone without Chemotherapy [24,25]. The first-line chemotherapy for AIDS associated KS (AIDS-KS) is liposomal anthracyclines [26-29]. Other cytotoxic agents tested include vinca alkaloids, bleomycin and etoposide [20,30,31]. Paclitaxel as a single agent have been shown to have activity against KS including some that had previously received anthracylines [20,32,33]. The outcome of KS is that of partial or complete remission,

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stabilization of disease, failure of treatment, relapse of disease or progression to death [12].

The objective of this study is to review the clinical presentation, treatment and outcome of AIDS-KS in a tertiary health facility in Nigeria.

METHODS

Records of all patients that were managed with AIDS-KS from January 2012 to December 2014 from the ART clinic, Clinical Haematology clinic and chemotherapy day care of the Department of Medicine of Aminu Kano Teaching Hospital Kano, Nigeria were reviewed and information on clinical presentation, therapy given and outcome were retrieved and recorded. Based on the unit protocol, all the patients were given eight cycles of combination of intravenous Adriamycin 35mg/m^2, Bleomycin 10iu/ m^2 and Vincristine 1.4mg/m^2 (ABV) fortnightly [34,35]. Those that failed ABV clinically or have relapse diagnosed histologically are given intravenous Paclitaxel 100mg/m^2 fortnightly [28,29,36]. Quantitative variables obtained are summarised as proportions while continuous variables are summarised as mean and median with distributions presented as standard deviation and 95% confidence interval. Data was analysed with STATA statistical software, version 11. Comparison of means was done using 2 tailed student's t test and a p value of 0.05 is considered statistically significant.

RESULT

Between January 2012 and December 2014, 3705 patients were recruited in the anti-retroviral therapy (ART) clinic of Aminu Kano Teaching Hospital out of which 24 were histologically found to have AIDS-KS giving a period prevalence of 0.65%. The mean age of the patients was 39.46 (±8.75) years with a Male:Female ratio of 2.4:1. Married patients constitute 62.5% and more than 60% are civil servants or engaged in business/trading (Table 1).

Table 1: Demographic Characteristics (n=24)

Parameter	Frequency (N =24)	Percentage (%)
Age		
Mean = 39.46 (±8.75) years		
Range = 25-55 years		
Sex		
Male	17	70.8
Female	7	29.2
M:F = 2.4:1		
Marital Status		
Married	15	62.5
Single	9	37.5
Occupation		
Business/Trading	9	37.5
Civil Servants	6	25.0
Commercial Drivers	3	12.5
Police	2	8.3
Others	4	16.7

Clinical Presentation

Based on the ACTG classification, 14 (58.3%) patients presented as poor risk group with 12 (50%) as T1I1S1 and 2 (8.3%) as T1I1S0. Six patients (25%) were diagnosed to have HIV as a result of KS. The remaining 75% were all on 1st line ARVs based on the National guidelines[37] with an average duration on treatment of 8.43 (±10.72) months before diagnosis of KS was made. Nine patients (37.5%) had treatment for tuberculosis before they were diagnosed with KS.

The mean CD4 count before chemotherapy for KS was 211.6 cells/ul (95%CI=140.2 – 283 cells/ul).

The KS lesions seen in 25% of cases were generally hyperpigmented patches/plagues seen all over the body and multiple cutaneous and mucosal nodules affecting the lower limbs with lymphoedema (Figure 1 a). However, about 50% had mucocutaneous and lymph nodes affectation. Visceral involvement comprising various combination of the chest, gastrointestinal tract, conjunctiva, tongue and hypopharyngeal lesions were seen in 25% of cases (Figures 1b and 1c).

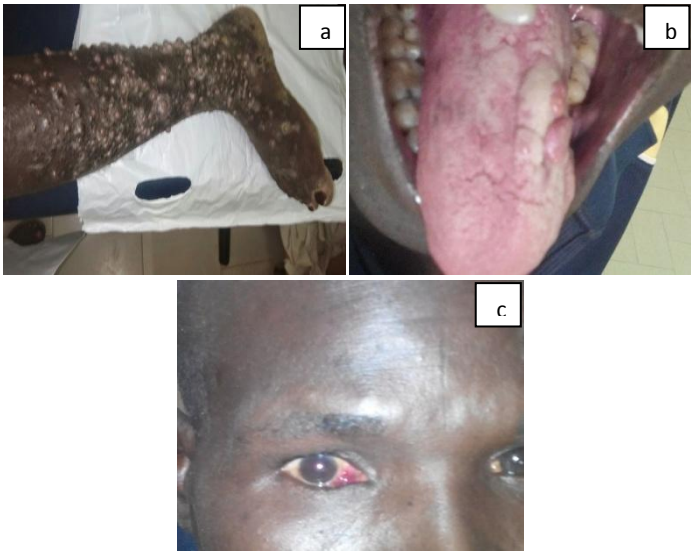

Figure 1: Lymphoedema in lower limbs (a), tongue (b), and conjunctiva (c)

Treatment Outcome

Treatments given to the patients include HAART for 2 patients with resolution of lesions and are on follow up for 4 months and 12 months as at the time of data collection. Four (16.7%) other patients, 2 males and 2 females absconded before therapy could be commenced.

The remaining 18 patients had chemotherapy in the form of combination of Adriamycin, Bleomycin and Vincristine (ABV) with variable outcomes (Figure 2). Ten were in either partial or complete remission determined based on the ACTG criteria[12] with a mean follow up time of 18.25 (±10.99) months. Three patients died while on ABV treatment and all of them had KS lesions in the lungs.

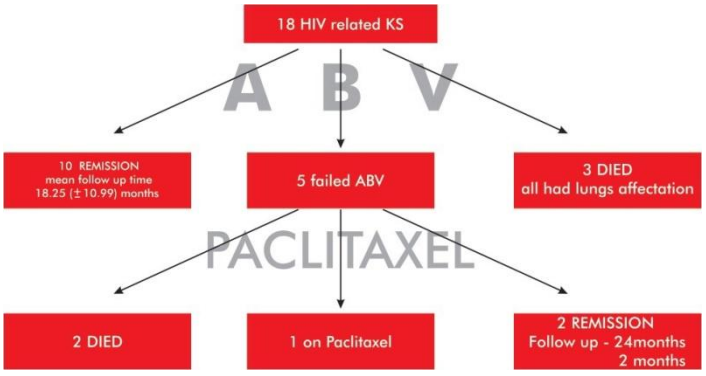

Figure 2: Flow chart showing outcome of chemotherapy

Five (27.8%) failed ABV and had Palitaxel given, with two of them in remission and on follow up for 8 months and 2 months at the time of this data collection. Two other patients died while on this second line

therapy and the remaining one patient was still on treatment with Paclitaxel (Figure 2).

A final mortality rate of 20.8% was recorded among these patients and the end of treatment 14 (58.3%) patient were in remission (Table 2).

Table 2: 0utcome of AIDS-KS

Outcome	Number (n=24)	Percentage (%)
Absconded	4	16.7
Remission	14	58.3
Death	5	20.8
On treatment	1	4.2
Total	24	100

The mean CD4 count after chemotherapy with ABV was 281.4 cells/ul (95% CI= 169.9 – 392.9 cells/ul). There is no statistically significant difference between CD4 count before and after chemotherapy (P>0.05).

Side effects recorded during chemotherapy were generally mild and include alopecia in 62.5% of cases while 75% had hyperpigmentation. A case of moderate neutropaenia following Paclitaxel was also reported.

DISCUSSION

The prevalence of 0.65% of AIDS-KS recorded in this study is lower than the post HAART era prevalences of 0.85% and 0.8% observed in studies from Abuja[38,39] and much lower than the prevalences of 1.4% and 1.6% reported from Zaria and Jos respectively [19,40] , all in Nigeria. This could be as a result of increased availability and accessibility of HAART recorded over the years in the country[37], the consequence of which is decrease in the incidence of the disease as reported [6-10]. The mean age at presentation of the disease of 39.46 years reported here is similar to reports from other studies in Nigeria[19,38,39] and South Africa[3,16], however we could not obtain information on homosexuality practice. The age range reported in this study of 25-55 years corresponds to the age ranges with the highest HIV seropositivity in Nigeria and also the ages when individuals indulge in high risk sexual activities [37]. The male predominance found in this study, though a little bit higher, is similar to many earlier reports [3,5,15,19]. However, a report from Jos, Nigeria gave higher ratio to females that was attributed to the study population that included women attending antenatal care. The presentation of majority of our patients (58.3%) as poor risk ACTG class is lower than the earlier report of 78.6% from the same region [19]. However out of this 58.3%, T1I1S1 constitute 50% which is similar to the 48% reported in the same study. This is not surprising as most patients with AIDS-KS have been reported to have low CD4 count even if they are on HAART [8]. Also this low CD4 count predisposes these patients to other opportunistic infections like tuberculosis which 37.5% of our patients had before they presented to us with KS. Other reports gave proportion of AIDS-KS patients treated for tuberculosis as 18% in South Africa and 20.4% in Zaria [3,19]. However, there is a report of KS in African AIDS patients with CD4 count of more than 350 cells/ul [41], which is concurred by studies that showed KS can develop among patients with good immune system as a result of Human Herpes Virus 8 (HHV8) infection despite good CD4 count [42-44]. The mean CD4 count of 211.6 cells/ul (95%CI=140.2 – 283 cells/ul) that our patients presented with is higher than that reported from the Zaria study of 165 (95%CI =97-425cells/ul) [19]. This could be explained by the fact that the Zaria study had more cases of poor risk patients (78.6%) based on the ACTG classification compared to our 58.3%, and since the CD4 count is used in the classification, it is logical for their average CD4 count to be higher than what is found in our study. Also ARV resistance and poor adherence to therapy by patients as reported may be a reason [22,23]. Furthermore the larger sample size of the Zaria study can also contribute to this disparity in CD4 count. The diagnosis of HIV was made in 25% of our cases when they presented with KS which is similar to reports from Brazil of about 25%, but much higher than the 7.1% reported from Zaria [18,19]. Visceral and other organs involvement was observed in about 25% of our cases and the mortality recorded in patients on ABV was all among patients that had Lung KS. This is consistent with reports that disseminated and visceral KS is commoner among AIDS patients and has high mortality rate [34,45,46]. Treatment given to our patients was consistent with what is obtained in the literature that early or good risk disease can show regression of lesions with HAART alone which was observed in 2 of our patients while in patients with aggressive and extensive mucocutaneous disease or with visceral KS, systemic chemotherapy and HAART is the treatment of choice [24,24,47]. This is necessitated because of the absence of Liposomal Dounorubicin in Nigeria and most African countries because of cost and logistics that involve cold chain [48]. The patients that failed ABV were treated with paclitaxel which has been shown to have activity against Anthracycline resistant KS with no significant interaction with HAART [28,29,36]. No significant change in CD4 count was noticed among our patient after chemotherapy which is similar to other reports [19,36]. The response rate of 58.3% we recorded is within the range of 50- 88% response reported both within and outside Nigeria [17,19,48,49]. The 16.7% abscondment and the overall mortality of 20.8% noted in this study have been recently reflected in a reviews from South Africa and Zimbabwe that showed higher risk of dying and lost to follow up among patients with AIDS-KS especially those with low pre-treatment CD4 count [3,50]. Side effects of chemotherapeutic agents reported were generally mild and did not warranted postponement or discontinuation of therapy and are consistent with those that are reported when these drugs are used [49,51].

CONCLUSIONS

Kaposi Sarcoma is a common cancer among AIDS patient and a major cause of morbidity and mortality. Majority of our patients presented with advanced disease and classified as poor risk based on the ACTG classification. Patients with visceral affectation especially the lungs have poor outcome. Treatment of KS does not improve CD4 count in patients with HIV. There is need to clinically identify patients with KS in ART centres early in order to improve their outcome by initiating ARVs early. Combination chemotherapy using Adriamycin, Bleomycin and Vincristine should be used in place of Liposomal Daunorubicin and Paclitaxel use as a second line treatment should be encouraged.

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