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Trends and morphologic variants of Kaposi Sarcoma as seen in Nnewi, Anambra State, Nigeria

Felix Emeka Menkiti ^{1,*}, Cornelius Ozobia Ukah ¹, Ifeoma Oluchukwu Menkiti ², Chisom Godswill Chigbo ³ and Igwebuike Victor Onyiaorah ¹

¹ Department of Anatomic Pathology and Forensic Medicine, Nnamdi Azikiwe University, Nnewi Campus, Anambra state, Nigeria.

² School of Nursing, Nnamdi Azikiwe University Teaching Hospitals, Nnewi, Anambra State, Nigeria.

³ Research society, Nnamdi Azikiwe University Teaching Hospitals, Nnewi, Anambra State, Nigeria.

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Abstract

Kaposi sarcoma (KS) is a human herpes virus type 8 (HHV-8) driven neoplasm with varying morphologic features and attendant diagnostic dilemma. This study presents the trend of KS in our environment and the different morphologic variants, with a view to arousing awareness and reducing missed and delayed diagnosis. KS accounted for 18.34% and 59.66% of vascular neoplasms and malignant vascular neoplasms, respectively with most KS occurring in the background of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). The frequency peaked in 2013 and began to decline with a fairly even sex distribution. There are diverse variants of KS that can pose diagnostic challenges. Hence, there is need for this awareness to enhance prompt and accurate diagnosis.

Keywords: Kaposi Sarcoma; Morphology; Trends; Variants; Vascular

1. Introduction

Over the past few decades, the interest in Kaposi sarcoma (KS) has been renewed due to its association with HIV/AIDS. KS is one of the AIDS defining neoplasms, classified as a low grade sarcoma. KS presents in four epidemiological forms, including classic, endemic, iatrogenic, and AIDS-associated, all having a common aetiologic agent HHV-8 (Human Herpes Virus-8).¹ The incidence of KS has decreased globally since the advent of highly active anti-retroviral therapy (HAART) for the treatment of HIV/AIDS.² According to GLOBOCAN 2020, KS ranked 33rd among cancer cases, accounting for 0.18% of new cancer cases worldwide,³ but ranks 20th in Nigeria, accounting for 0.94% of new cancer cases with a cumulative risk of 0.06.⁴ In a study done in South-eastern part of Nigeria, KS accounted for 1.31% of solid cancers and 15.38% of sarcomas.⁵

Accurate diagnosis requires morphologic evaluation, with KS being characterised by vascular slits formed by atypical spindle cells containing red cells and admixed with inflammatory cells and occasional hyaline globules.⁶ However, morphology alone is not sufficient to confirm diagnosis or exclude mimics of KS. Hence, the need to subject lesions with features suggestive of KS to immunohistochemical confirmation.^{5,7} Moreso, in recent times, there has been an increasing awareness and reporting of wider histologic variants of KS, some of which are unusual and easily missed.⁸⁻¹⁰ Some researchers have opined that some of these variants may have prognostic implication; hence failure to identify a given lesion as KS could lead to delayed diagnosis or inappropriate management.¹¹ Pathologists therefore, must be aware of this to avoid misdiagnosis, which is common with KS and KS-like lesions.⁵

* Corresponding author: Felix Emeka Menkiti

Department of Anatomic Pathology and Forensic Medicine, Nnamdi Azikiwe University, Nnewi Campus, Anambra state, Nigeria.

This study is aimed at assessing the trend of KS and the different morphologic patterns as seen in Nnewi, Anambra state Nigeria over a 16-year period. This is to highlight and create awareness of these pictures to reduce misdiagnosis, as well as encourage utilisation of confirmatory tests on KS-like lesions.

2. Material and methods

This is a descriptive 16 years retrospective study that involved all biopsies with a morphologic diagnosis of KS and confirmed using HHV-8 LNA1 immunohistochemistry. The formalin-fixed paraffin-embedded tissue blocks and clinical request forms of cases that met inclusion criteria were retrieved from the archives of Histopathology Department of Nnamdi Azikiwe University Teaching Hospital (NAUTH) and Pathocon Specialist Clinic & Research Institute, both in Nnewi, Anambra State, Nigeria, between the period of January 2006 and December 2020. Fresh sections were prepared and stained with haematoxylin and eosin (H and E) stains and examined using multi-headed compound light microscope (@CARL ZEISS).

The data analysis was done using the IBM, Chicago Statistical Package for Social Sciences (SPSS) software version 20.0, and the results presented in tables and charts.

3. Results

A total of 387 vascular lesions were recorded in the years under review (including 223 benign, 45 borderline and 119 malignant vascular lesions), 71 of which were diagnosed morphologically and immunohistochemically (using HHV-8 LNA1 antibody) confirmed as KS. KS therefore accounted for 18.34% and 59.66% of vascular neoplasms and malignant vascular neoplasms, respectively.

KS was noted to be at its peak in the third decade, affected 35 males and 36 females in a male to female ratio of 1.0:1.0; however, more females (58.93%) were affected by the HIV/AIDS-associated KS (see *Table 1*).

Table 1 Demographic distribution of KS

Age range	HIV/AIDS-Associated		Non-HIV/AIDS-Associated		Total
	Male	Female	Male	Female	
1-10	1	1	1	0	3
11-20	1	1	2	0	4
21-30	8	11	1	0	20
31-40	4	9	1	0	14
41-50	5	6	2	1	14
51-60	3	3	1	1	8
61-70	1	2	1	1	5
71-80	0	0	3	0	3
	23	33	12	3	71
Total	56		15		

Almost 80% (56/71) of the KS lesions were associated with HIV/AIDS. Most (41/71) of the lesions were noted to involve the lower limbs (*Figure 1*). These lesions were largely diagnosed at the morphologic nodular stage (see *Figure 2*).

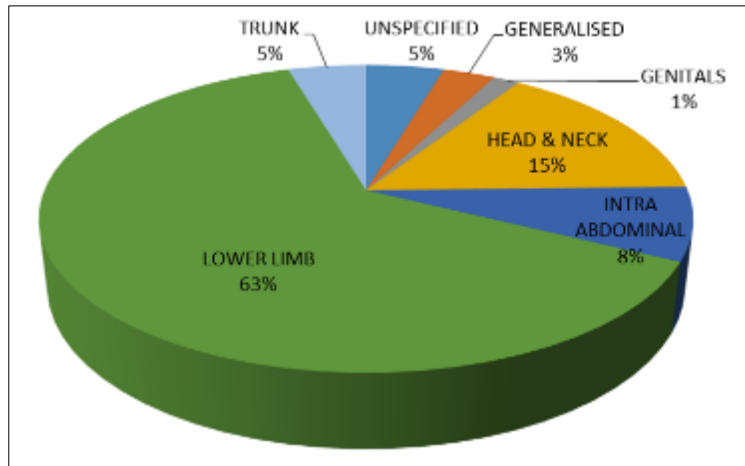


Figure 1 Anatomic site distribution of KS

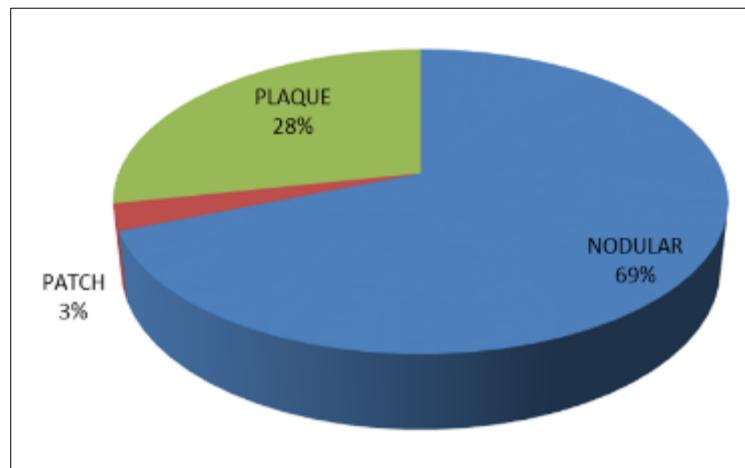


Figure 2 Morphologic stage distribution of KS

Figure 3 showed a gradual decline in the frequency of KS from 2006 to 2011, a sharp rise thereafter to reach a peak in 2013, followed by a gradual decline. The rise was noted to be largely in association with HIV/AIDS (see *Figure 4*) with a fairly uniform distribution in both sexes (see *Figure 5*).

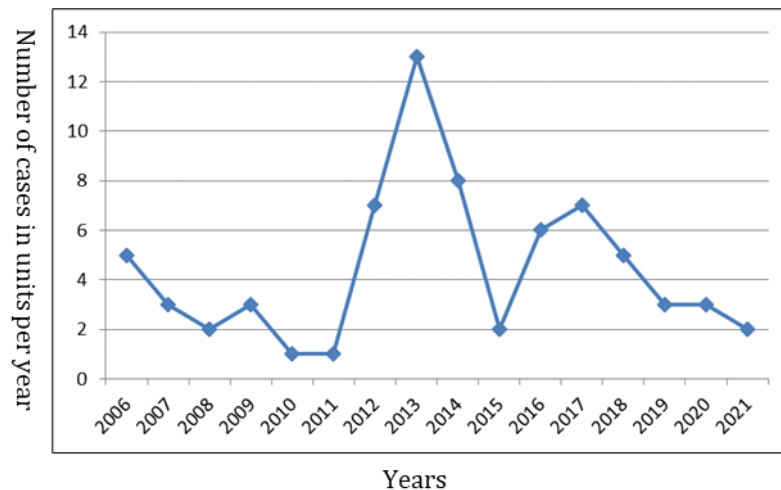


Figure 3 Yearly trend of Kaposi Sarcoma across the year 2006-2021

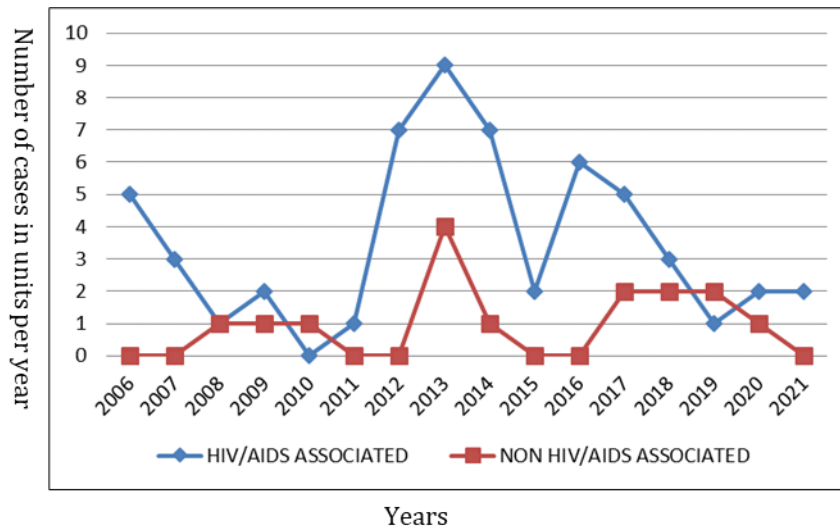


Figure 4 Yearly trend of KS according to classification across year 2006-2021

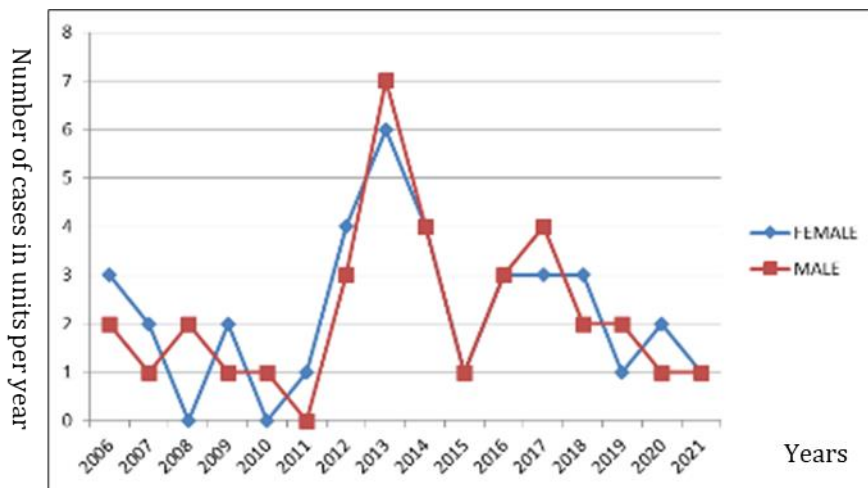


Figure 5 Gender trend of Kaposi Sarcoma across the year 2006-2021

3.1. Morphologic variants of KS observed

Figures 6 (a-h) show the morphologic variants noted in this review, other than the classic morphologic pictures of the different stages. These included epithelioid, cavernous haemangioma-like, lymphangioma-like, telangiectatic, bullous-type, pyogenic granuloma-like, micronodular, acanthotic and verrucous variants.

Epithelioid KS consisted of sheets and nests of epithelioid cells having pleomorphic and irregular nuclei with scant cytoplasm. There are extravasated red blood cells, numerous mitotic figures and scattered inflammatory cells (see *Fig 6a*). *Telangiectatic KS* is composed of variably sized, ectatic, congested vascular channels amidst foci of typical nodular KS (see *Figures 6b-d*) lined by HHV8-LNA-1 positive endothelial cells. *Cavernous haemangioma-like KS* shows cavernous channels with flattened endothelium admixed with plump spindle cell proliferation interspersed by vascular slits, inflammatory cells and extravasated red cells under a hyperkeratotic squamous epithelium; the spindle and endothelial cells being HHV-8 LNA1 positive (see *Figures 6e-f*). *Pyogenic granuloma-like* is characterized by lobulated capillary-caliber vascular proliferation with features consistent with KS spindle cell proliferation and HHV8-LNA-1 immunopositivity (see *Figures 6g-h*). *Lymphangioma-like KS* shows dermal inter-anastomotic, irregularly shaped, caving and variably atypical endothelial-lined channels in a background of typical KS spindle cells (see *Figures 6i-j*). *Acanthotic KS* displays dermal atypical spindle cells interspersed by inflammatory cells and slit-like channels containing red cells with overlying acanthotic and hyperkeratotic epidermis (see *Figure 6k*). *Micronodular KS* shows a small, circumscribed but unencapsulated, proliferating atypical spindle cell characteristic of KS within the reticular dermis (see *Figure 6l*). *Bullous KS* features consistent with KS lesions, but the overlying epidermis has sub-epidermal bullae,

and the cells were positive for HHV-8 LNA1 immunostaining (see *Figures 6m-n*). *Verrucous KS* shows verruciform epidermal hyperplasia and hyperkeratosis overlying a dermal characteristic KS lesion (see *Figure 6o*).

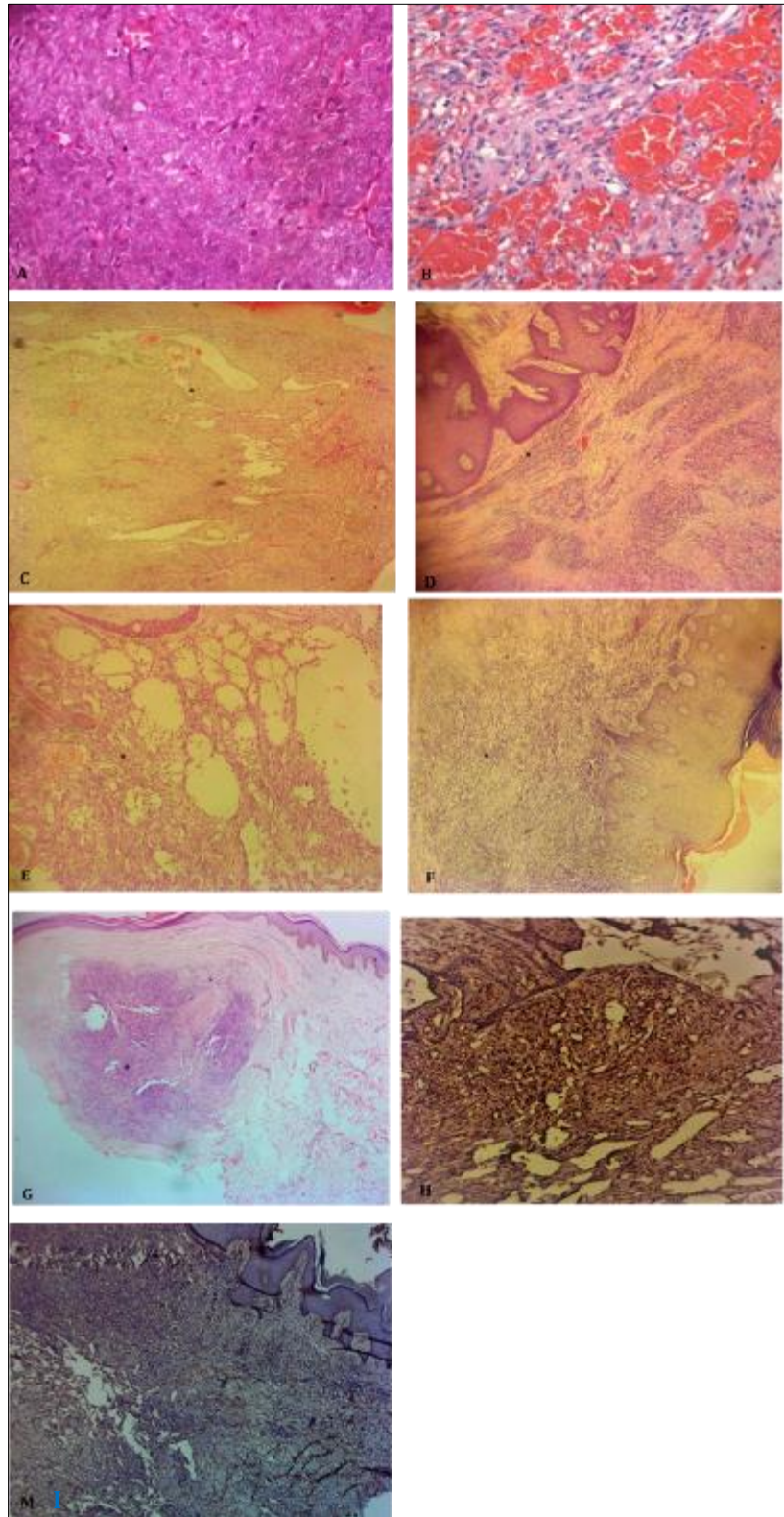


Figure 6 Photomicrographs showing the different morphologic variants epithelioid (a: H&E x100), telangiectatic (b: H&E x100), cavernous haemangioma-like (c: H&E x100), pyogenic granuloma-like (d: H&E x50), lymphangioma-like (e: H&E x100), acanthotic (f: H&E x50), micronodular (g: H&E x50), Bullous (h: HHV8 immunohistochemistry x100) and verrucous (i: HHV8 immunohistochemistry x50).

4. Discussions

KS is a Human Herpes Virus-8 (HHV-8) driven neoplasm with variable clinical course and occurring in four epidemiological setting.¹² It was first reported by Moritz Kaposi in 1872. Its incidence was reportedly increased over the years linked to HIV/AIDS pandemic but has declined globally due to the introduction of HAARTS, accounting for about 0.2% of cancer incidence and mortality.¹³ despite this global decline, KS still accounts for 0.94% and 0.87% of cancer incidence and mortality respectively, with a 5-year prevalence of 1.20%.¹⁴

KS accounted for 18.34% and 59.66% of vascular neoplasms and malignant vascular neoplasms, respectively, making it the commonest malignant vascular lesion in this study. A study done in northern Nigeria reported KS as the most common malignant vascular neoplasm.¹⁵ Forae *et al.* in the south south part of Nigeria also reported that KS accounted for 79/269 vascular lesions diagnosed over 20 years period, accounting for approximately 89% of borderline and malignant vascular neoplasm.¹⁶ KS is therefore a fairly common vascular neoplasm in our environment. KS has been reported to occur over a wide age range with a peak that varies between the third and fifth decades of life.¹⁷⁻¹⁹

The trend over the years indicated a steady growth from 2006 to 2013, after which there was a sharp decline, a stepwise rise and then a stepwise steady decline. We noted here that the burden of KS over the years was majorly contributed to by the HIV/AIDS association, which has slight female preponderance; though KS overall displays a fairly even sex distribution. The study by Forae *et al.* indicated a rise after year 2005 to reach a peak in 2008, then a little drop to a still significant value that is fairly sustained between 2009 and 2014.¹⁶ We may not fully define the reason for the initially rise in our study, but could be possibly explained by increased campaign and awareness of HIV/AIDS and testing as coordinated by the establishment of national agency for the control of AIDS (NACA) and a National Strategic Framework in 2004/2005.²⁰ It is plausible to state that a sustained strategic plan against HIV/AIDS with targeted reach of the rural communities, is still required, not only to eradicate the HIV/AIDS pandemic but also KS.

KS is morphologically characterized by spindle cells forming slits containing red bloodcells, admixed with inflammatory cells and occasional presence of periodic acid-Schiff (PAS)stain positive hyaline globules.¹⁰ However, KS clearly has the ability to develop into lesions of varying morphologic appearance relating to the stages of the lesion, including patch, plaque and nodular stages. Most of the lesions in this study were morphologically diagnosed at the nodular stage and, the lower limb is the commonest affected anatomic site. This finding is similar to that reported in studies related to KS in most studies in Africa. Although this late morphology (nodular stage) may be related to late presentation due to ignorance, poverty and poor access to health care in Africa, as well as the fact that most are HIV/AIDS-associated, thus having rapid progression,²¹ no explanation has been given for the lower limb predilection of this lesion.

We noted in this study some morphologic variants other than the conventional type. These included epithelioid, cavernous haemangioma-like, lymphangioma-like, telangiectatic, bullous-type, pyogenic granuloma-like, micronodular, acanthotic, verrucous and hyperkeratotic variants. The morphologic diversities of KS have been reported in literatures, noting various variants.²²⁻²⁴ It has also been suggested that certain variants, such as anaplastic KS and possibly lymphangioma-like KS, might have prognostic relevance.²⁵⁻²⁶ It is therefore important that pathologists be able to recognize these variants in order to avoid potential misdiagnosis, delayed diagnosis and mismanagement of afflicted patients.

5. Conclusion

KS presents varying morphologic diversities that pathologists and clinicians must be aware of to enhance prompt and accurate patient management. No gender predilection is noted in the occurrence of KS. There was a noticeable steady decline in its frequency in this last decade. Since its occurrence over time is related to HIV/AIDS, a sustained, coordinated, grassroots action against HIV/AIDS will help reduce the frequency in our environment.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

All the authors declare that there are no conflicts of interest.

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