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Full Length Research Paper

Kaposi Sarcoma: A review of 387 cases seen in Yaounde, Cameroon

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The introduction of highly active antiretroviral therapy has improved on survival and increased the life expectancy of HIV/AIDS patients. This increase predisposes to a high incidence of HIV-associated malignancies among these patients. Kaposi sarcoma is one of the commonest AIDS-related malignancy in our community and is sometimes the clinical presentation that heralds the infection. We were interested to find out the epidemiological and anatomo-clinical aspects of the disease in this population. Data of the Yaounde Population Cancer Registry on patients diagnosed with Kaposi sarcoma between 2004 and 2011 was reviewed in this retrospective population study. Epidemiological and anatomo-clinical data of the patient and the tumour were analyzed. Chi-squared tests were used for statistical analysis. 387 patients with Kaposi sarcoma, including 64% males and 37% females were found in 8 years, giving an annual average of 48. About 55% of the disease was AIDS-associated. The age range for patients was 1-86 years at an average of 42.01 years and median of 40 years. The male average age was 42.4 years and 36.1 years for females. In males the disease is significantly more located in the skin, while the digestive tract with exception of the stomach is a significantly more topographic site for the tumour in females. 3 patients were HIV negative. There is no difference among the sexes for location of the tumour in the stomach, lymph nodes and lung. Kaposi sarcoma is common our community, mostly affects males at mid age, and is predominantly AIDS-related. The tumour location is sex-dependent at certain sites. HIV negative persons are not immune to the disease. HIV serology is recommended for all patients who present with a Kaposi sarcoma and concomitantly, all HIV seropositive patients should be screened for the disease.

Keywords: Kaposi, sarcoma, AIDS, Yaounde.

INTRODUCTION

Kaposi's sarcoma (KS) is a systemic disease that can present with cutaneous lesions with or without internal involvement. Since Moritz Kaposi (Kaposi, 1872) first described this malignant neoplasm the disease has been reported in five separate clinical settings, with different presentations, epidemiology, and prognosis (James et al., 2005). The viral cause for this cancer was discovered in 1994 (Chang et al., 1994). All of these forms are infected with Kaposi sarcoma herpes virus (KSHV) and

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Table 1. Topographic distribution of KS.

Site	Number of cases	%
Skin	289	66.0
Stomach	72	16.4
Lymph node	33	7.5
Mouth/tonsil/pharynx	23	5.3
Anus/colon/rectum	3	0.7
Bronchus	3	0.7
Others-eye, testis, vulva	15	3.4
All sites	**438***	**100**

*The tumour was located at multiple sites amongst some patients.

are different manifestations of the same disease with different clinical aggressiveness, prognosis and treatment. Classic Kaposi sarcoma; as originally described was a relatively indolent disease affecting elderly men from the Mediterranean region, or of Eastern European descent. Countries bordering the Mediterranean basin have higher rates of KSHV/HHV-8 infection than the remainder of Europe (Iscovich et al., 1998; Fenig et al., 1998). The clinical types include:

1. Endemic KS, which has two types, African cutaneous Kaposi sarcoma and African lymphadenopathic Kaposi sarcoma was described later in young African people, mainly from sub-Saharan Africa. It is a more aggressive disease that infiltrated the skin extensively, especially on the lower limbs. This type is not related to HIV infection. KS is prevalent worldwide (Cook-Mozaffari et al., 1998; Olsen et al., 1998).

2. Immunosuppression-associated Kaposi sarcoma had been described, but only rarely, until the advent of calcineurin inhibitors (such as ciclosporines, which are inhibitors of T-cell function) for transplant patients in the 1980s, when its incidence grew rapidly. The tumor arises either when an HHV8-infected organ is transplanted into someone who has not been exposed to the virus or when the transplant recipient already harbors pre-existing HHV-8 infection (Qunibi et al., 1998; Luppi et al., 2000).

3. AIDS-associated Kaposi sarcoma or Epidemic KS was described during the 1980s as an aggressive disease in AIDS patients. It is over 300 times more common in AIDS patients than in renal transplant recipients. In this case, HHV-8 is sexually transmitted among people also at risk for sexually transmitted HIV infection (Beral et al., 1990). Some AIDS patients have complete resolution of the lesions and prolonged remission while on highly active antiretroviral therapy (HAART). Consequently, HAART is considered first-line treatment for these patients, though they may require other concomitant treatments (Iscovich et al., 1998; Cook-Mozaffari et al., 1998; Fenig et al., 1998; Antman and Chang, 2000). Although KS is now well-established to be caused by a viral infection, there is widespread lack of awareness of this even among persons at risk for KSHV/HHV-8 infection (13 Caceres), the virus which is responsible for all varieties of KS.

MATERIALS AND METHODS

For a retrospective period of 8 years between January 1 2004 and December 31 2011, data on patients diagnosed with KS and captured by the Yaounde Cancer Registry was reviewed. The epidemiologic, anatomic and clinical data on the tumour and patients was retrieved and analyzed. Cases out of the study period were rejected. Chi-squared tests were used for data analysis.

RESULTS

A total of 387 cases of KS involving 438 sites were observed. There were 244 males (63%) and 143 females (37%) diagnosed with KS in eight years, giving an annual average of 55 tumour sites among 48 patients. The age range for males was 1-85 years, median 44 years and mean 42.4 years. For females, the age range was 2-86 years, median 25years and mean of 36.1 years. The disease is predominantly AIDS-associated (34% males and 21% females). In males KS is significantly more located in the skin than in females, while the digestive tract including the mouth, tonsils and pharynx, but with exception of the stomach is a significantly more topographic site in females. There is no significant difference among the sexes for location of the tumour in the stomach, lymph nodes and lung. Incidence of the disease is not influenced by level of education of the patients.

Table 2. Distribution of KS by age and by sex.

Age (years)	Sex		Total	%
	Male	female		
0-9	6	5	11	2.9
10-19	9	3	12	3.1
20-29	19	38	57	14.7
30-39	56	53	109	28.2
40-49	78	18	96	24.8
50-59	44	11	55	14.2
60-69	13	4	17	4.4
70-79	11	1	12	3.1
≥80	1	4	5	1.3
Unknown	7	6	13	3.3
All ages	**244**	**143**	**387**	**100**

Table 3. KS distribution in specific sites by sex

Topography	Male	%	Female	%
Skin	194	79.5	97	67.8
Lymph nodes	19	7.8	15	10.5
Stomach	11	4.5	7	4.9
Anus/colon/rectum	1	0.4	2	1.4
Bronchus/lung	1	0.4	2	1.4
Mouth/tonsil/pharynx	9	3.7	14	9.8

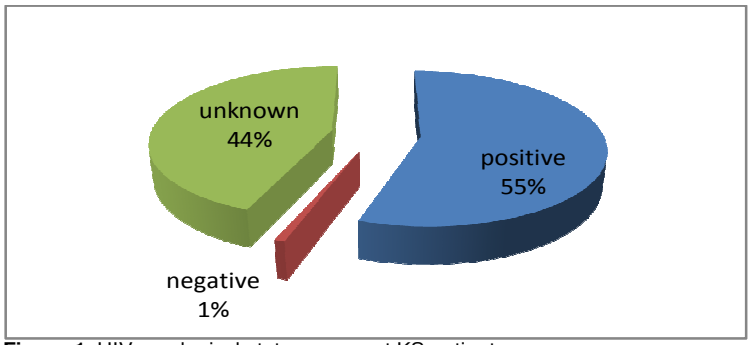

Figure 1. HIV serological status amongst KS patients.

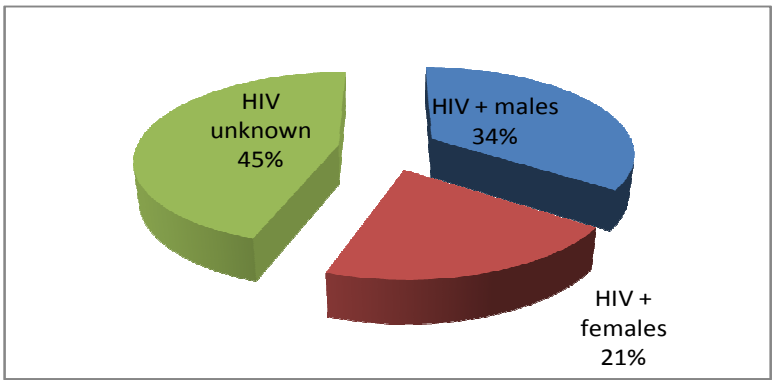

Figure 2. Sex distribution of HIV+ patients with KS

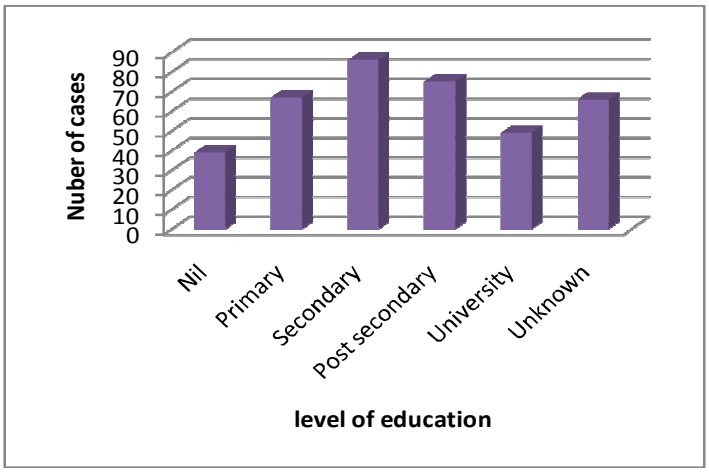

Figure 3. Educational level of KS patients.

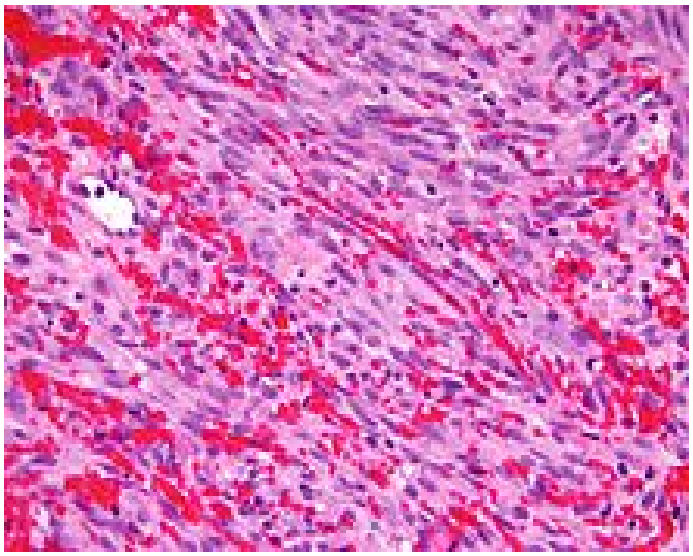

Figure 4. Micrograph of a Kaposi sarcoma showing the characteristic spindle cells, high vascularity and intracellular hyaline globs. H&E stain.

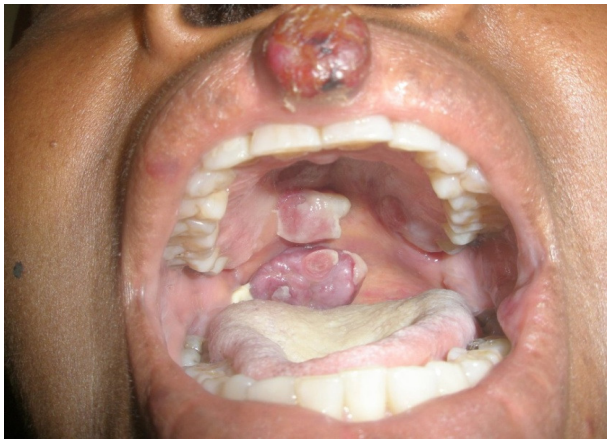

Figure 5. Labial and palatine location of KS in an HIV + patient. The candida-coated tongue is common finding.

DISCUSSION

Cancer has been found to be a public health problem in Cameroon (Doh et al., 2007) with KS representing about 6.9% of the national cancer burden (Enow Orock, 2012). In an earlier study, KS was reported to be the commonest AIDS-associated malignancy in the country, and was found among 30.6% of HIV/AIDS patients (Enow Orock, 2012). The 6.9% burden in this population reported above is higher than the 3-5 % found in Kenya and Tanzania (Hutt, 1984). There has been an upsurge of KS in the past decades in this community where the previous rate of KS was 10.4% in males and 0.9% in females from 1968 to 1973 (Jensen et al., 1978), and no case registered between 1995-1996 (Parravicini et al., 1997). This low incidence is similarly observed in Ibadan where only 3 cases in males and 1 case in females were reported between 1998 and1999 (Cancer in Africa. Epidemiology and Prevention, 2003).

Endemic African Kaposi sarcoma has accounted for 10% of cancers and has been seen in a male-to-female ratio of 15:1, a rate higher than the 1.8:1 that we found in our series. The Kampala Cancer Registry has shown a significant alteration in the incidence of Kaposi sarcoma in the era of AIDS. In Uganda, Kaposi sarcoma has caused almost one half (48.9%) of cancer cases in men and 17.9% in women (Gantt et al., 2010). The incidence in men (30.1 cases per 100,000) represents a more than 10-fold increase in men since the 1950s and is approximately 3 times the incidence found in women (11 cases per 100,000). In neighboring Zambia, the disorder was particularly aggressive among children, more than 80% of whom were HIV seropositive. Kaposi sarcoma was found to represent as much as 25% of childhood cancers (Gantt et al., 2010). These values are higher than the incidence of 5.6/100.000 in males and 2.9/100.000 in females that we found in Yaounde (Enow Orock, 2012). The incidence in boys and girls was approximately the same in childhood (birth to 14 years), with small peaks in girls younger than 5 years and boys aged 5-9 years. Subsequently, a progressive rise in incidence peaked in women aged 25-29 years and in men aged 35-39 years. This pattern is similar to our observation in this study (table 2).

HHV-8 has been linked convincingly with all 4 types of KS, an association that is necessary, but not sufficient, to develop KS. Immunosuppression appears to be the most significant cofactor. KSHV is also transmissible via organ transplantation (Parravicini et al., 1997) and blood transfusion (Hladik et al., 2006).

Testing for the virus before these procedures is likely to effectively limit iatrogenic transmission. In our study, 55% of patients were HIV positive out of 56% of patients whose HIV serological status was known (98.2%). Among a high proportion of our patients, the HIV serological status remains unknown (45%) (see Figure 1 and II).

Kaposi sarcoma is described in 3 forms (localized nodular, locally aggressive, and generalized) and in 6 stages (patch, plaque, nodular, exophytic, infiltrative, and lymphadenopathic). It occurs most frequently in mucocutaneous sites, typically the skin of the lower extremities, face, trunk, genitalia and oropharyngeal mucosa. It also commonly involves lymph nodes and visceral organs, most notably the respiratory and gastrointestinal tracts (Mitsuyasu, 1987). KS is typically found on the skin, but spread elsewhere is common, especially the mouth (Figure 5), gastrointestinal tract and respiratory tract. Growth can range from very slow to explosively fast, and is associated with significant mortality and morbidity (Dezube, 1996).

Lymphadenopathic Kaposi sarcoma affected 12% of total cases in Uganda while we observed a rate of 7.5%. Of 73 Ugandan children with epidemic Kaposi sarcoma from the Uganda Cancer Institute in Kampala (from 2004-2007), 37 were boys and 36 were girls, with a median age of 10.1 years (range 2-18 years) (10). The average male-to-female ratio was 1.76:1, with male predominance higher in children older than 5 years (2.5:1 ratio) than in children younger than 5 years (1.4:1 ratio). In our series, among 23 children aged 0-19 years with KS, 15 were boys against 8 girls, with similar age and sex proportions among children. In neighboring Nigeria, the prevalence of HIV-related Kaposi sarcoma seems to be increasing, probably owing to more females having HIV disease (Onunu et al., 2007).

Gastrointestinal involvement is common in those with transplant-related or AIDS-related disease, and it may occur in the absence of skin involvement. The gastrointestinal lesions may be silent or cause weight loss, pain, nausea/vomiting, diarrhea, bleeding (either vomiting blood or passing it with bowel motions), malabsorption, or intestinal obstruction (Danzig et al., 1991). In our series, 6.3% of cases were located in the GIT with majority of these found in the stomach (table 3). The mouth is reportedly involved in about 30% of cases, and is the initial site in 15% of AIDS-related KS. In the mouth, the hard palate is most frequently affected, followed by the gums (Nichols, 1993). In this study, the commonest sites of the disease were the skin (67.8%), lymph nodes (10.5%), oropharynx (9.8%0 and the stomach (4.9%). We found 9.8% of our patients to have oropharyngeal tumours (table 3).

Although KS may be suspected from the appearance of lesions and the patient's risk factors, definite diagnosis can be made only by biopsy and microscopic examination, which will show the presence of spindle cells (Figure 5). Detection of the KSHV protein LANA in tumor cells confirms the diagnosis. Histological confirmation was done in 287/387 (74%) patients in this study. In AIDS patients, Kaposi sarcoma is considered an opportunistic infection.

With the rise of HIV/AIDS in Africa, where KSHV is widespread, KS has become the most frequently reported

cancer in some countries. KS is one of the commonest AIDS-related malignancy in our community and is sometimes the clinical presentation that heralds the infection (Enow Orock and Ngowe, 2013). It is the fifth commonest cancer among both sexes, third commonest in males and fourth in females (Enow Orock and Ngowe, 2013). This trend which has occurred in the past ten years has been largely attributed to the AIDS pandemic. The 20-59 years age group is most affected in both sexes with peak at the 30-39 years. This age group is also that most affected by AIDS. The pattern of the disease among both sexes is the same - low in children and young teenagers and also low among third generation elderly patients. Although patients of secondary and post secondary educational levels are more affected in this study, there is no significant difference in the level of education among the patients (p>1.5) (figure 3).

Kaposi sarcoma is rare but not excluded in HIV negative patients, and is associated with HHV-8 infection (Iman et al., 2011). The first cases were reported as far back as 1872 as a form of the cancer in older people of eastern Mediterranean origin. In this study, 3 patients were found to have the disease with a negative HIV serology (Gönen et al., 2006). These were 2 males aged 1 and 42 years respectively, and a-3-years-old female.

CONCLUSION

Kaposi sarcoma is a common malignancy in our community, and the predominant type is AIDS-associated. The disease incidence is not influenced by the educational level of the individual. The target age groups coincide with that of HIV infection, and it is sometimes the heralding sign of the infection, though HIV negative persons are not immune to the disease. There appears to be a predilection of the tumour for particular sites among males and females. HIV serology is recommended for all patients who present with a KS and concomitantly, all patients, irrespective HIV sero-positive and negative patients should be screened for KS. Further in-depth studies are recommended to document trends of the disease in this community.

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