Pattern of head and neck malignant neoplasms in HIV-infected patients in Kenya


Abstract. HIV-infected patients face a greater risk of developing malignant disease. The most commonly reported neoplasms of the head and neck region include Kaposi’s sarcoma (KS) and non-Hodgkin’s lymphoma (NHL). There is also an increased risk of oral squamous cell carcinoma (SCC).

A descriptive cross-sectional study including HIV-infected patients with neoplastic and non-neoplastic lesions was conducted. Of the 200 participants, 116 (58%) were male and 84 (42%) female with an age range of 18–61 years (mean 37 years). The females were significantly younger (mean 33 years) than the males (mean 37 years) (t test; 2.57; \( P < 0.05 \)). The prevalence of neoplastic lesions in this study was 27%; 37 (68%) patients had KS, 9 (17%) had SCC, 7 (13%) had NHL and 1 (2%) had Burkitt’s lymphoma. More females than males presented with lesions of KS and SCC compared with NHL. The youngest patient presented with SCC at 18 years (mean 35.7 years), followed by KS at 23 years (mean 36.3 years) and NHL at 33 years (mean 43.9 years). Most study participants (97%) were in stage III/IV of the disease and the remaining 3% in stage II. In this study, the most common malignant neoplasms were KS, SCC and NHL, manifesting in a younger age group than in the non-HIV group of patients.

Keywords: HIV; malignancy; head and neck.

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The global AIDS epidemic shows no signs of abating since its first detailed clinical description in 1981\(^2\). According to the current UNAIDS report, the number of people living with HIV worldwide in 2007 was 33.2 million (30.6–36.1 million). Sub-Saharan Africa remains the most seriously affected region; more than 68% of adults and nearly 90% of children infected with HIV live in this region and more than 76% of AIDS deaths in 2007 occurred there. It is estimated that 1.7 million (1.4–2.4 million) people were newly infected with HIV in 2007, bringing to 22.5 million (20.9–24.3 million) the number of people living with the virus\(^4\). In Africa, AIDS has almost reversed gains in life expectancy and reductions in childhood mortality\(^5\). Most countries in Africa lack the economic capacity and infrastructure to handle the economic and health costs of the disease. Heavily affected countries in sub-Saharan Africa could lose more than 20% of their Growth Development Potential by 2020\(^6\).

HIV infection and subsequent immunosuppression results in an increased risk of developing malignant disease. In 1996 it was reported that malignancies that were diagnosed more frequently in patients with AIDS than in the general population included Kaposi’s sarcoma (KS), non-Hodgkin’s lymphoma (NHL), melanoma,
oral malignancies associated with HIV-Related Diseases) 2. The prevalence of AIDS group IVD (CDC classification of HIV infection) may reflect local head and neck manifestations, but recognition of these lesions has increased and it now seems that nearly 100% of patients with AIDS have both neoplastic and non-neoplastic lesions. 

HIV-infected individuals have a two-fold increase in the risk of malignant disease. Oral malignancies associated with HIV infection may reflect local head and neck disease or represent systemic malignant disease. The presence of oral malignancies varies with risk factors for transmission of HIV, including unprotected sexual activity, contact with blood or blood products, and injection drug abuse; and differs geographically based on behaviour, viral cofactors, HIV therapy and genetic variation. Squamous cell carcinoma (SCC) is the most common cancer in the head and neck region, but it is overshadowed by KS and NHL in patients with HIV. SCC has been seen in excess in HIV-infected populations. Oral KS (OKS) is the most prevalent AIDS-associated malignancy. In more than 20% of patients with KS, the oral cavity is the initial site of presentation. It is an endothelial cell, multicentric, malignant neoplasm, and frequently involves the palate, gingivae and tongue. OKS has been reported to be the first sign of KS in up to 70% of cases, as well as the most common sign of HIV infection. KS in an HIV-infected patient is classified as AIDS group IVD (CDC classification of HIV-Related Diseases). The prevalence of AIDS-associated OKS is 0–12% in Africa and 0–38% in the USA and Europe. NHL is a malignancy of the lymphoid tissue, considered to be a complication of HIV disease. It was not until 1985 that the CDC included NHL as an AIDS-defining diagnosis. NHL is the second most common malignancy affecting people with HIV infection in Western countries. The anatomical distribution of NHL is not altered in the presence of HIV infection in the head and neck region (63%). Primary oral NHL was rare before the AIDS era, constituting only 4–5% of extranodal NHL. Of these tumours, approximately 20–35% originated in the palate and only 35% showed osseous involvement. NHL of the oral cavity account for 3% of all malignant lymphomas in patients with HIV infection. The oral cavity may be the first or only site of involvement, NHL presents as a firm elastic often reddish or purplish swelling, with or without ulceration. The gingivae, palatal mucosa and fauces are sites of predilection. SCC has been reported in HIV-infected patients, although epidemiological evidence documenting an increased risk of this has not been convincing. Case reports appear in the literature, some involving younger people without other risk factors commonly associated with SCC. In addition to tobacco and alcohol use, human papilloma virus (HPV) infection, immunodeficiency, and possibly genetic changes represent risk factors for SCC in HIV infection. In general, this malignancy has been described in a younger age group and in individuals lacking the common risk factors associated with oral cancer and may be associated with a poorer overall survival. Flaitz et al. reported four patients in whom the tumour appeared as an ulcer or fungating mass or erythroplasia. SCC of the upper aerodigestive tract in HIV-infected individuals may be more aggressive than in those who are not HIV-infected. In one study, the overall experience with 30 cases of SCC of the upper aerodigestive tract in HIV-infected patients, stage III or IV cancer was found in all but one patient at presentation. In contrast, the advanced stage occurred in only 49% of the non-infected population. This is a descriptive cross-sectional study to determine the pattern of occurrence of head and neck malignancy among HIV-infected patients at the Kenyatta National Hospital in Nairobi, Kenya. 

Material and methods
This study was approved by the Ethics, Research and Standards Committee of the Kenyatta National Hospital and the University of Nairobi (Reference number KNH-ERC/01/3317). All consecutive patients were included, the selection criteria were age > 18 years and voluntary informed consent. The study was conducted over 8 months. HIV-positive patients whose HIV status had been confirmed through laboratory examination (using the fourth generation enzyme linked immunosorbent assay) were included in the study. A general head and neck examination was performed and the presence of non-neoplastic lesions (candidiasis, aphthous ulceration) and/or neoplastic lesions (KS, NHL, SCC) was recorded. An incisional biopsy under local anaesthesia using a strict aseptic technique was performed on all lesions suspected of being malignant. Histopathological analysis of the specimens was performed primarily by a histopathologist using haematoxylin and eosin staining.

Of the 250 patients identified, 200 were included in the study, the remainder could not be included because of discordant seropositive results. Others were discharged from the hospital, some declined to participate and others succumbed to HIV. There were 132 patients from the wards and 68 from the outpatient clinics among whom 116 were males and 84 females. 

Results
The age range among the study participants was 18–61 years (mean 37 years); among females it was 18–57 years (mean 38 years). 

Fig. 1. Distribution of HIV-associated non-neoplastic lesions among the participants.
33.5 years); and among males 18–61 years (mean 37.3 years). Most patients (88%) were 18–34 years for females and 35–45 years for males; the minority were 55 years or older.

Of the 200 patients included, clinical examination revealed that the presence of oral manifestations (both neoplastic and non-neoplastic) increased with the progressive stages of the disease. The most prevalent non-neoplastic lesions were hyperplastic candidiasis followed by erythematous candidiasis, angular cheilitis, aphthous ulceration and herpetic ulcers (Fig. 1).

Among the neoplastic lesions, 37 (68%) patients presented with KS, 9 (17%) with SCC, 7 (13%) with NHL and 1 (2%) with Burkitt’s lymphoma (BL) (Fig. 2). The clinical and histological manifestations of the various neoplastic lesions are shown in Figs. 3–5. Most KS lesions were seen on the palate followed by the maxillary alveolus and gingivae, unlike NHL and SCC which presented mainly in the maxillary and mandibular alveolus (Table 1). The age distribution of patients with malignant lesions varied, the youngest patient with SCC was 18 years old followed by a 23 year old with KS and a 33 year old with NHL. NHL appeared in an older age group compared with SCC and KS (Table 2). In this study, a higher number of females (20, 54%) than males (17, 46%) presented with KS. More females (6, 67%) than males (3, 34%) presented with SCC, the converse was true for NHL with 6 (86%) males compared with 1 (14%) female. All patients with neoplastic lesions were in stage III and IV of HIV disease; none was in stage II. The only malignancy that appeared in stage III was KS (1%), the remainder were in stage IV. The most prevalent malignancy in stage IV was KS then SCC followed by NHL.

Of the participants, 29% (57) and 19% (37) had a history of alcohol and tobacco consumption, respectively. Malignancy in these groups was 23% and 27%, respectively. According to the WHO clinical staging classification, 7 patients (3.5%) were in stage II, 86 (43%) in stage III and 107 (53.5%) in stage IV of the disease (Fig. 6).

Discussion

The results presented here show a similar pattern of head and neck malignancy in HIV-infected patients as reported in other studies. The prevalence of an oral neoplastic lesion in this group of HIV patients is 27% (95%CI); the true prevalence in...
any population is 21–33%. HIV-infected patients have an overall two-fold increase in the risk of developing malignant disease, with the following sequence of presentation: KS, NHL and SCC (2). The head and neck region was the initial and only site of presentation for most of the neoplastic lesions and the frequency of occurrence was KS/OKS (68%), SCC (17%), NHL (13%) and BL (2%). SCC, was the second most common neoplastic lesion, contrary to the report of NITTAYANTA and CHUNGPA-NICH20. The malignancies presented at an earlier age than is generally observed in non-HIV infected patients.

KS was most prevalent among females with a ratio of female to male of 1:0.85. In the developed world the incidence of HIV-related KS began to decline before highly active anti-retroviral treatment (HAART) became available, but became more pronounced thereafter. In contrast, the prevalence of KS has risen alarmingly in Africa15. Since the emergence of AIDS, KS has become more frequent in both genders, the male to female ratio changing from 19:1 to 1.7:1, particularly in East Africa27. There is no apparent reason why females are more affected than males. The site predilection was in accordance with the findings of LAGER et al.16 with the palate being the most common site9. AIDS patients with OKS have a higher mortality rate than those with skin involvement and KS has been identified as a prognostic factor for patients not taking HAART24. The second most prevalent neoplasm after KS/OKS was SCC; the patients had a mean age of 35.6 years. The youngest patient was 18 years of age and the female to male ratio was 2:1. This was unusual as in non-HIV-infected patients males more frequently develop SCC due to their consumption of alcohol and tobacco. Most of the afflicted had an advanced and aggressive form of the disease at presentation. SCC, the most common cancer in the head and neck region, is overshadowed by KS and NHL in patients with HIV infection4,27. An overall younger (less than 45 years) population is affected by HIV-associated SCC8. The results of a study in non-HIV infected patients at the same hospital, showed a relative frequency of oral cancer of 2–3%, with a peak incidence in those aged 50–60.
years. In this study, 29% and 19% of the patients who used alcohol and tobacco, respectively, developed the neoplasm. Patients with malignancy had a history of exposure to tobacco and/or alcohol, suggesting that carcinoma may develop in these patients as a result of a multifactorial aetiology including viral stimulation and immune dysfunction. It is important to note that these young patients had no history of tobacco or alcohol consumption. Patients in the present study were of a younger age, had an advanced form of malignancy and were in stage IV of the HIV disease, this is in keeping with the findings of other studies. This clearly shows that HIV infection accelerates the development of SCC by impairing normal immune surveillance mechanisms related to HIV infection. The alteration in the age distribution of SCC mandates aggressive screening of all HIV-infected patients.

Although, NHL is the second common malignancy in HIV-infected patients, in this population it was the third common. In comparison to KS and SCC, NHL presents in older individuals with a mean age of 43.9 years. NHL, in the non-HIV infected group appears in the fifth to sixth decade with an equal female to male ratio. NHL in the HIV group equally affects males and females. In this study, the age of the patients with NHL was approximately 10 years younger; in accordance with other studies. In the present group, the male to female ratio was 6:1, most presented in stage IV of the disease with the alveolar ridge and palate as the most common extra-lymphatic sites. The distribution and course of NHL is unique and a high level of suspicion for NHL is required in all patients with HIV infection.

References


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