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HIV Disease

Ranula: another HIV/AIDS associated oral lesion in Zimbabwe?

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AIM: To show that sublingual ranula is associated with HIV/AIDS and as such should be considered an HIV/AIDS associated oral lesion in Zimbabwe.
OBJECTIVES: To retrospectively study the prevalence, age and gender distribution, the HIV serostatus of ranula patients and the trend in prevalence of ranula and Kaposi's sarcoma (KS) in patients at the two largest referral Oral and Maxillofacial Surgery specialist centres in Harare, Zimbabwe. To use this information to infer an association between ranula and HIV/AIDS in Zimbabwe.
DESIGN: Descriptive study with a retrospective and prospective component.
SETTING: Oral and Maxillofacial Surgical clinics at specialist referral hospitals, Harare Central Hospital and Parirenyatwa Government Hospital, Harare, Zimbabwe.
SUBJECTS: Eighty-three cases of ranula were studied: 45 cases retrospectively and 38 consecutively. A total of 231 cases of KS were studied retrospectively.
METHODS: Histopathologic records of patients who presented with ranula and KS during the period January 1981 to September 2003 were studied. Gender and age were recorded for each case. Thirty-eight ranula patients studied consecutively during the period June 1999 to September 2003 were consented for HIV testing.
RESULTS: There were 83 cases of ranula; 43.4% male and 56.6% female. There were 231 cases of KS, 61.2% male and 38.8% female. Male to female ratio was 1:1.3 for ranula and for KS was 1:0.6. Ranula was predominant in the 0–10 year age group (73.5%) while KS was most common in the 21–40 year age group (76.4%). Ranula and KS both had a marked rise in prevalence from 1992 to 2003. A total of 88.5% of the ranula cases tested HIV positive with 95% in the 0–10 year age group.
CONCLUSION: There was a rising prevalence of ranula which mirrors that of KS (an HIV/AIDS associated oral lesion) and that 88.5% of ranula patients were HIV positive with 95% of them in the 0–10 year age group. Sublingual ranula should thus be considered another HIV/AIDS associated lesion in Zimbabwe, especially in children.
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Keywords: ranula; oral manifestation; HIV/AIDS; sublingual salivary gland

Introduction

Human immunodeficiency virus (HIV) infection first recognized in the early 1980s has since spread rapidly within the developing world and affecting mostly the adult age groups, which are most productive socially, reproductively and economically (Holmes and Stephen, 2002). Several papers describing the wide spectrum of oral manifestations of HIV/AIDS have been published. There are, however, unique differences in these oral manifestations in the various regions with unusual lesions appearing in HIV-infected individuals in developing countries (Patton *et al*, 2002). The following have been described: oral Kaposi's sarcoma (KS) is generally not a common finding in many other African studies (Arendorf and Holmes, 2000) unlike the Zimbabwean experience (Jonsson *et al*, 1998; Chidzonga, 2003); cancrum oris (noma) in Zimbabwe (Chidzonga, 1996); in South Africa (Naidoo and Chikte, 2000); in Lesotho (Adedoja *et al*, 2002); in Mali (Faye *et al*, 2003); in Nigeria (Ibeziako *et al*, 2003); in South East Asia penicilliosis marneffei has been suggested as another HIV/AIDS defining illness (Nittayananta, 1999). Thus, it is incumbent upon researchers in HIV/AIDS endemic developing countries to document unusual lesions or unusual presentation of known lesions of HIV/AIDS in their countries. It is in this context that the current study was conducted to provide evidence for an association between ranula and HIV/AIDS and propose its inclusion as an HIV/AIDS associated oral lesion in Zimbabwe.

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Human immunodeficiency virus associated salivary gland disease (HIV-SGD) is defined as the presence of xerostomia and or swelling of the major salivary glands common among children but uncommon among adults (Schiodt *et al*, 1992; Schiodt, 1992a). This has also been noted in Zimbabwe (Chidzonga, 2003). The prevalence of sublingual ranula in our Oral and Maxillofacial Surgical clinics was low in the past but since early 1999 it was noted that there was a rather marked increase in the number of patients presenting with sublingual ranula. Could this be another manifestation of HIV-SGD? What evidence could be presented to associate sublingual ranula with HIV-SGD? The prevalence of KS in Zimbabwe is reflective of the HIV/AIDS disease burden in the country (Chokunonga *et al*, 1999). Is there any similarity in the prevalence trends of ranula and KS? Surely any oral lesion that has a similar prevalence trend to oral KS should be considered an oral HIV/AIDS associated lesion!

The aim of the present study was to show that sublingual ranula is an HIV/AIDS associated oral lesion in Zimbabwe.

The objectives were to retrospectively and partly prospectively document the prevalence, age and gender distribution, determine the HIV serostatus of ranula patients and the trends in prevalence of ranula and KS (an established HIV/AIDS associated oral lesion) in patients seen at the two largest referral Oral and Maxillofacial Surgery specialist centres in Harare, Zimbabwe, and thereby propose an association between ranula and HIV/AIDS disease in Zimbabwe.

Methods

A retrospective analysis of biopsy records at Harare Central Hospital and Parirenyatwa Government Hospital for the period January 1981 to September 2003 was carried out recording all cases of ranula and KS by year, age and gender. Additionally, during the period June 1999 to September 2003, cases of ranula presenting at both hospitals were consecutively recorded by year, age, gender and HIV serostatus, was determined for consenting patients.

Results

Over the 23 year period (January 1981 to September 2003) 83 cases of ranula, 43.4% ($n = 36$) male and 56.6% ($n = 47$) female were recorded. There were 231 cases of KS of which 53 had either gender or age not stated, thus only 178 cases had complete data, 61.2% ($n = 109$) male and 38.8% ($n = 69$) female. The male to female ratio was 1:1.3 for ranula and 1:0.6 for KS.

Figure 1 shows trends in prevalence of ranula and KS over the study period, 0 for ranula and 1 for KS in 1981 to a high of 11 in 1995 for ranula and 24 and 25 for KS in 1995 and 1996, respectively.

Figure 2 comparing the age distribution of ranula and KS shows that ranula predominantly occurred in the 0–10 year age group with another peak in the 11–20 year age group. KS had the highest incidence in the 21–30 year age group with also another peak in the 31–40 year age group.

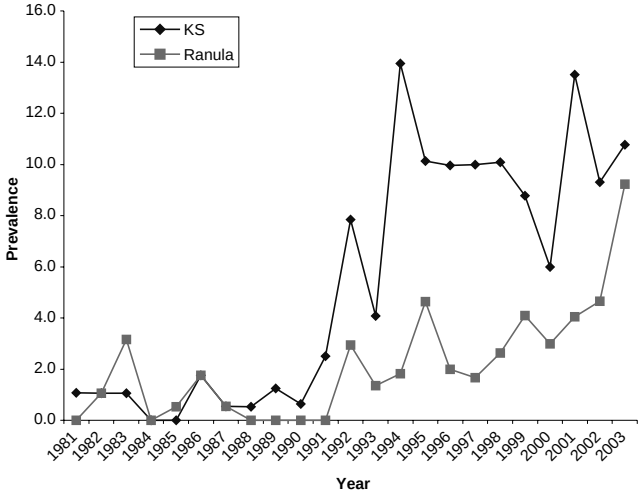

Figure 1 Trends in the prevalence of ranula and KS over the 23 year period

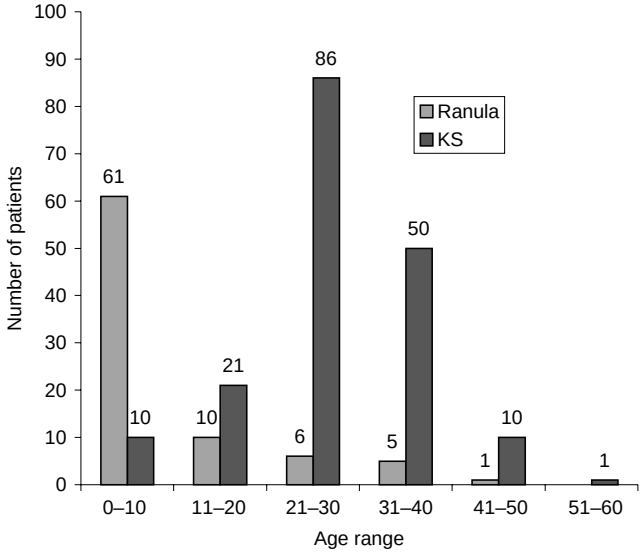

Figure 2 Comparison of age distribution of patients with ranula and intra oral Kaposi's sarcoma

Figure 3 a and b showing the distribution of KS and ranula by age and gender shows that more females than males in the 0–10 year age group were affected by ranula. In KS more males than females in the 21–30 year age group were affected.

Table 1 shows that of the 38 cases of ranula studied consecutively and offered HIV serotesting only 26 (68.4%) agreed to undergo the test of which 23 (88.5%) tested HIV positive with 3 (11.5%) testing negative using the ELISA method. Among the HIV positive patients 95% were in the 0–10 year age group.

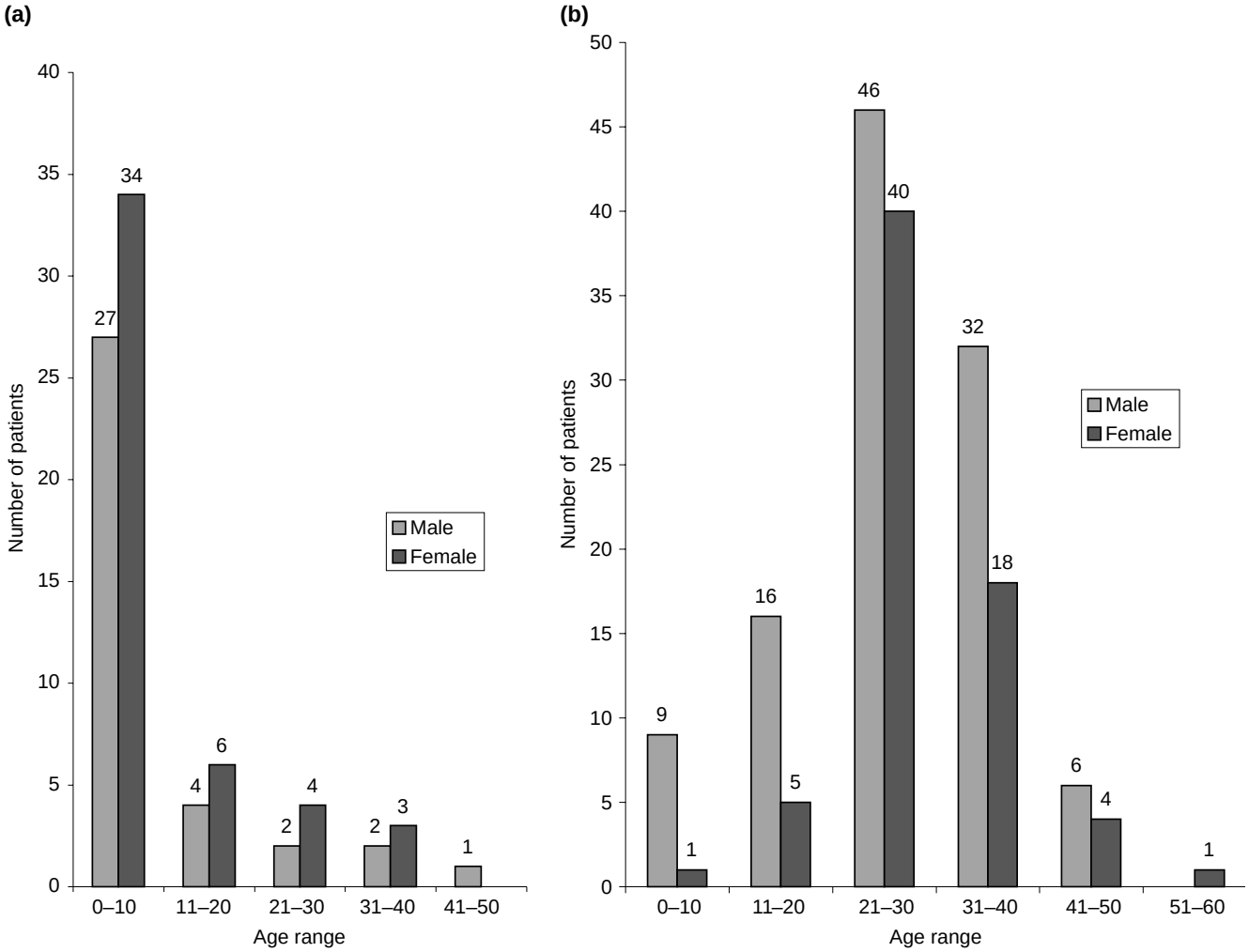

Figure 3 (a) Distribution of ranula by gender. (b) Distribution of Kaposi's sarcoma by age and gender

Table 1 HIV serology results for 38 patients

Year	*Total Number of cases*	*Number of cases consenting to HIV test*	*Number of cases HIV positive (%)*	*Number of cases HIV negative*
1999	7	7	6 (85.7)	1
2000	5	3	3 (100)	0
2001	6	3	3 (100)	0
2002	8	6	4 (66.7)	2
2003	12	7	7 (100)	0
Total	38	26	23 (88.5)	3

Discussion

KS is one of the established HIV/AIDS associated oral lesions worldwide and as such its prevalence/incidence is reflective of the HIV/AIDS load in that particular setting. In Zimbabwe the age-specific incidence rates of KS in 1990–1992 and 1993–1995 show peaks in the 20–40 year age group for both males and females in the number of cases over the years since 1981 (Chokunonga *et al*, 1999). This same picture is shown by the prevalence of KS at our Oral and Maxillofacial Surgical clinics (Figure 1). A similar prevalence peak during the same time period was also shown by ranula suggestive of some association with an event occurring during this period. This could be HIV/AIDS related as in KS. The increase in the prevalence of KS mirrors the prevalence of HIV/AIDS in the community. The cases of ranula have been on the increase from 1981 to 2003 (Figure 1). This mirrors the increase in oral KS, an HIV/AIDS associated oral lesion. KS prevalence in our clinics increased during the years 1992 to 2003. A similar increase in prevalence of KS in Zimbabwe reflective of the HIV/AIDS burden in the country was also noted

during this period (Chokunonga *et al*, 1999). The common factor here is HIV/AIDS disease.

There is a striking difference in the age distribution of KS and ranula (Figure 2): 73.5% of the ranula cases were between the ages of 0 and 10 years with only 5.6% cases of KS in this age group. KS had 76.4% of the cases in the 20–40 year age group with only 13.3% cases of ranula. The noted age distribution of KS is reflective of the age group most commonly succumbing to HIV/AIDS in Zimbabwe (UNAIDS/WHO Epidemiological Fact Sheet, 2002). The very young age group associated with ranula may be explained by the fact that HIV-SGD is common among children but uncommon among adults (Schiodt, 1992b). This is also the age group succumbing to HIV/AIDS disease mainly due to parent to child transmission in Zimbabwe.

The HIV-SGD usually includes xerostomia and or swelling of the major salivary glands, lymphoepithelial lesions, cysts and intraglandular lymph nodes along with diffuse interstitial lymphocytosis. A study on HIV positive Africans from Cameroon showed severe HIV-SGD compared with HIV positive American patients (McArthur *et al*, 2003). Marked fibrosis was also noted in African minor salivary glands. This fibrosis noted in African minor salivary glands could also be present in the Zimbabwean population and may result in blockage of the sublingual gland ducts and hence the ranula. Diffuse infiltrative lymphocytosis syndrome was also noted to be high in West Africans (McArthur *et al*, 2000). The same study showed that severe salivary gland duct atypia (96%) was the feature most strongly associated with HIV/AIDS. Could these be the possible changes that would result in ductal blockage and hence the ranula?

The fact that 88.5% ($n = 23$ of 26) of the ranula patients were HIV seropositive indicates strong association of sublingual ranula with HIV/AIDS. However, there is the possibility of self-selection bias for testing favouring those who were HIV –positive. This becomes more compelling in children whose parents had died of AIDS as testing would then confirm their HIV status. Whatever the reason is for consenting or declining HIV testing, 88.5% positive test in patients with ranula lends strong support to the association between ranula and HIV/AIDS. Among the HIV-positive patients 95% were in the 0–10 year age group suggestive of perinatal transmission. This high figure tallies with findings in pregnant women in Harare where a prevalence rate of 30.4% for HIV-1 was noted (Mbizvo *et al*, 1996). The HIV-seroprevalence of our clinic referral base can be approximated to be around 33.7% as per UNAIDS/WHO Epidemiological Fact Sheet (2002) on HIV/AIDS and Sexually Transmitted Infections, Zimbabwe 2002 update.

From the above evidence ranula should be considered another HIV/AIDS associated oral lesion in Zimbabwe.

Recommendations for further study of ranula in Zimbabwe should include case–control studies on ranula, CD4 and CD8 lymphocyte counts, evaluation of HIV viral load, immunoglobulin profiles of the fluid contents, collagen I content, infiltrative lymphocytosis, the ductal nature of the sublingual gland, longevity of ranula patients compared with KS patients post-KS diagnosis and the effect of antiretroviral therapy.

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