PATHOLOGICAL CHANGES ASSOCIATED WITH HIV/AIDS IN PAROTID GLANDS

BY

HERBERT ISAAC NGUVUMALI, DDS

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF DENTISTRY IN ORAL PATHOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

2008

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the University of Muhimbili Health and Allied Science a dissertation entitled: *Pathological changes associated with HIV/AIDS in parotid glands.* in partial fulfillment of the requirements of the Degree of Master of Dentistry (Oral Pathology).

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(SECOND SUPERVISOR)

Date: 25th November 2008

DECLARATION AND COPYRIGHT

I, Herbert Isaac Nguvumali, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature..... Date: 25th November, 2008

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May God bless you all.

DEDICATION

This work is dedicated to my parents Isaac and Lydia whose guidance and prayers enabled me to pursue Medicine.

ABSTRACT

Background

Opportunistic infections and other conditions in salivary glands are now known to be associated with human immunodeficiency virus (HIV) infection. However, a very scant information is available concerning the type and the magnitude of salivary gland pathological conditions that are associated with HIV infection and Acquired Immune Deficiency Syndrome (AIDS).

Objectives

The aim of this study was to determine the type and frequency of pathological changes that occur in parotid glands of HIV infected individuals and compare the findings with a cohort of HIV seronegative cases as seen at Muhimbili National Hospital.

Study design

This was a prospective cross sectional study.

Inclusion criteria

All clinical autopsies done in Morbid Anatomy Unit at Muhimbili National Hospital who had informed consent from relatives and or doctors. Also all medicolegal cases authorized by police.

Exclusive criteria

All decomposed bodies and bodies staying for more than 24 hours from time of death. Also bodies without consent.

Material and Methods

The study included 142 autopsy cases from Muhimbili National Hospital (MNH) mortuary that were seen between January and December 2006. Tissue specimens from

parotid glands for histological analysis and blood samples for HIV sero-status were collected from each autopsy body. Enzyme Linked Immunosorbent Assay (ELISA) was used to determine HIV sero-status whereas routine haematoxylin and eosin (H&E) as well as special stains such as Ziehl Neelsen (ZN) and Grocott's were employed to determine the histological diagnosis of various diseases of parotid glands in HIV infected and HIV negative study participants.

Results

Between January and December 2006, a total of 1431 medicolegal autopsy cases were carried out in the Morbid Anatomy Unit of Muhimbili National Hospital of which 142 cases were included in the study. These cases died from head injuries, haemorrhagic shock and poisoning and medical causes. Among the 142 autopsy cases, 23.2% (n = 33) were confirmed to be HIV seropositive, whereas 76.8% (n = 109) were HIV seronegative. Out of the 33 cases with HIV infection, 63.6% (n=21) were histologically diagnosed to have various disease conditions affecting the parotid gland. In contrast, only 12.8% (n = 14) of HIV negative group had parotid gland pathological conditions. The frequency of parotid gland disease conditions between HIV positive and HIV negative groups was statistically significant (p value=0.002).

In respect to type of disease conditions found in this study, non specific chronic sialadenitis (NSCS) was the commonest pathological condition that affected both groups. However, NSCS was significantly frequent in HIV group affecting 36.4% in contrast to only 12.1% in HIV negative group (p value = 0.042). NSCS was classified mild when it destroyed 5% of the parenchyma. Moderate NSCS covered less than 10% while severe

non NSCS covered more than 10% of the glandular parenchyma. On the other hand, the study revealed that there was no difference in disease severity between the two groups. In the HIV – seropositive group 30.8% had mild NSCS versus 34.6% in the HIV – seronegative group. Also 3.8% in the HIV - seropositive group the severity of NSCS was moderate in comparison to 7.7% found in the HIV – seronegative group. In severe NSCS both groups had 11.5%.

Other infectious conditions that are rarely described in parotid salivary gland were distinctly encountered in HIV infected patients. Such conditions included tuberculosis (12%, n = 4), cryptococcosis (9.1%, n=3) and histoplasmosis (1 case). On the other hand only one case of lymphoepithelial cyst was encountered. Neither KS nor NHL was seen in this study.

Conclusion

Inspite of relatively limited sample size, this study has illustrated that more pathological alterations are found in parotid salivary gland of HIV-patients than in individuals with HIV-negative serostatus. About two thirds (63.6%) of HIV-positive patients were found to have various pathological alterations in parotid glands as opposed to only 12.1% found in HIV- negative study group resulting into ratio of 4.97:1 respectively. NSCS was the commonest disease condition encountered in both groups but was three times frequent (36.4%) in HIV-positive group than in HIV-negative group (12.1%), making a ratio of 3:1, respectively. Additionally, the study has also revealed that even the very rare diseases that are of opportunistic nature are not infrequently encountered in parotids of HIV-positive patients. These include tuberculosis, cryptococcosis and histoplasmosis.

These findings form a baseline data in planning preventive and therapeutic measures for HIV- patients with salivary gland ailments.

Recommendation

Since about two thirds (63.6%) of HIV- seropositive patients are likely to have various pathological alterations in parotid glands in this study, it is recommended that conversely, in view of the fact that patients with HIV infection are at high risk of developing parotid disease, they should also be examined to exclude parotid gland disorders. However, larger sample size of the similar study is needed to precisely ascertain the phenomenon.

LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
AKS	AIDS related Kaposi's Sarcoma
DDS	Doctor of Dental Surgery
DPX	Dextrene Polystyrene Xylene
ELISA	Enzyme linked Immunosorbent Assay
H&E	Haematoxylin and Eosin
HIV	Human Immunodeficiency Virus
KS	Kaposi's Sarcoma
M.DENT	Master of Dentistry
M.MED	Master of Medicine
M.D	Doctor of Medicine
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
NHL	Non Hodgkin's Lymphoma
NSCS	Non specific chronic sialadenitis
OR	Odd's Ratio
PAS	Periodic Acid Schiff
PhD	Doctor of Philosophy
UNAIDS	United Nations Programme on HIV/AIDS
WHO	World Health Organization

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INTRODUCTION AND REVIEW OF LITERATURE

Human Immunodeficiency Virus (HIV) infected patients face many challenges, including head and neck pathological alterations. While most of these pathological disorders are not different in type from those encountered by individuals who are HIV seronegative, there are obvious differences in frequency and severity between the two groups. The lack of a competent immune system in HIV infected patients can have an impact on the course and progression of head and neck diseases and may require more aggressive approach in the management in order to avoid complications which can result into serious health consequences.

Infection with HIV presents with myriads of symptoms in the head and neck region. Salivary glands are among the head and neck affected tissues and may present with various pathological changes such as inflammation, various infections, cystic lesions and neoplastic conditions (Ihrler et al, 1996). Sooy et al, in 1987 discovered that 41% of HIV infected individuals presented for the first time with parotid related symptoms. However, few years later (1996) Ihrler et al. reported that 51% of HIV patients were found to have salivary gland lesions. Three years later Vargas et al. in different studies reported the same 51% prevalence of parotid gland lesions in HIV infected individuals. Over the years, a number of studies have reported various pathological entities that can affect the parotid gland of HIV patients. Increase in HIV/AIDS disease, results in increased frequency of opportunistic diseases, which seem to affect salivary glands.

In 1999 Mandel and Hong discovered that in the initial phase of the disease, inflammatory conditions predominate, usually associated with body reaction to HIV infection itself. During this phase there is proliferation of lymphoid tissue with gradually

parenchymal atrophy, followed by lymphoepithelial hyperplasia of ducts and the formation of large lymphoepithelial cyst, which are the predominant lesions affecting 3-6% of HIV infected patients. These cystic lesions usually cause parotid enlargement and sometimes this can be the first manifestation of HIV infection (Ihrler et al, 1996; Vargas et al, 2001). Vargas et al, 2003 found that 29% of HIV seropositive patients had nonspecific chronic sialadenitis, 10% had mycobacterium tuberculosis, 6% had lymphoepithelial cyst, 2% were diagnosed with histoplasmosis, 3% with cryptococcosis and 1% of the cases were diagnosed with non Hodgkin's lymphoma. The later was encountered during the late stage of disease progression.

Nevertheless, the few available African studies (Bem et al, 1992) have shown that HIV associated oral lesions are also very common in sub-Saharan Africa. These studies have also pointed out that the occurrence of diseases in the oral region is potentially influenced by HIV disease stage, ethnicity, social economic status, diet, genetics as well as the access to health care facilities as seen in findings in other parts of the world. Such African studies include those from Zambia whereby Bem et al, 1992 studied the pathology of parotid glands in 261 HIV-seropositive patients. He reported that 0.8%, (n = 2) had Kaposi's sarcoma, 0.8% (n = 2) had mycobacterium tuberculosis and multiple cystic parotid lesions constituted 1.5%. (n = 4).

LYMPHOEPITHELIAL CYST (LEC)

This is a progressive autoimmune chronic inflammatory process primarily of parotid gland in which dense infiltrates of lymphocytes replace the acini and the residual ductal elements are stimulated to undergo hyperplasia forming irregularly shaped islands of squamous epithelium. From the beginning of HIV era lymphoepithelial cyst has been

reported to be associated with HIV infection in parotid glands. It was reported that 6% of HIV infected adults examined by Schiodt et al, in 1998, specifically experienced parotid gland enlargement due to cystic lymphoepithelial lesions compared to 0.5% before the HIV era. Parotid enlargement due to lymphoepithelial cysts have frequently been found in paediatric AIDS patients.

In 2001, Vargas and co-workers reported 30% prevalence of lymphoepithelial cyst in paediatric cases with AIDS. The lymphoepithelial cysts in parotid glands are usually bilateral in HIV patients compared to occasional reports of unilateral swellings in HIV seronegative patients. Pathological changes in HIV-infected patients are more severe and in HIV-seronegative patients are mild (Vargas et al, 2001).

Lesions are usually multicystic with size ranging from 0.5 to 5 cm in diameter and usually the superficial lobe is affected (Ihrler et al, 1996). Salivary glands react to injury or obstruction by undergoing atrophic degeneration and necrosis. Thereafter, replacement of the parenchyma by inflammatory cells occurs and ultimately fibrous scarring. Bacterial or viral infections of the gland or other immunological reactions to autoantigens may result into degeneration, necrosis and fibrosis as well. However, the pathogenesis of the lymphoproliferative changes in the parotid gland remains unclear.

NON SPECIFIC CHRONIC SIALADENITIS (NSCS)

Non specific chronic sialadenitis (NSCS) in parotid glands has been reported to increase in prevalence in HIV patients. NSCS is a chronic inflammatory condition characterized by chronic inflammatory cell infiltrates mainly lymphocyte aggregation which varies from mild, moderate to intense. Mandel and Hong, in 1999 graded it mild when it involved 5% of the gland parenchyma, moderate when it covered 5 - 10% and intense

when it affected more than 10%. Vargas et al, in 2003 found that non specific chronic sialadenitis was the most common alteration in parotid gland of HIV infected patients. Mandel and Hong in 1999 revealed that NSCS is associated with the reaction of the body to HIV infection itself. This immunological reaction to autoantigens may result into degeneration, necrosis and tissue fibrosis resulting into xerostomia due to glandular tissue destruction.

MYCOBACTERIUM TUBERCULOSIS

This is primarily a chronic granulomatous infection of the lungs caused by *Mycobacterium tuberculosis*. Mycobacterium tuberculosis is the leading infectious disease in HIV-1 infected people with more than two million new cases annually worldwide (UNAIDS/WHO, 2000). Mycobacterium tuberculosis is also the main cause of death in HIV infected patients. Before the HIV era, mycobacterium tuberculosis in parotid glands was extremely rare but there have been several reports on increased prevalence of this disease. Vargas and co-workers in 2003 reported tuberculosis prevalence of 10% in HIV/AIDS parotid glands. The morphological pattern of tuberculosis observed by Vargas and co-workers in parotid glands of HIV/AIDS patients was characterized by numerous macrophages full of mycobacteria and poorly organized granulomas which indicate low cellular immune response of these HIV patients (Lewin Smith et al, 1998).

HISTOPLASMOSIS

Histoplasmosis is a chronic lung infection commonly found in the Mississippi valley due to inhalation of spores of *Histoplasma capsulatum*. It may have associated intraoral lesions consisting of a chronic ulcer resembling malignancy. However in few cases, the

disease may disseminate to other organs and tissues including the parotid glands (Ihrler et al, 1996).

Most cases of lung histoplasmosis are asymptomatic and only 1% of the infected individuals develop a detectable pneumonia. Both HIV-seropositive and HIV-seronegative patients with lung histoplasmosis normally develop fever, malaise, cough and dyspnoea mimicking pulmonary tuberculosis. Infection by histoplasmosis in lung tissue develops into granulomas and cavitation which in HIV/AIDS patients this is often followed by wide dissemination of the disease to the regional lymphnodes and adjacent anatomical structures including parotid glands.

In chronic phase, dissemination to the skin and oral mucous membranes may be the first signs of the infection. Oral lesions of histoplasmosis occur primarily on the gingiva, tongue, palate and buccal mucosa. These intraoral lesions start with granuloma then turn to be chronic ulcers with raised, rolled borders and induration of the surrounding tissue. Clinical appearance of histoplasma oral ulcer resembles carcinoma or tuberculous ulcer. Progression of gingival lesions may cause loss of the alveolar bone and loosening of teeth. In such cases cervical lymphadenopathy is common and brain involvement may occur. In the study done by Vargas et al in 2003, they reported a prevalence of 2% of parotid gland histoplasmosis in HIV patients, which was extremely rare before HIV era.

Histologically, histoplasmosis is characterized by formation of multiple small granulomas composed of histiocytes which contain histoplasma organisms. In HIV patient, the fungus grows abundantly in macrophages. In HIV-negative patient, histoplasma stimulates an epithelioid cell granulomatous reaction which resembles non caseous tuberculosis. Calcification is a characteristic of old necrotic lesion. Histoplasma has a rigid cell wall

about 3 microns in diameter whereby during fixation, the protoplasm retracts from the rigid wall, leaving a clear space that gives appearance of unstained capsule.

CRYPTOCOCCOSIS

Cryptococcosis is a chronic fungal infection commonly occurring as an opportunistic infection in immunocompromised patients due to HIV infection. Cryptococcosis is caused by *Cryptococcus neoformans*, a round to oval yeast about 5 to 10 microns in diameter that reproduces by budding. Birds especially pigeons excrete cryptococcal spores without themselves suffering from the disease. Inhalation of the spores is the usual mode of infection and therefore the lung is the primary site of localization. From their primary site cryptococci may disseminate widely by the blood stream to the skin, liver, spleen, adrenals, parotid glands or other tissues in severely immunosuppressed patients. Clinically, some patients present with oral ulcers that penetrate into bone or palate. Vargas et al (2003) reported 3% prevalence of cryptococcosis in parotid glands among the HIV/AIDS autopsied cases, all found in parenchyma. In two out of the three, the fungus was seen involving the intraparotid lymphnodes.

Histologically the tissue response to cryptococcus is extremely variable depending on the level of immunity in immunusuppressed patients and they may evoke no inflammatory reaction whereas in normal reactors the fungi induce a chronic granulomatous reaction. Histologically the later normally shows the presence of macrophages, lymphocytes and foreign body giant cells. Neutrophils and suppuration may also occasionally be seen. Cryptococcus has a distinctive heavy prominent gelatinous capsule that creates an apparent clear halo in tissue sections or exudates. Macrophages and multinucleated giant cells containing fungal organisms are seen in clusters or singly

NEOPLASTIC CONDITIONS

The increased prevalence of neoplastic lesions in parotid gland of HIV patients has been reported. Among the HIV/AIDS reported cases are Kaposi's sarcoma (KS) and Non - Hodgkin's lymphoma (NHL). Parotid gland involvement by neoplastic lesions occurs generally at the advanced stage of HIV/AIDS.

KAPOSI'S SARCOMA

Kaposi's sarcoma (KS) is an angio-proliferative lesion affecting skin, mucosa, lymph nodes and viscera. This neoplastic lesion was first described by Moritz Kaposi (1872) as a slowly progressive, idiopathic, multiple pigmented skin lesions, presenting with purplish nodular lesion predominantly involving the extremities of elderly Mediterranean men.

Subsequently, a number of studies have been carried out and more information has been documented in regard to KS. Presently, four forms of KS which are histologically similar but clinico-epidemiologically different have been described. These are classical/sporadic form, endemic African form, iatrogenic transplant associated form seen in immunosuppressed organ recipient and epidemic or AIDS related form. AIDS related Kaposi's sarcoma (AKS) is the most aggressive and the commonest malignant tumour in AIDS patients (Ablashi et al., 2002; Safai et al., 1992). Histologically, Kaposi's sarcoma develops through early stages of patch, plaque to late stage of tumorous lesion (Oettle, 1962). Abundant spindle shaped cells, vascular slits and inflammatory cells characterize the lesion in the late stage.

The sex ratio of Kaposi's sarcoma in East Africa has dropped due to HIV infection from male/female ratio of 19:1 to 1.7:1 (Thomas, 2001). Chances for developing Kaposi's

sarcoma in HIV patients is 100 to 300 times than in HIV negatives (Frisch et al, 2001). In Mosha's study (2005) the prevalence of HIV infection in OKS was 97.4%, which showed a significant causal association. In Mosha's study the mean age of patients with OKS was 30.1 years with a range of 5-58 years and male to female ratio of OKS was 0.28:1.

As a rule it is extremely rare to find KS in parotid glands. However, during HIV era, Kaposi's sarcoma has also been reported in salivary glands (Vargas et al., 2003). Parotid gland Kaposi's sarcoma was described primarily in homosexual men along with epidemic Kaposi's sarcoma (Shiboski et al, 1996, Goedert et al, 1996). Parotid gland involvement is usually found in conjunction with KS in other sites (Castle et al., 2000). The study by Castle and co-workers had six patients who presented clinically with a mass in the submandibular (n = 4) and parotid (n = 2) glands. Five patients were HIV-seropositive (3 homosexual males, one infected by a contaminated blood transfusion, and one with an unknown risk factor).

Histologically, the tumours exhibited the usual features of KS, which is a spindle cell vascular proliferation arranged in fasculated bundles and extravasated erythrocytes. In African setup where heterosexuality is the predominant mode of HIV transmission, there is a need of establishing whether KS is among disorders that can occur in HIV salivary glands.

NON HODGKIN'S LYMPHOMA (NHL)

Non-Hodgkin's Lymphoma (NHL) is a group of malignant lymphoproliferative neoplasms classified as low, intermediate and high grades. NHL has been increasing with increase in HIV infection in the USA (Chassagne-Clement et al; 1999). Two percent of all NHL are found in the head and neck region (Freeman et al; 1972). It has been

established that 70-90% of NHL found in HIV infected patients have a high grade type with exclusively B-cell immunoblastic variant of Burkitt's like lymphoma (Hansen et al; 2000; Franceschi et al, 1999; Said, 1997).

Kaaya and co-workers, 2006, reported on low frequency of malignant lymphoma in Tanzania and Africa in general despite the ongoing HIV/AIDS epidemic. They also reported on overall increasing tendency for malignant lymphoma in Tanzania from 1991-1994 whereby there was a clear increase in year 1993. There are few reports on parotid NHL in HIV infected individuals. Vargas et al, (2003) reported only one case with NHL of parotid gland out of 100 study subjects with HIV/AIDS.

Dunn and co-workers reported on 23 patients with primary salivary gland lymphoma who were diagnosed between 1990 and 2001. The sites of involvement were the parotid gland in 13, the submandibular gland in 9 and the minor salivary gland in one case. Further studies are needed to find out the prevalence of NHL in parotid glands of HIV cases and establish the causal association with HIV infection in Tanzania which is in sub-Saharan Africa where there are majority of HIV patients. Also such studies will enable proper planning and management of patients with NHL.

RATIONALE OF THE STUDY

Globally there are about 40 million people living with HIV infection and over 60% of world's cases are found in sub-Saharan Africa (UNAIDS/WHO, December 2004). Tanzania which is within Sub-Saharan Africa a region mostly affected by HIV/AIDS pandemic had about 1.8 million people living with HIV in the year 2003 (NACP report number 18, 2004). Almost all HIV infected persons are at risk of developing various illness and later succumb to death as a result of opportunistic infections and/or neoplastic

established that 70-90% of NHL found in HIV infected patients have a high grade type with exclusively B-cell immunoblastic variant of Burkitt's like lymphoma (Hansen et al; 2000; Franceschi et al, 1999; Said, 1997).

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lesions in the parotid glands.

For the control and management of infections and neoplastic lesions affecting the parotid gland associated with HIV/AIDS, data on type and the magnitude of this problem should be known. Globally, especially in the sub-Sahara Africa, the association between parotid gland lesions and HIV infection has been scantly reported and the association has not been clearly established, which justify further studies. Matee et al. (2000) in their study involving Tanzanian patients reported an association of HIV infection and parotid gland enlargement where they reported 20% of AIDS patients who had parotid enlargement compared to 11.9% of HIV-seropositive and 5.1% of HIV-seronegatives. However, the study did not identify the types of diseases that caused parotid enlargement. This study will therefore provide baseline data on the types and frequency of pathological changes that occur in parotid glands of HIV infected cases.

OBJECTIVES

Broad Objective

To determine the type and frequency of pathological changes that occur in parotid glands of HIV infected cases.

Specific Objectives

1. To determine the HIV serostatus of medicolegal and clinical autopsy cases at Muhimbili National Hospital (MNH) from January to December, 2006.
2. To determine the frequency of pathological lesions that occur in parotid glands of HIV infected autopsies and compare with frequency of pathological lesion in HIV negative autopsies.
3. To identify the types of pathological lesions that affect parotid glands of HIV -

infected cases in comparison to those seen in parotid gland of HIV negative cases.

HYPOTHESIS

There is a high frequency and various types of parotid gland pathological lesions in HIV infected patients than in HIV seronegative cases.

MATERIALS AND METHODS

Study area

The study samples were collected at Muhimbili National Hospital Mortuary which receives bodies from Dar es Salaam and Coast regions which have a population of 3.5 million people (Population Housing census, 2000). The hospital is also a teaching facility for Muhimbili University of Health and Allied Sciences (MUHAS). Tissue specimens were processed and analysed in the Department of Pathology, MUHAS in collaboration with the Microbiology and Immunology Unit of MNH. The Pathology Department at MUHAS has a capacity of processing routine surgical pathology and cytological specimens for microscopical examination. Special stains and immunohistochemistry procedures can also be performed on request.

Sampling

The study population included autopsy cases that were received between January and December, 2006. This was a prospective cross sectional study whereby tissue specimens and blood samples were taken from parotid glands of fresh human bodies that had died within twenty four hours.

Inclusion Criteria

Inclusion criteria for this study was as follows:-

(i) All clinical autopsies done in Morbid Anatomy unit at Muhimbili National

Hospital who had informed consent from relatives and/or doctors.

(ii) All medicolegal cases authorized by police.

Exclusion Criteria

Bodies with the following characteristics were not considered as study samples.

(i) All decomposed bodies and bodies staying for more than 24 hours from time of death

(ii) Bodies without informed consent.

Clinical examination

Thorough clinical observation of each body was done. It involved external examination of clinical features suggestive of immunosuppression. Such features included cachexia, dehydration, hair thinning, vascularitis, pigmentation of skin and lymphadenopathy. Parotid glands of both sides were examined externally to see whether they were enlarged. Palpation was also done to rule out any anatomical alterations of parotid glands.

Collection of study specimens

Blood for HIV screening

About 2mls of blood was collected from each body using vacutainer or disposable syringes in aseptic way and was placed in a sterile bottle. All blood samples were submitted to Microbiology and Immunology unit of MNH for HIV testing. An alternative confirmatory strategy technique for detecting HIV antibodies using enzyme- linked immunosorbent assays (ELISA) was applied (Urassa et al; 1992). All blood samples were secreened using Enzygnost ant-HIV-1 and 2 Plus ELISA (Behring, Marburg, Germany). All reactive sera were then tested using Wellcozyme HIV-1 recombinant ELISA (Murex, Dartford, UK). Specimens which were reactive in both assays were considered as HIV-1 seropositive, and those which were non reactive in the first assay were considered as

HIV-1 sero-negative. Western Blot analysis was done for only those with discordant results (Nkengason et al, 1998; Urassa et al; 1992; Urassa et al; 2002).

Tissues for histological studies

A 2 cm superior-inferior incision was made at the mandibular angle at both right and left sides to expose the superficial lobe of the parotid gland. The tissue specimen measuring 2x2x1 cm was excised from each lobe and fixed in 10% buffered formalin solution for 24 hours. The volume ratio of tissue to fixative was 1: 10. Specimens were then submitted to the histopathology laboratory for processing, staining and microscopical examination.

Preparation of Histological Sections

Tissues were routinely processed and embedded in paraffin using low melting point (55°C). Six sections of five microns thick each were cut using a microtome machine from paraffin embedded tissue and mounted on glass slides. Sections were then placed on the slides, put on hot plate to reduce the amount of wax and then cleared in xylene and hydrated in descending order of absolute alcohol, 95%, 80% and 70% alcohol to water. Sections were then stained by Haematoxylin and Eosin (H& E). Also Ziehl Neelsen and Grocott methanamine silver special stains were used to stain the tissue sections. Dehydration followed in ascending order and mounting was done by Dextrene Polystyrene Xylene (DPX).

Haematoxylin and eosin (H&E) staining

This was performed on paraffin-embedded tissues for microscopical examination. Five µm thick sections were sectioned from formalin fixed and paraffin embedded tissue specimens and mounted on a glass slide. Sections were de-waxed by placing the slides on the hot plate to reduce wax and then cleared in xylene. Thereafter rehydration was done

by treating the tissues with absolute alcohol, followed by 95% alcohol and then 70% alcohol to water. Then sections were stained by H&E. Sections were then washed with running tape water followed by dehydration in ascending order of alcohol and clearead in xylene and mounting using Dextrene Polystyrene Xylene (DPX).

Ziehl Neelsen's (ZN) stain

This stain was perfomed for the purpose of identifying acid fast bacilli. The formalin fixed, paraffin embedded five micron thick sections were deparaffinized in xylen and hydrated to water. The deparraffinized and dehydrated tissue sections were then flooded with ZN solution as recommended by Culling (1974). Ziehl Neelsen working solution preparation was done by dissolving 1 gm of basic fuchsin in 10 mls of ethyl alcohol. This was combined with 100 mls of 5% phenol. The slides were then heated on the back of the specimen by a bunsen burner flame until stain steam raised and were left for 15 minutes to cool. Thereafter the slides were washed in running tape water to remove excess stain. Differentiating tissues from excess staining material was done using 3% hydrochloric acid in 70% alcohol until tissues were pale pink in colour. Tissue sections were then washed in running tape water for 10 minutes and counterstained using 0.1% methylene blue for 15 seconds. Sections were then washed with running tape water followed by dehydration in ascending order of alcohol and cleared in xylene and mounted using DPX. Acid fast bacilli were seen as red rods, while cell nuclei stained blue, red blood corpuscles stained pink whereas other tissue constituents stained pale blue.

Positive control specimens that contained mycobacterium tuberculosis were processed together with the study specimens. Lymphnode tissue confirmed to be ZN positive was used as positive control specimen. A normal lung tissue which was ZN negative was used

as a negative control.

REPORTING

All histological specimens were examined and reported by the author and counterchecked by a qualified Pathologist.

GROCOTT'S STAIN

Grocott's stain (modified methenamine silver) was employed to identify *Cryptococcus neoformans* and *Histoplasma capsulatum* fungi according to method by Grookham et al. (1991). A five microme thick sections from formalin fixed and paraffin embedded tissue specimens were subjected to Grocott's stain. Sections were deparaffinized in xylene and hydrated to distilled water and then treated with 2% chromic acid before being microwaved at 60°C for 45 seconds and allowed to cool for 5 minutes. Later sections were washed in tape water, rinsed in distilled water and placed in 1% sodium metabisulfite for 1 minute at room temperature. Sections were then washed in tape water, rinsed in distilled water in three changes before subjecting them in methenamine silver solution. Section microwaving was done at 60°C for 70 seconds until tissue changed to brown paper bag. Slides were then agitated in the hot methenamine silver solution, rinsed in distilled water in two changes and placed in 0.5% gold chloride for 1 minute until they changed grey. Sections were then washed in distilled water, treated in 5% hydrochloride acid for 3 minutes followed by washing them in tape water and distilled water respectively. Sections were later dehydrated in ascending order of alcohol, cleared in xylene, mounted using DPX then cover slip was applied.

Cryptococcus neoformans which stain black with Grocott's stain appeared round surrounded with large clear halo. *Histoplasma capsulatum* appeared black round

intracellular structures in phagocytic cells. Positive control specimens that contained the fungal organisms under study were processed together with the study specimens. A lymph node with fungi was used as a positive control whereby the negative controls was achieved by using the lung tissue which had no fungal organisms.

STATISTICAL METHODS

DATA MANAGEMENT

Data analysis was done using SPSS computer software. The Chi-square test was used to determine associations between dependent and independent variables, with statistical significance set at $p < 0.05$.

ETHICAL ISSUES

Permission to conduct the study on bodies dying from various causes was sought from the government. The MUHAS Research and Publication Clearance Committee approved the study. All autopsy case's information in this study was confidential and their identities were not revealed. Autopsy case's information were obtained from the clinical files and police forms that ordered autopsy to be conducted (Police form 99).

RESULTS

1.0 DEMOGRAPHIC DATA

Between January and December, 2006 a total of 1431 medicolegal autopsies were carried out in the Morbid Anatomy Unit of Muhimbili National Hospital. During this period, 142 autopsies met inclusion criteria. Out of the 142 autopsies there were 116 (81.7%) males and 26 (18.3%) females. The age distribution ranged from 3 to 85 years with mean age of 32.9 ± 13.9 years. Majority of the cases (70%) were between 20-39 years. The youngest study cases was 3 years old male child who died of

2.2 CAUSE OF DEATH

The distribution of autopsy cases by causes of death and HIV-serostatus is shown in Table 2. The highest cause of death in both HIV-seropositive and HIV-seronegative cases was head injury which accounted for 39.4% and 57.8% of all causes of death for seropositive and for seronegative cases respectively. Other causes of death in descending order were haemorrhagic shock (19.0%), respiratory insufficiency (14.8%), poisoning (6.3) and other medical causes (6.3%) for all cases. There were no statistically significant differences in cause of death by serostatus ($\chi^2 = 6.431$; $p = 0.169$)

Table 2 Distribution of autopsy cases by cause of death and HIV serostatus

	HVI-serostatus		
Cause of death	**HIV-seropositive**	**HIV-seronegative**	**TOTAL**
	n (%)	**n (%)**	**n (%)**
Head Injury	13 (39.4)	63 (57.8)	76 (53.5)
Respiratory Insufficiency	7 (21.2)	14 (12.8)	21 (14.8)
Haemorrhagic shock	10 (30.3)	17 (15.8)	27 (19.0)
Poisoning	2 (6.1)	7 (6.4)	9 (6.3)
Other Medical Causes	1 (3.0)	8 (7.3)	9 (6.3)
Total	**33(100.0)**	**109 (100.0)**	**142 (100)**

$\chi^2 = 6.431$; $p = 0.169$

3.0 HIV SEROSTATUS

Thirty three cases (23.2%) out of 142 autopsy cases tested positive with ELISA test for HIV, whereas, the remaining 109 (76.8%) were HIV-seronegative. All HIV-seropositive cases served as study group while the HIV- negative group of 109 cases provided a

control cohort of this study. In respect to causes of death of HIV-positive versus HIV-negative groups, no statistical difference was observed in the two groups (p-value = 0.564) (Table 1). Of the 33 cases that were HIV-seropositive, nine cases had HIV/AIDS related lesions in the parotid glands (Table 4).

3.1 Age and sex

In both HIV-seropositive and HIV-seronegative groups, there were substantially more males than females, respectively. The HIV-positive group comprised of 25 (75.8%) males and 8 (24.2%) females, whereas in the control HIV-negative cluster, there were 91 (83.5%) males and 18 (16.5%) females. Figure 1 illustrates HIV-serostatus according to sex. On the other hand, proportional-wise more women were infected 30.8% (8/26) than men 21.6% (25/116).

The peak age group for both HIV-positive and HIV-negative was 20-39 years. The range of HIV-positive group was from 3 to 80 years with mean age of 33.8 years (SD ± 15.4). Similarly, the ages of HIV-negative cases ranged from 16 to 85 years with mean age of 32.6 years (SD ± 13.6). Figure 2 shows distribution of age groups in respect to HIV status. Similar distribution in regard to sex (p-value = 0.24) and age (p-value = 0.216) was observed in the HIV-positive versus HIV-negative groups.

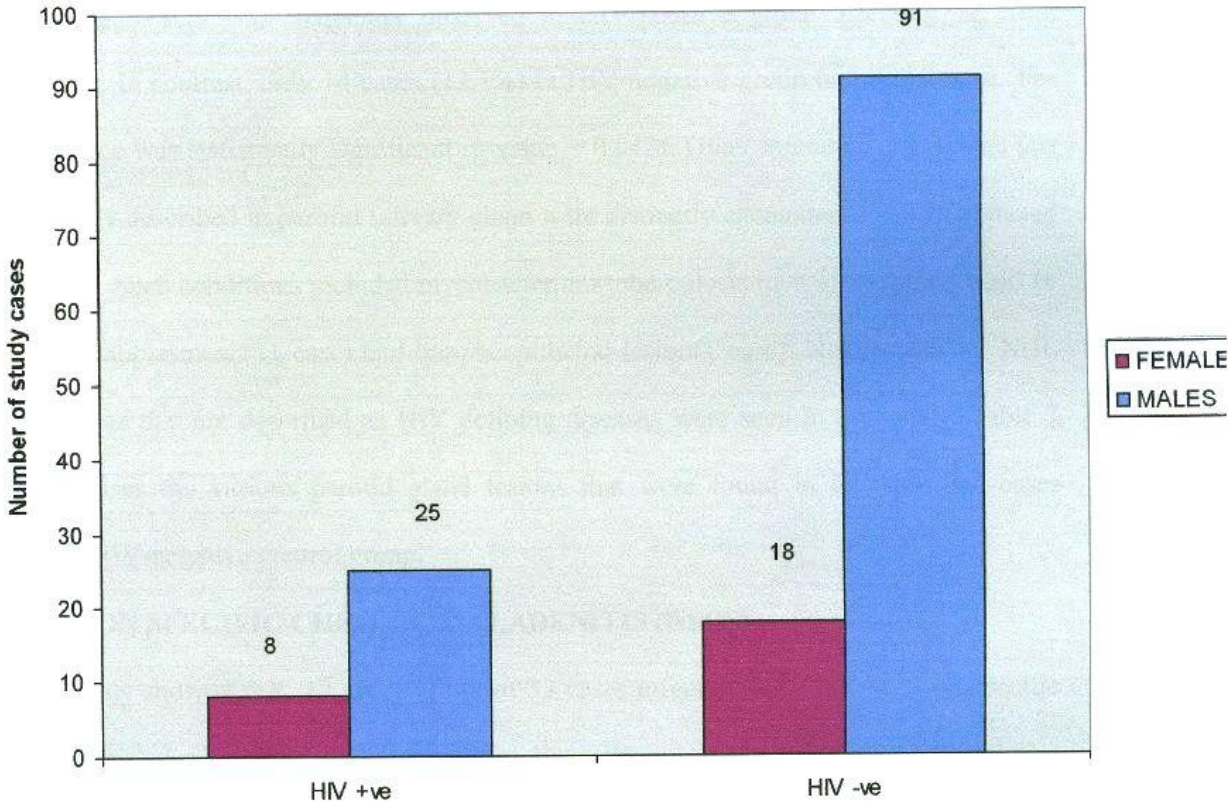
3.2 External examination

Thorough external examination of autopsy cases revealed that only seven (21.2%) out of the 33 cases with HIV infection had one or a combination of signs of immunosuppression. These signs included cachexia only (4 cases), both skin rashes and cachexia (2 cases) and one case with a combination of cachexia, skin rashes and oral thrush. The remaining 26 cases with HIV infection had normal external appearance with

good nutritional status as per gross examination. On the other hand, among the 109 control HIV-negative group, only 2 cases (0.9%) had features of poor nutritional status.

The frequency of immunosuppressive features in HIV-positive study group was significantly higher than in HIV-negative control group (p-value = 0.041). No enlargement of parotid gland was observed in any of HIV-positive nor in HIV-negative autopsy cases.

FIGURE 1: Distribution of autopsy cases by HIV-serostatus and sex



PAROTID GLAND LESIONS

Pathological conditions were encountered in parotid glands of HIV-positive than in HIV-negative group. Among the 33 cases with HIV infection, 21 cases (63.6%) were

histologically diagnosed to have various disease conditions affecting the parotid gland. In contrast, only 14 cases (12.8%) out of 109 of HIV-negative group had various pathological alterations in the parotid gland. The statistical difference in frequency of parotid gland disease conditions between HIV positive and HIV negative groups was highly significant (p-value = 0.002).

In respect to type of disease conditions found in this study, non specific chronic sialadenitis (NSCS) was the commonest pathological condition that affected both groups. However, NSCS was frequently observed in HIV-positive group affecting 12 cases (36.4%). In contrast, only 14 cases (12.1%) in HIV-negative group had the disease. The difference was statistically significant (p-value = 0.042). Other infectious conditions that are rarely described in parotid salivary gland were distinctly encountered in HIV infected patients. Such conditions included mycobacterium tuberculosis (n = 4), cryptococcosis (n = 3), histoplasmosis (1 case) and lymphoepithelial lesion(1 case). Neither KS nor NHL conditions that are described as HIV defining diseases were seen in this study. Table 2 summarises the various parotid gland lesions that were found in HIV-positive cases versus HIV-negative control group.

2.3.1 NON SPECIFIC CHRONIC SIALADENITIS (NSCS)

This study showed that, 12 (36.4%) out of 33 cases infected with HIV had non specific chronic sialadenitis (NSCS) whereas out of 109 HIV-seronegative cases only 14 (12.8%) cases were diagnosed with the condition. The prevalence of NSCS was significantly higher in HIV-positive study group than in HIV-negative control group (p-value = 0.042). In both the histologic features were similar.

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FIGURE 2 Distribution of autopsy cases by HIV-serostatus and age groups

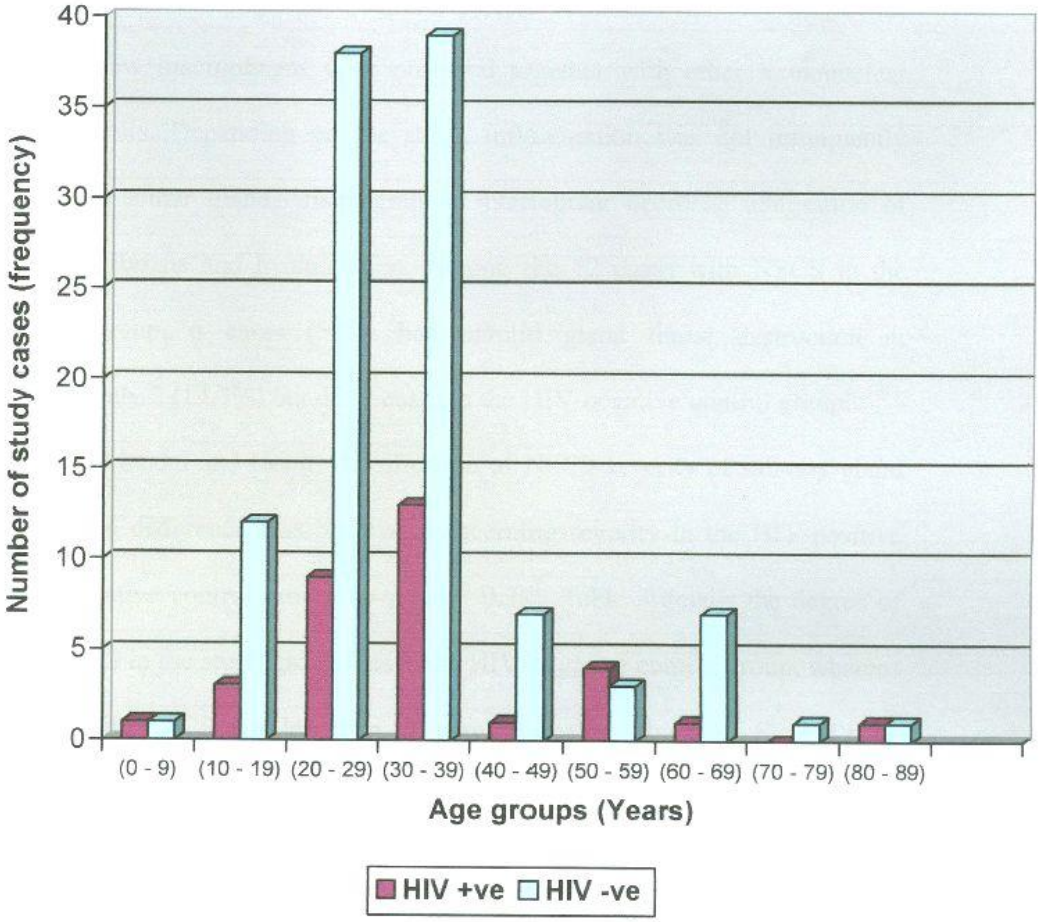


Table 3: Distribution of parotid gland lesions according to HIV-serostatus

Histological lesion	HIV-serostatus		
	HIV-seropositive n (%)	HIV–seronegative n (%)	Total n (%)
Non-specific chronic sialadenitis	12 (34.3)	14 (40.0)	26 (74.3)
Tuberculosis	4 (11.4)	0.0	4 (11.4)
Cryptococcosis	3 (8.6)	0.0	3 (8.6)
Histoplasmosis	1 (2.9)	0.0	1 (2.9)
Lymphoepithelial cyst	1 (2.9)	0.0	1 (2.9)
TOTAL	**21 (60.0)**	**14 (40.0)**	**35 (100.0)**

NSCS was histologically characterized by variable infiltration of mononuclear inflammatory cells namely lymphocytes and plasma cells. Occasionally where was infiltration of few macrophages were observed together with other mononuclear inflammatory cells. Depending on the stage, inflammation was not infrequently associated with acinar glands disintegration, interlobular necrosis, congestion of blood vessels, fibrosis and hyalinization. Among the 12 cases with NSCS in the HIV-positive group, 6 cases (50%) had parotid gland tissue destruction in comparison to only 2 (14.3%) out of 14 cases in the HIV-negative control group.

In reference to Mandel and Hong, classification of NSCS severity of salivary gland tissue (1999), no difference was observed concerning severity in the HIV-positive versus HIV-negative control groups (p-value = 0.28). Table 3 details the degree of severity of NSCS in the study group versus the HIV-negative control group, whereas Plate I shows mild NSCS with less than 5% parenchymal involvement. Plate II is an illustration of moderate NSCS covering less than 10% and Plate III demonstrates severe NSCS covering more than 10% of the glandular parenchyma.

Table 4: Severity of Non specific chronic sialadenitis in respect to HIV serostatus

	HIV serostatus		
Severity of sialadenitis	HIV-seropositive	HIV-seronegative	Total
Mild	8 (30.8)	9 (34.6)	17 (65.4)
Moderate	1 (3.8)	2 (7.7)	3 (11.5)
Severe	3 (11.5)	3 (11.5)	6 (23.1)
TOTAL	**12 (46.2)**	**14 (53.8)**	**26 (100)**

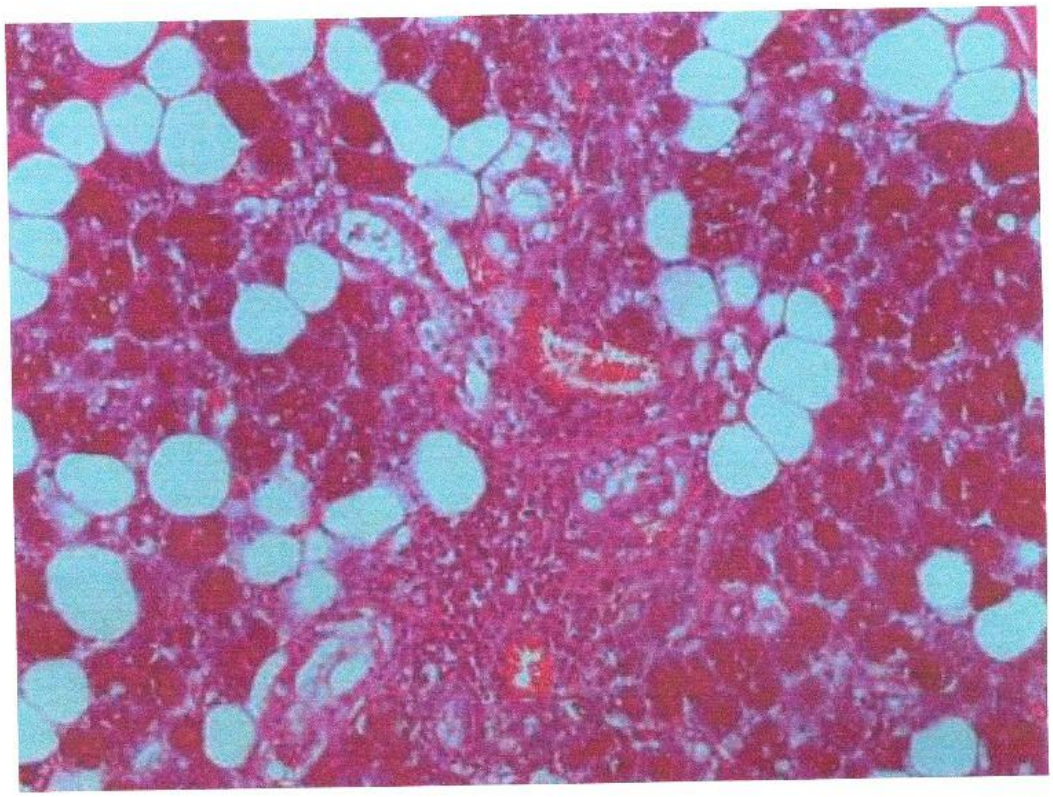


PLATE I
Parotid gland section showing mild infiltration of mainly lymphocytic inflammatory cells with minimal or no glandular destruction.[H&E x 40]

2.3.2 MYCOBACTERIUM TUBERCULOSIS

Mycobacterium tuberculosis of parotid glands was encountered in 4 (12.1%) HIV-seropositive autopsy cases. All cases with parotid gland tuberculosis were known cases of pulmonary tuberculosis, which was the main cause of their deaths. The 4 autopsy cases with parotid gland tuberculosis, were composed of 3 males and one female with ages ranging from 36 to 50 years.

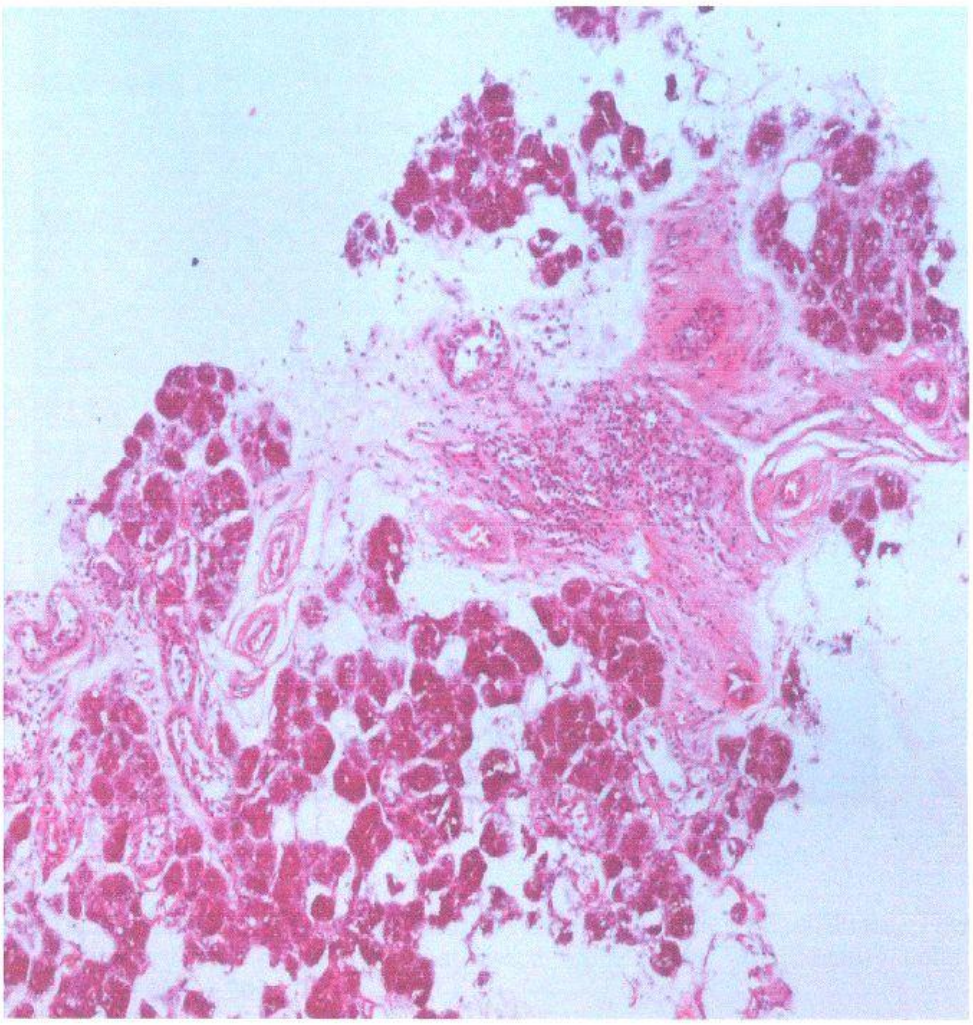


PLATE II

Section of parotid gland showing moderate non specific chronic sialadenitis. This was accompanied with glandular destruction and fibrosis. [H&E x 20].

Additionally these autopsy cases with parotid gland mycobacterium tuberculosis were characterised by one or more features of immunosuppression namely cachexia, skin rashes and oral thrush. In three autopsy cases, the tuberculous lesions were encountered in the intraparotid lymphoid tissue whereas in one case,

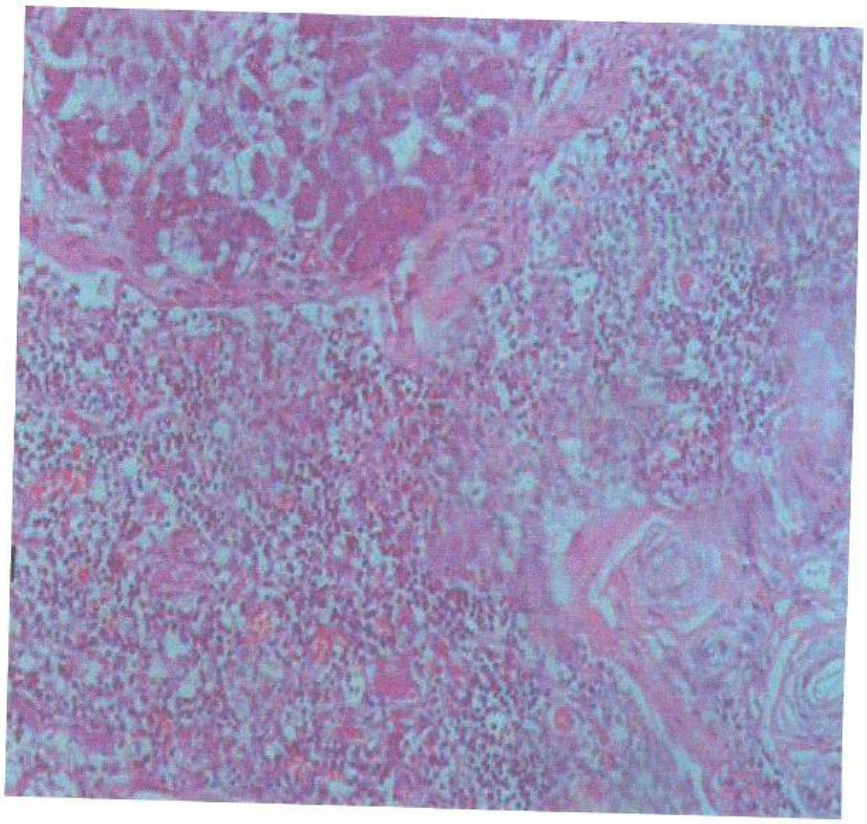


PLATE III
Section of parotid gland tissue with severe lymphocytic cell infiltrate. There is destruction of salivary parenchymal tissue replaced by inflammatory cells and fibrosis. [H & E x 20].

the lesions were found in both lymphoid tissue and glandular parenchyma of parotid gland. Also mycobacterium tuberculosis of parotid gland was characterised by poorly formed granulomas that were composed of caseous necrosis-like areas, epithelioid cells, Langerhan's giant cells and lymphoplasmic infiltrates. Mycobacterium tubercle bacilli were visualized by Ziehl Neelsen stain where they appeared as red rods (PLATE IV).

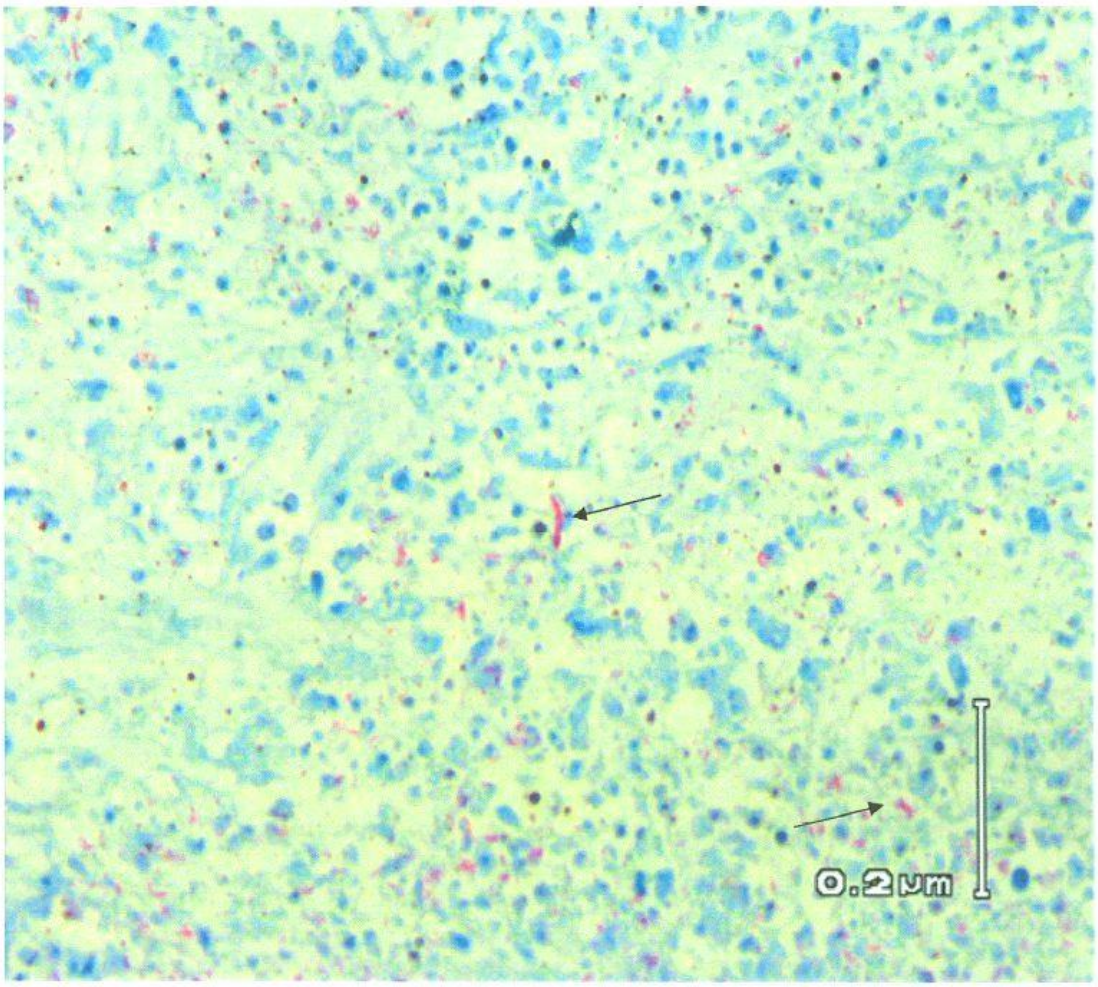


PLATE IV
Section of the parotid gland lymphoid tissue showing red stained mycobacterium tuberculosis bacilli [ZN stain X 40]

2.3.3 PAROTID GLAND CRYPTOCOCCOSIS

There were three cases with HIV disease that had cryptococcosis as confirmed by Grocott's stain. These comprised of 2 males and one female with ages ranging from 24 to 57 years and mean age of 37 years. One male and a female died of motor traffic accident and the third case who was a male died from haemorrhagic shock after an assault. Weight loss and skin rashes were other features that were observed in two cases with

cryptococcosis. The other case in this group of cryptococcosis was of good nutritional status and had neither rashes nor oral thrush.

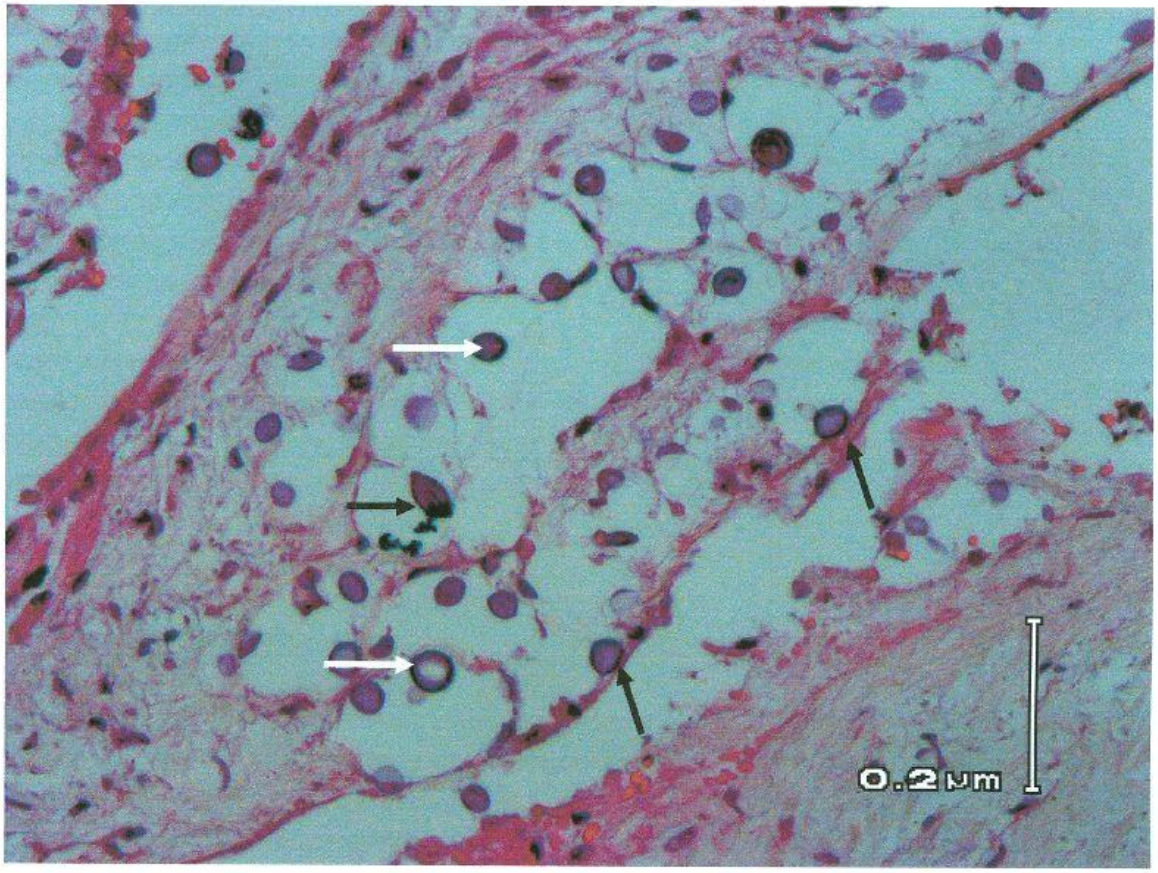
Characteristic histological features of cryptococcosis were of macrophagic pattern which contained cryptococcal micro organisms. All three cases with cryptococcosis had the disease in the parotid gland parenchyma (PLATE V). *Cryptococcus neoformans* was surrounded by a clear halo due to its enlarged gelatinous capsule.

2.3.4 HISTOPLASMOSIS

Only one case which was HIV-seropositive was diagnosed with histoplasmosis of the parotid gland. The deceased was a male aged 28 years. On physical examination, he had all signs of immunodepression. He died of head injury due to motor traffic accident. Histological section showed macrophages containing histoplasma organisms which were in clusters or singly. These microganisms stained black with Grocott's stain. Histoplasmosis fungal infection was confined in the parotid gland parenchyma and was not seen in the intraparotid lymphoid tissue (PLATE VI).

2.3.5 LYMPHOEPITHELIAL CYST

Only one case with lymphoepithelial lesion (LEC) was encountered in this study. The case with LEC was HIV positive male aged 56 years who died due to pulmonary mycobacterium tuberculosis. The lymphoepithelial lesion was characterized by a cystic lesion which had eosinophilic amorphous material. The cavity was surrounded by heavy lymphocytic cell infiltrate, congested blood vessels, fibrosis and fat degeneration



P LATE V
Section of a parotid gland showing spores of *cryptococcus neoformans* organisms [Grocott's stain x 40].

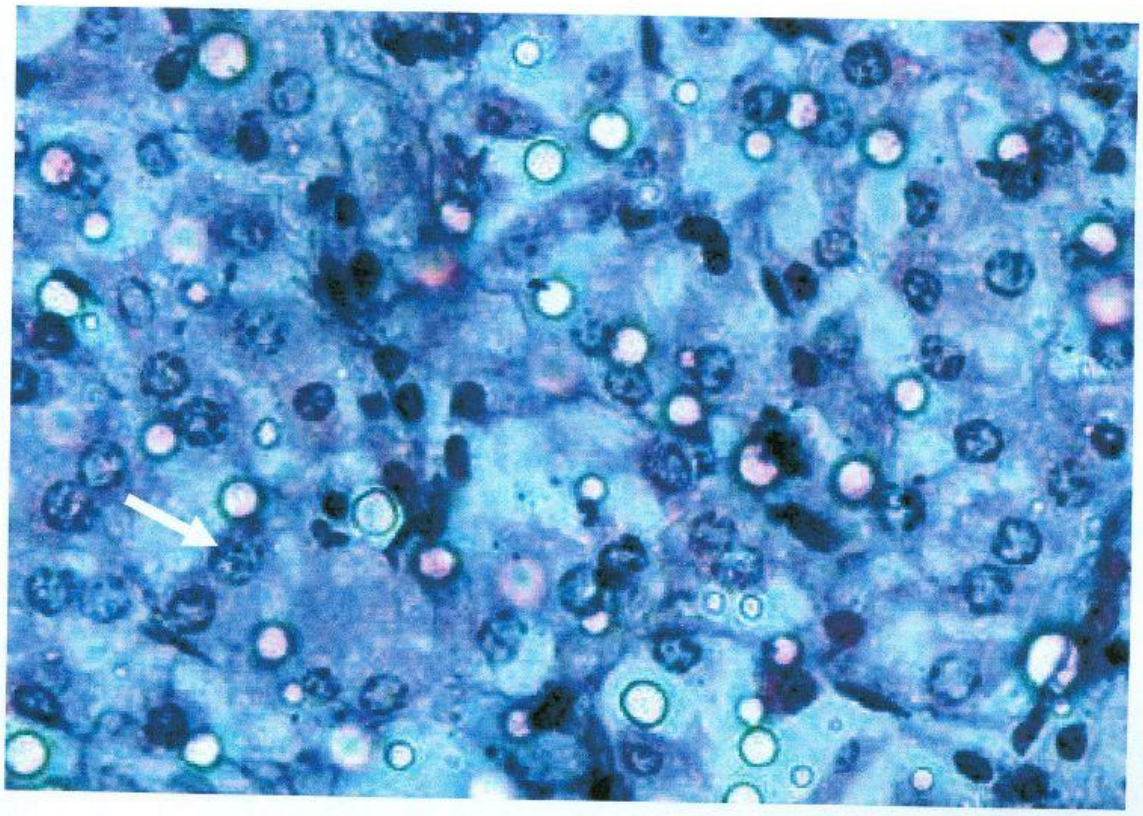


PLATE VI
Parotid gland section showing black stained *histoplasma capsulatum* microorganisms [Grocott's stain x 40]

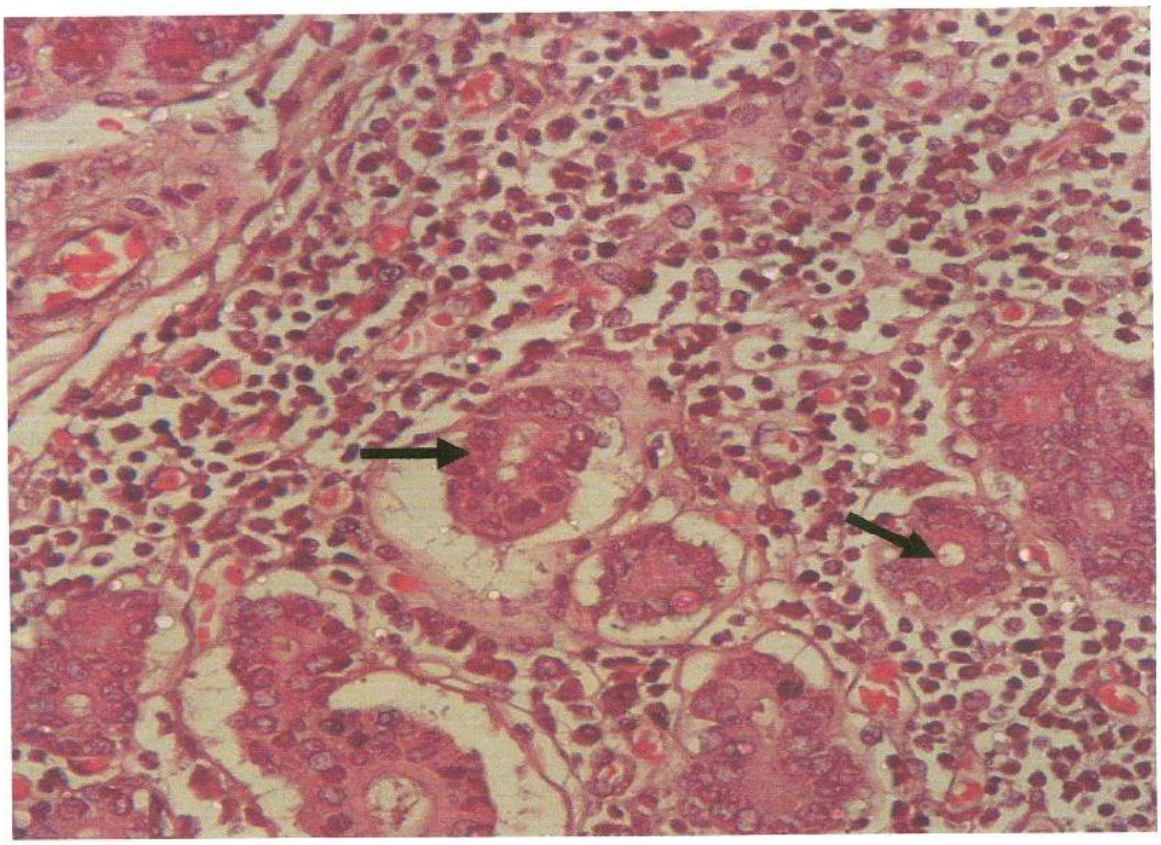


PLATE VII
Section of parotid gland showing lymphoepithelial lesion [H & E X 40].

DISCUSSION

Among the 142 autopsy cases, 23.2% (n = 33) were confirmed to be HIV seropositive, whereas 76.8% (n = 109) were HIV seronegative. Out of the 33 cases with HIV infection, 63.6% (n=21) were histologically diagnosed to have various disease conditions affecting the parotid gland. In contrast, only 12.8% (n = 14) of HIV negative group had parotid gland pathological conditions.

In respect to type of disease conditions found in this study, non specific chronic sialadenitis (NSCS) was the commonest pathological condition that affected both groups. However, NSCS was significantly frequent in HIV group affecting 36.4% in contrast to only 12.1% in HIV negative group. Other conditions included tuberculosis (12%, n = 4), cryptococcosis (9.1%, n=3) and histoplasmosis (1 case). On the other hand only one case of lymphoepithelial cyst was encountered.

This study has focused on establishing the types of pathological processes that can affect the parotid glands of autopsy cases with HIV infection. This is the first study of its kind in Tanzania to identify specific disease conditions that affect the salivary glands of HIV infected individuals using medical legal autopsy cases. Dealing with autopsy cases allowed collection of enough tissue and blood specimens for a detailed histological analysis and blood screening for HIV, respectively. Such studies have also been carried out in Brazil (Vargas et al, 2001, 2003) and in Germany (Ihrler et al, 1996). Besides that studies on salivary gland in patients with HIV infection have also been reported by Sooy et al, in 1987. The prevalence of pathological lesions in HIV parotid glands in this study was 63.6%. compared to 41% of Vargas, Matee 33% and Bem 26.4%. Parotid gland lesions prevalence seems to be on increase probably due to increase in HIV infection.

From the findings of this study, it has been established that non specific chronic sialadenitis is the commonest condition that can affect the salivary glands of HIV positive subjects at the early stage of the disease. NSCS was followed by mycobacterium tuberculosis (11.4%), cryptoccocosis (8.6%), histoplasmosis (2.9%) and lymphoepithelial cyst (2.9%). Reported prevalences by Vargas were NSCS (29%), mycobacterium tuberculosis (10%), cryptococcossis (3%), histoplasmosis(1%) and lymphoepithelial cysts (6%). In a study done by Bem et al, 1992 in Zambia, they reported on prevalence of mycobacterium tuberculosis as (0.2%), KS (0.8%) and cystic lesions (1.5%). This could imply that Zambia has a low prevalence of Mycobacterium tuberclosis campared to Tanzania.

The study group had a mean age of 33.8 years with men (81.6%) being the majority. The predominating young age and male gender of this group reflects the possibility of having a cohort that is physiologically vigorous, economically dynamic and socially active group. This may point out toward a sexually active individuals and therefore more risk of HIV infection.

The prevalence of HIV in this study was 23.2%. This is higher than the overall estimated prevalence in Tanzania which is 7% of the population (NACP Report, 2004). However, the type of autopsy cases that were recruited for this study could be the reason for high prevalence. The prevalence of HIV in Tanzania according to NACP report, 2004 ranges from 6% to 14%. This variation in prevalence of HIV infection depends on whether the data is from urban (11%) or rural (5%), men (6%) or women (8%) or regional wise (Mbeya being the highest 14%). This indicates that in situation where a researcher deals with special group it is possible to get indices that are two or three folds of the mentioned

figure.

NON SPECIFIC CHRONIC SIALADENITIS

This study has clearly shown that NSCS is a predominating lesion in parotid gland of HIV- infected cases. Thirty six percent of HIV-infected study autopsy cases revealed various degrees of NSCS compared to only 12.8% controls with HIV-negative serostatus. Similar findings were reported by Vargas et al. (Vargas et al, 2001, 2003) who documented 29% NSCS prevalence in HIV - infected cases. This portrays that the risk of getting NSCS of parotid gland in HIV- infected person is three times than in HIV-seronegative cases. Statistical analysis between the two groups was highly significant with p-value = 0.042.

MYCOBACTERIUM TUBERCULOSIS

It is worth to note that five cases (15.2%) in HIV-positive study group had pulmonary tuberculosis while four (12.1%) of them in addition to pulmonary tuberculosis had parotid glands mycobacterium tuberculosis. None was found with the disease in the HIV-seronegative cases. This finding is consistent with other reported studies regarding the prevalence of tuberculosis of parotid gland in HIV patients. Vargas, in 2003 reported a similar prevalence of 10% with parotid gland tuberculosis in a cohort of 100 autopsy cases. It is a fact that, tuberculosis of parotid gland was very rare before HIV era, however, this is not the case in post HIV era. Pulmonary tuberculosis has been on increase globally with an estimated one third of the world's HIV infected population being infected with mycobacterium tuberculosis (Mfinanga et al, 2003, Mizra et al, 2003, Kusner et al, 2005, Campbell et al, 2006). Approximately 3-4 million people are diagnosed each year, causing deaths of nearly one million people each year mainly in developing world (Singh et al, 2000, Bezabih et al, 2000, Mizra et al, 2003). In three

cases the mycobacterium tuberculosis granulomatous lesions were found in the parotid gland lymphoid tissue while the fouth case had the disease in both lymphoid tissue and parenchyma. Same findings were reported by Vargas, 2003 who reported intraparotid lymphnode involvement in all 10 cases of mycobacterium tuberculosis reflecting the lymphatic dissemination of mycobacteria. Parenchymal spread of mycobacterium tuberculosis is by macrophages which contain the macroorganisms. Mycobacterium tuberculosis was characterized by poor granuloma formation, epithelioid cells, Langerhan's giant cells and caseous necrosis. Vargas, 2003 and Lewin Smith, 1998 also reported the same findings of poorly organized granulomas microscopically which may reflect low cellular immune response of HIV/AIDS subjects against the infection. Poorly organized granulomas in HIV infection, few lymphocytic cell infiltrate and few acid fast *mycobacterium tuberculosis* bacilli in mixed primary and secondary mycobacterium tuberculosis infection might result into missing diagnosis of mycobacterium tuberculosis infection (Robbins et al, 1999).

CRYPTOCOCCOSIS AND HISTOPLASMOSIS

It is worthy noting that all cases with parotid gland cryptococcosis were HIV-seropositive whereas in the control group there was none. Vargas et al, (2003) reported cryptococcosis prevalence of 3% in HIV parotid glands. He also reported that cryptococcosis in parotid glands was rarely encountered before the HIV era. The findings of this study are consistent with those of Vargas and co-workers that cryptococcosis is an expected finding in HIV parotid glands than it used to be before the HIV era. Vargas also reported that this infection was located in the glandular parenchyma which agrees with findings of this study whereby all the three cases were located in the glandular parenchyma.

The tissue reaction to cryptococcus varies from scant or no inflammation to a non suppurative granulomatous reaction with variable degrees of necrosis (Monteil et al, 1997). In the present study, scanty lymphocytic cell infiltrate was seen. This finding emphasizes the fact that cryptococcosis is an opportunistic infection that is likely to affect patients with compromised immunity (Vargas et al, 2001).

Only one (3%) HIV-positive study subject was diagnosed with histoplasmosis of the parotid gland. There was no histoplasmosis in the HIV-negative group. In a study done by Vargas and co-workers, (2003), they reported 1% prevalence of histoplasmosis in a cohort of 100 autopsy cases. Histoplasmosis of parotid gland which was unknown before the HIV era and although still very low in prevalence, it is not infrequently encountered in parotid glands of HIV cases. The detection of histoplasmosis in the parotid gland in HIV study subjects has been considered to be an important outcome measure in HIV infection, contributing to staging and prognosis systems (Greenspan and Greenspan, 2002). In a Thai study, the presence of oral histoplasmosis was associated with systemic histoplasmosis. More studies with larger sample size are recommended in order to precisely establish the magnitude of parotid gland histoplasmosis in HIV infected individuals.

OTHER LESIONS

There was only one patient in the HIV-positive group who had lymphoepithelial lesion and there was no disease in the HIV-negative group. Schiodt, 1998 and Vargas, 2001 each reported twice as much (6%) prevalence of lymphoepithelial cysts in parotid glands of their study subjects. In 2001, Sperling et al, 1990 reported 30% prevalence of lymphoepithelial cysts in paediatric cases with AIDS. Before the HIV era, parotid

enlargement due to lymphoepithelial cysts was 0.5%. The rise in proportion of LEC shows an association with HIV infection. This study involved adult population who have less prevalence of LEC compared to children and it also had one child and this could have attributed to low LEC prevalence.

Parotid gland Kaposi's sarcoma was not seen in this study. It has been reported that approximately 30% of HIV positive patients eventually develop Kaposi's sarcoma during their lifetime (Levine, 1994; Said, 1997). Kaposi's sarcoma is established as AIDS-defining neoplasm (Parkin et al, 2000) and was primarily found in homosexual men along with epidemic KS (Shiboski et al, 1996, Goedert et al, 1996). Mosha (2005) reported on the relationship of different histological diagnoses and HIV infection that, 38 out of 39 (97.4%) screened cases of oral KS were HIV-positive (p-value = 0.0003). The reason for missing KS in this study could be attributed to early stage of HIV infection in the majority of the study cases and probably also there are few cases of KS in parotid gland of HIV infected cases. Castle et al, 2000 reported that parotid gland involvement is usually found in conjunction with KS in other sites. Thorough physical examination on bodies of these study subjects revealed no suspicious lesion of KS in it's different stages namely patchy, plaque and nodular. Further studies are needed to establish the causal association between HIV infection and Kaposi's sarcoma in parotid glands.

Non Hodgkin's lymphoma is another AIDS defining neoplasm which was not seen in this study. NHL has been increasing with increase in HIV infection in the USA (Chassagne-Clement, 1999). Two percent of all NHL are found in head and neck region (Freeman et al, 1972). However, Kaaya et al, 2006 reported on overall increasing tendency for malignant lymphoma in Tanzania from 1991-1994 whereby there was a clear increase in

year 1993. Vargas, 2003 reported one case with NHL of parotid gland out of 100 study subjects. NHL was not seen in the study subjects probably due to small sample size or majority were in early stages of HIV infection leading to low frequency of the NHL. It is also possible that NHL is a rare condition in parotids of HIV infected cases. More studies are needed using large sample size to establish relationship of NHL with HIV infection for serving life of HIV infected patients.

Subjective complaint of dry mouth (Xerostomia) and salivary gland hypofunction have been associated with HIV infection (Nazareth et al, 2000). Xerostomia was reported in 10% of 375 American Homosexual males with HIV infection (Silverman et al, 1986), 9% of 74 HIV infected Dutch patients (Schulten et al, 1989), 26% of 100 Greek male and female HIV infected individuals (Laskaris et al, 1992) and 80% of 20 Peruvian HIV positive patients (Gillespie and Marino, 1992). Patients with HIV infection develop opportunistic infections such as NSCS, mycobacterium tuberculosis cryptococcosis histoplasmosis and lymphoepithelial cysts which destroy salivary glands and cause decreased salivary flow. Saliva plays a significant role in oral homeostasis. It is responsible for mouth cleansing and food digesion. A patient with reduced salivary flow will complain of dry mouth (xerostomia), burning sensation and extreme discomfort. Recurrent dental caries, oral candidiasis, gingivitis and periodontitis are the most common complications associated with salivary gland hypofunction. Also, patients with xerostomia have difficulties with oral artificial appliances such as dentures because they traumatize the dry oral mucosa. Tanzania has only 120 Dentists serving a population of 38 million people. Therefore, prevention and early management of opportunistic infections is mandatory for better management of HIV infected individuals.

CONCLUSION

This study has illustrated that more pathological alterations are found in parotid salivary gland of HIV patients than those without the disease. Therefore parotid gland lesions can be considered as a potential public health problem in this era of increasing incidence of HIV infection in Tanzania. NSCS was the commonest disease condition encountered in both groups but was significantly higher (36.4%) in HIV-seropositive study group than the HIV-seronegative control group (12.1%) making a ratio of 3:1, respectively. This finding is important for diagnosis and management of HIV infection and to patients with parotid gland lesions.

RECOMMENDATIONS

1. Since two thirds of HIV - infected patients are likely to have various pathological alterations in parotid glands, all patients with parotid gland lesions should be screened for HIV – infection.

2. On the other hand, patients with HIV infection should be examined for parotid gland diseases.

3. More studies with larger sample size should be done to further elucidate the relationship of HIV infection and parotid gland diseases. These studies will also show the magnitude of parotid gland pathological conditions.

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