

Clinical Experience with Parotid Gland Enlargement in HIV Infection: A Report of Five Cases in Nigeria

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Abstract

A changing picture of oral lesions associated with HIV/AIDS has been documented. With the use of antiretroviral therapy, salivary gland swellings and other less common conditions associated with HIV/AIDS are now becoming more common. Our review of the literature showed the presence of parotid swelling in HIV-1 infection has increased from a range of 5-10% to 20% in AIDS. However, to the best of our knowledge, none from sub-Saharan Africa, which is the epicenter of the HIV infection and where access to antiretroviral therapy is poorest, has been primarily reported in literature.

This report documents five cases of bilateral parotid gland enlargement as the presenting clinical manifestation of HIV/AIDS. The combination of a fine needle aspiration (FNA) biopsy, ultrasound imaging, and histological diagnosis increased the accuracy of diagnosis. While two patients had access to antiretroviral therapy, other modes of management were cystic aspiration and parotidectomy. One of the patients treated with parotidectomy had facial nerve injury, and the short-term aesthetic outcome between surgical treatment and antiretroviral therapy did not appear different. However, all our patients were lost to follow-up within a 2-year period.

For a resource-constrained environment like Nigeria where stigma and discrimination is high and access to antiretroviral therapy is limited, there is a need to understand how best to manage a lymphoepithelial lesion in HIV/AIDS patients.

Keywords: Parotid swellings, HIV infection, lymphoepithelial cyst

Citation: Owotade FJ, Fatusi OA, Adebisi KE, Ajike SO, Folayan MO. Clinical Experience with Parotid Gland Enlargement in HIV Infection: A Report of Five Cases in Nigeria. J Contemp Dent Pract 2005 February;(6)1:136-145.

Introduction

HIV infection has spread rapidly within developing countries since it was first diagnosed in the early 1980s. In particular the African continent has been the worst affected with the sub-Saharan Africa harboring about 70% of the world's infected population.¹ Even within this endemic region, the burdens of the disease vary significantly from country to country. Nigeria, with a seroprevalence level of 5.8% and a population of 3.5 million HIV infected individuals, is presently ranked as the fourth worst affected nation in the world after South Africa, India, and Ethiopia.¹



Poverty is a principal contributory factor to the epidemic in this region as it increases the vulnerability to HIV infection, while the infection itself impoverishes individuals as well.² Thus, a vicious cycle of poverty and HIV infection is set into motion. Poverty has also affected the effectiveness of managing the infection with very few having access to single antiretroviral drugs such as the highly active antiretroviral therapy (HAART). As of this writing, only 15,000 out of the 3.5 million HIV infected persons are on antiretroviral drugs.³ Improved access to antiretroviral drugs, early diagnosis, and prompt treatment of opportunistic infections remains the primary focus of HIV infection management in the sub-Saharan region, including Nigeria.

The role of dentists in the early diagnosis of HIV infection has been highlighted in previous studies.^{4,5} Oral lesions have been observed since the

beginning of the epidemic with approximately 10% of the HIV infected population presenting oral manifestations as a first stage of their disease.⁶ These oral lesions usually have diagnostic and prognostic roles in the management of HIV infection.⁷ The diagnostic potential of oral lesions is based on the fact some oral lesions, such as candidiasis, have been found to be strongly associated with HIV, while others like major salivary gland swellings are less likely to be associated. However, with adequate management of HIV infection, oral lesions, such as candidiasis, no longer predominate; oral diseases such as HIV salivary gland diseases and oral warts are becoming more commonly seen in HIV infected individuals.⁸ Oral lesions are still strongly associated with the clinical stage of HIV infection, and the presence of these lesions can be used as additional markers of immunosuppression and AIDS.⁹ This fact is supported by Eyeson et al.⁷ who observed the prevalence and severity of these oral lesions inversely correlates with the level of immunosuppression. This highlights the role of oral lesions as a prognostic indicator.

Salivary gland diseases are also important as diagnostic and prognostic indicators in HIV infection. These salivary gland diseases include the enlargement of major salivary glands (with or without hypofunction) and xerostomia.¹⁰ In early lesions the submandibular and sublingual glands are often initially affected and enlarged.¹¹ However, as the disease progresses, more parotid gland swelling can be observed.^{9,12} As many as 5-10% of patients with HIV-1 infection have been reported to have parotid swelling¹³ with the incidence increasing to as high as 20% in AIDS patients.¹⁴

There are several case reports in the literature on parotid gland enlargement in HIV infection.^{14,15} However, the authors could not find any report in the literature about sub-Saharan Africa, which is the region worst affected by the epidemic. This paper presents five cases of parotid gland enlargement seen in HIV infected persons in Nigeria and reports on the differing modes of management in a resource-constrained environment with poor access to antiretroviral therapy. The implications for the overall health of these patients are also discussed.

Report of Cases

Five patients (1 male and 4 female) with ages ranging from 18 to 54 years (mean age of 33.8) were diagnosed with lymphoepithelial cysts of the parotid gland in two maxillofacial centers in Nigeria over a 5-year period. All patients presented with bilateral parotid gland swellings with durations ranging from 6 months to 2 years. Swelling started in one gland in all of the patients a few months before the other gland became involved. All patients presented in the hospital because of aesthetic concerns (Figure 1). None reported with pain. The lesions were cystic in consistency in 4 of the 5 patients. In the fifth patient, the lesion was firm.



Figure 1. Bilateral parotid gland swelling in HIV infection.

Table 1 summarizes the clinical features of the patients. Laboratory investigations revealed three out of the five patients were positive for HIV I and II, while two had HIV I. The histological sections of the parotid lesions showed a fibrous connective tissue stroma densely infiltrated by lymphocytes organized into follicles and germinal centers that surround islands of epithelial tissue (Figure 2). Also seen were some plasma cells and histiocytes.

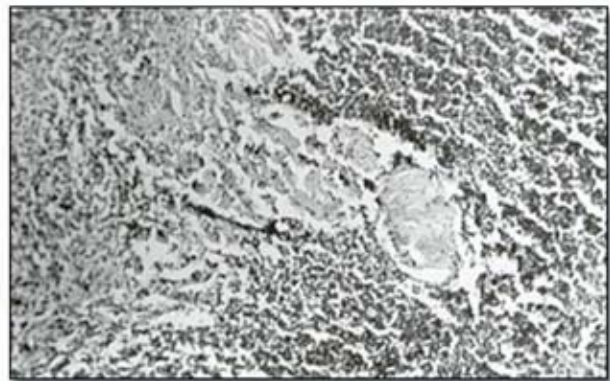


Figure 2. Fibrous connective tissue stroma with lymphocyte infiltration.

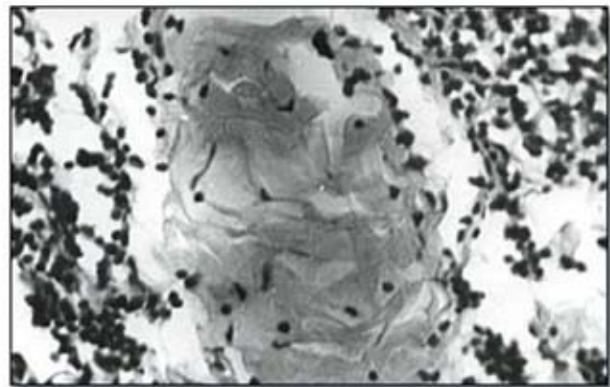


Figure 3. Amyloid deposit in lymphoepithelial lesion of the parotid gland.

Eosinophilic deposits believed to be amyloid were present in some areas (Figure 3).

The histological features were consistent with benign lymphoepithelial lesions of the parotid glands. Ultrasonographic investigation in one of the patients showed a bilateral cystic swelling in the parotid area, which contained clear fluid. No eddy was demonstrated (Figure 4).

Two patients underwent bilateral parotidectomy, while three had courses of antiretroviral therapy

Table 1. Clinical features of patients.

Number	Age	Gender	Presentation of Swelling	Duration (months)	Consistency
1	58	F	Bilateral	12	Cystic
2	18	M	Bilateral	6	Cystic
3	28	F	Bilateral	36	Cystic
4	23	F	Bilateral	12	Cystic
5	35	F	Unilateral	24	Firm

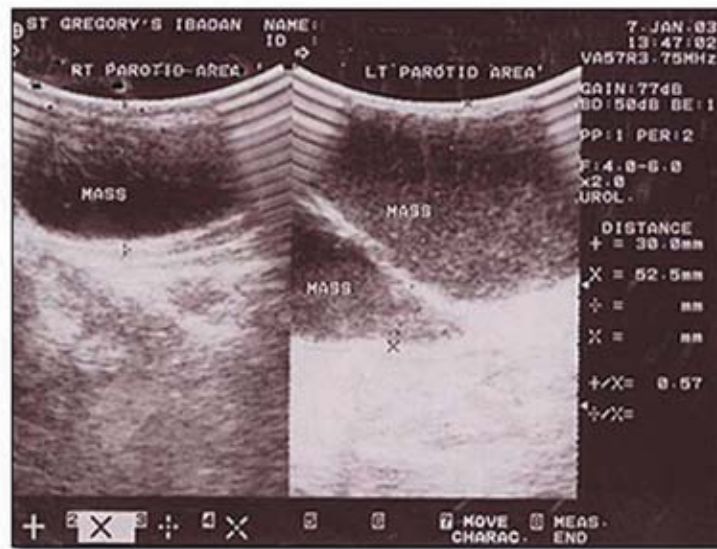


Figure 4. Ultrasound picture of salivary gland lesion showing hypochoic cystic areas.

Table 2. Treatment and outcome.

Number	Treatment	Complications	Outcome
1	Cystic aspiration + ARV	Nil	Lost to follow-up
2	ARV	-	Nil
3	Bilateral parotidectomy + ARV	Bilateral facial nerve weakness	Improvement with use of neurobion
4	Parotidectomy	-	Lost to follow-up
5	Nil	-	Lost to follow-up

ARV = Antiretroviral therapy.

before being lost to follow-up (Table 2). One of the three patients on antiretroviral therapy received it as the only instituted regimen, another received it along with cystic aspiration, while the third had surgery (bilateral parotidectomy) combined with antiretroviral therapy.

One of the patients was followed up two years post surgery. The result of surgery was satisfactory. The inability to follow-up with all patients on a long-term basis makes reporting treatment outcome difficult.

Discussion

Lymphoepithelial lesions in the parotid gland are uncommon benign entities with increasing incidence in association with HIV infec-

tion since 1980.¹⁶ The lesions are thought to reflect a localized manifestation of a persistent generalized lymphadenopathy associated with HIV infections.¹⁷ However, it remains unclear whether lymphoepithelial cysts in parotid glands in HIV patients develop from pre-existing salivary gland inclusions in intra parotid lymph nodes or from a lymphoepithelial lesion of the salivary parenchyma. Ihrler et al.¹⁸ demonstrated a secondary lymphatic infiltration of salivary parenchyma provokes a lymphoepithelial lesion of the striated ducts with basal cell hyperplasia. DiGiuseppe et al.^{17, 19}, and other researchers showed benign lymphoepithelial lesions of the parotid gland associated with HIV infection results from the involvement of intra-parotid lymph nodes by persistent generalized lymphadenopathy.²⁰

Viral load in an HIV infection was also found to be significantly and positively associated with gland enlargement with a linear trend.²¹ The virus is believed to alter the expression of strategic cellular genes. McAther et al.²² showed HIV virus altered the mRNA expression of the intracellular matrix and basement membrane, thereby, producing associated salivary gland disease. The lesion usually presents as a bilateral cystic swelling with an associated cervical lymphadenopathy and pain.^{23, 24} These swellings often create cosmetic concerns, as was the case in our patients; four patients presented with bilateral parotid swelling. The fact the swellings were firm in our subjects may signify an early phase of the lesion preceding cystic changes.

Diagnosis of the cystic lymphoepithelial lesion of the salivary gland can be made through the use of fine needle aspiration (FNA). The FNA procedure in skilled hands can be a very useful, simple, and cost-effective procedure for the diagnosis. The cellular component within the fluid may be exceedingly scanty or absent making diagnosis difficult and at times impossible.²⁵ However, a definitive diagnosis can be made with an overall accuracy of 73.6%-91%²⁵⁻²⁷ with sensitivity and specificity of 84.8% and 93.7%, respectively.²⁶ The use of the FNA biopsy can be enhanced by adequate clinical history, examination, and radiographic examination.

The use of imaging techniques such as computer tomography and ultrasound in the diagnosis of salivary gland diseases has been highlighted in the literature.^{28, 29}

Ultrasound offers a simple, rapid imaging technique for ascertaining the nature of glandular histology; with cystic lymphoepithelial lesions, sonolucent areas are noticed. This imaging technique often helps to differentiate parotid gland enlargement due to HIV infection from many other causes of parotid enlargement.²⁹ However, the ability to make a definitive diagnosis is dependent on the expertise of the radiologist. In one of the cases wherein an ultrasound was done, the radiologist made a diagnosis of bilateral parotid cystic masses with no observed sonolucent areas, however, a definitive diagnosis was only arrived at following histology.

Histology remains the most reliable means of confirming a diagnosis. Irhler et al.¹⁸ reported histological and immunological studies of specimens from 100 patients with lymphoepithelial cysts of the parotid gland revealed a continuous morphological spectrum of change within the salivary parenchyma demonstrating that secondary lymphatic infiltration provokes a lymphoepithelial lesion of striated ducts with basal cell hyperplasia. The involvement of a myoepithelial cell was also observed.¹⁸ Histological reports from our reported cases showed this pattern of massive lymphoepithelial infiltration. However, the morphological spectrum of change could not be demonstrated due to the small number of cases.

Varied treatment modalities have been preferred for benign lymphoepithelial cysts of the parotid gland. This varies from simple aspiration to surgical resection, pharmacotherapy, or radiotherapy. Suskind et al.²⁴ reported the use of doxycycline sclerotherapy in the management of a child. The definitive therapy for cystic lymphoepithelial lesions of the salivary gland is surgical excision. However, most HIV positive patients managed with antiretroviral therapy, which often showed regression of the lesion.^{15, 23, 30} Treatment with low dose radiotherapy as an alternative to antiretroviral therapy is also recommended for HIV positive individuals depending on the individual circumstances.³⁰ Surgical treatment is probably not necessary in the majority of HIV associated cases. However, the use of cystic aspiration alone has been found ineffective.³⁰

Among our patients, treatment varied from parotidectomy to cystic aspiration with or without antiretroviral therapy. In all the cases the diagnosis of HIV status was secondary to the oral presentation (parotid swelling). The treatment outcome of patients reported in this study could not be determined because all the patients were eventually lost to follow-up. Our experience of nerve damage in one of the surgically operated cases is not unusual. The fact antiretroviral therapy alone is adequate for the management of the aesthetic complications in most patients with lymphoepithelial cysts would reduce the need for surgery and the possible complications associated with surgery. Where antiretroviral

therapy is ineffective and aesthetic concerns remain a major issue, surgery may still be a treatment option.

Conclusion

Parotid gland enlargement may be the presenting clinical manifestation of HIV/AIDS in the African as in other races. Correct identification of salivary lymphoid infiltrates has important implications for the prognosis and patient management. The use of imaging techniques and FNA biopsy in combination with histological reports may help increase the accuracy of diagnosis and

differentiation of the lesion from other parotid lesions like Sjorgren's syndrome and marginal zone B-cell lymphoma.³¹ For Nigeria, there is a need to understand how to manage this lesion in HIV/AIDS patients as this condition is fairly recent. The esthetic complications that may be associated with an unmanaged case and surgical complications from managing the lesion may complicate issues for people living with HIV/AIDS who live in an environment where stigma and discrimination is high and lack of access to antiretroviral therapy, due to poverty, is difficult to obtain.

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