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Diagnostic ultrasound patterns of parotid glands in HIV patients

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Abstract
Aim: The aim of this study was to determine parotid gland changes in HIV patients using ultrasound.
Methods: In this prospective clinical study, ultrasound scans were performed on 50 patients aged between 20–60years.
Results: There were four main distinct ultrasound pathological patterns in the parotids, i.e. lymphocytic aggregations (LAs), lymphoepithelial cysts (LECs), fatty infiltration (FI) and lymphadenopathy only. There were additional subdivisions depending on the presence of echogenic foci and intraparotid lymphadenopathy. Of all these only two patterns were noticed in the present study. 46% cases showed LEC and only 2% cases showed FI.
Conclusions: In conclusion diagnostic ultrasound is the most appropriate imaging modality to investigate the parotid glands in HIV-positive patients.

Keywords: Diagnostic ultrasound, parotid glands, HIV patients

Introduction
Human immunodeficiency virus (HIV) infection was first recognized in Uganda in 1982. By the end of 2003, 70% of the world's affected population were living in the sub-Saharan region of Africa, and in Uganda alone 78, 000 people died in 2003 [1]. Even though HIV prevalence in world has reportedly fallen from 30% in 1987 to 6.1% in 2007, it still remains very high, and acquired immunodeficiency syndrome (AIDS) is still claiming thousands and lakhs of lives each year. The oral cavity is frequently the initial site of symptoms in patients with HIV infection. The task of maintaining a healthy oral environment falls largely to the salivary glands [2]. Parotid swelling in patients with HIV is often associated with salivary gland disease, such as inflammatory disorders, infections, neoplasms and benign lymphoepithelial cysts (BLECs). BLEC is characterized by bilateral parotid gland swelling and cervical lymphadenopathy, and the presence of BLECs can serve as an initial clinical manifestation of HIV [3].
With the recent availability of local expertise and equipment, ultrasound investigation provides noninvasive diagnosis and obviates surgical intervention.
Ultrasound imaging is already widely accepted worldwide for diagnosis of soft tissue swellings of the head and neck region and is used by some researchers for imaging the parotid glands in HIV patients[4]. Based on this the present study was done on HIV positive patients to assess the parotid gland changes using ultrasound.

Aims and objectives
This prospective clinical study, using ultrasound imaging, was performed on HIV-positive patients in Kamineni institute of Dental Sciences, Narketpally:
1. To determine the condition of the parotid glands, with and without enlargement
2. To determine the prevalence of the main ultrasound pattern groups.

Inclusion criteria
1. Patients who were HIV positive by both direct and indirect method.
2. Those who are on HAART and not on HAART treatment were included in the study.
3. Patients aged between 20-65years were included in the study.

Exclusion criteria

1. Those who were too weak to walk to the ultrasound department
2. All critically ill patients; those with draining abscesses in the parotid area; those who had any surgical intervention in the parotid glands, facial nerve palsy, meal related swellings or any signs of rheumatoid arthritis.

50 HIV positive patients who were positive by both direct and indirect method and who were admitted in the KIMS hospital for some other issues were selected in the study. Out of 50, 28 of them were female and 22 were male. In the present study no one showed parotid swelling. Informed consent was taken from all the patients and ultrasound was performed on them.

Ultrasound scanning was performed using a broadband linear probe at a frequency between 5 MHz and 12 MHz. Scanning was performed by Radiologist and always in the presence of one of two other experienced ultrasound radiologists.

For each patient in the study, at the time of the ultrasound scan, a detailed report was written in consultation with the other radiologist present. In the parotid glands, all relevant features were carefully recorded, i.e. echotexture of the whole gland, echogenicity, size and margins of each nodule, detection of lymph nodes as well as their size and position, whether intraparotid or peri/extraparotid, the presence or absence of echogenic foci and any associated vascularity as determined using colour Doppler ultrasound. For each patient, a diagnosis was made based on the pattern of sonographic features. Where the left and right sides were asymmetrical, diagnosis was made based on the more severely affected side.

Table 1 Sonographic features in the parotid gland, how they are described, what they look like and how to interpret them

Feature	*Descriptors of individual feature*	*Appearance*	*Interpretation*
Echogenicity	Isoechoic	Mid-grey, medium echoes	Normal parotid gland
	Anechoic	Black, no echoes	May be cyst, neoplasm or other
	Hypoechoic	Dark grey, weak echoes	May be fatty degeneration
	Hyperechoic	Light grey or white, strong echoes	
Echotexture	Homogeneous	Even texture	Normal parotid gland
	Heterogeneous	Mixture of high and low echogenicity, coarse texture	
Heterogeneous echotexture	Hypoechoic or anechoic areas or nodules	Dark grey or black	May be cyst, lymph node, neoplasm or other
	Size	Measure using electronic cursors	
	Shape	Round or other	
	Margins	Distinct or not	
	Number	Single or multiple	
	Distribution	Local or whole gland	
	Posterior acoustic enhancement	Increased echo strength in the area beyond ("behind") a nodule	Associated with cystic lesion (because fluid inside the cyst allows better transmission of ultrasound)
	Echogenic foci	Small white spots, mobile or stationary, scattered or clumped	May be debris or particles (clumps of cells, protein or other) suspended in fluid; if strong, echoes may be microcalcifications
	Posterior acoustic shadow	Black (vertical) stripe typically beyond echogenic foci, may be narrow or wide	Associated with microcalcifications or possibly gas bubbles (narrow); associated with mandible (wide). Caused by ultrasound being unable to penetrate calcified structures

Table 2 Categorization of sonographic patterns that form the main diagnoses in parotid glands; proposal for a new classification system

Diagnosis	*Pattern of features*
Normal parotid	Homogeneous and isoechoic Occasional normal intraparotid lymph nodes
Lymphocytic aggregations	Heterogeneous appearance "Coarse" echotexture Diffuse mainly small hypoechoic or anechoic areas interspersed within normal isoechoic areas Moderate to ill-defined margins Size usually less than 5 mm Not associated with posterior acoustic enhancement Subgroups Internal echogenic foci May be microcalcifications Intraparotid lymphadenopathy
Lymphoepithelial cysts	Heterogeneous appearance Prominent round hypoechoic area Well-circumscribed margins Size usually > 5 mm, up to several cm Internal septa Posterior acoustic enhancement Subgroups Internal echogenic foci May be microcalcifications Intraparotid lymphadenopathy
Fatty infiltration	Whole gland hypoechoic, with posterior attenuation Subgroup Intraparotid lymphadenopathy
Lymphadenopathy	Oval-shaped hypoechoic areas or nodules Echogenic hilum with hilar blood flow seen on colour Doppler

Results

Table 1

Total no of patients	Male	Female
50	22	28

Table 2

	Male(22)		Female(28)	
No.of patients	HAART 13	Not HAART 09	HAART 11	Not HAART 17
Normal parotid gland	4	5	7	10
LEC	6	3	4	7
FI	-	1	-	-

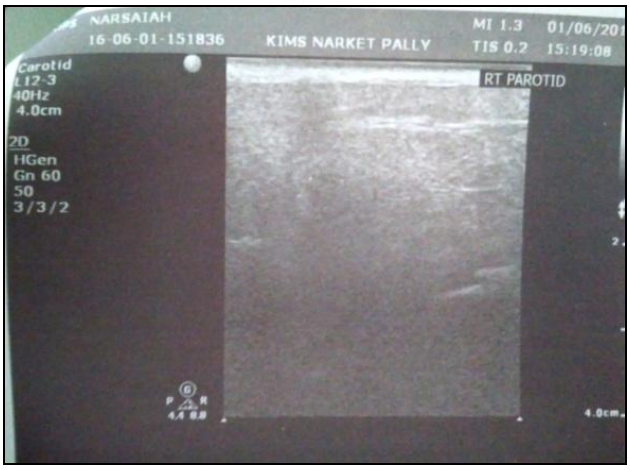

Fig 1: Normal parotid gland.

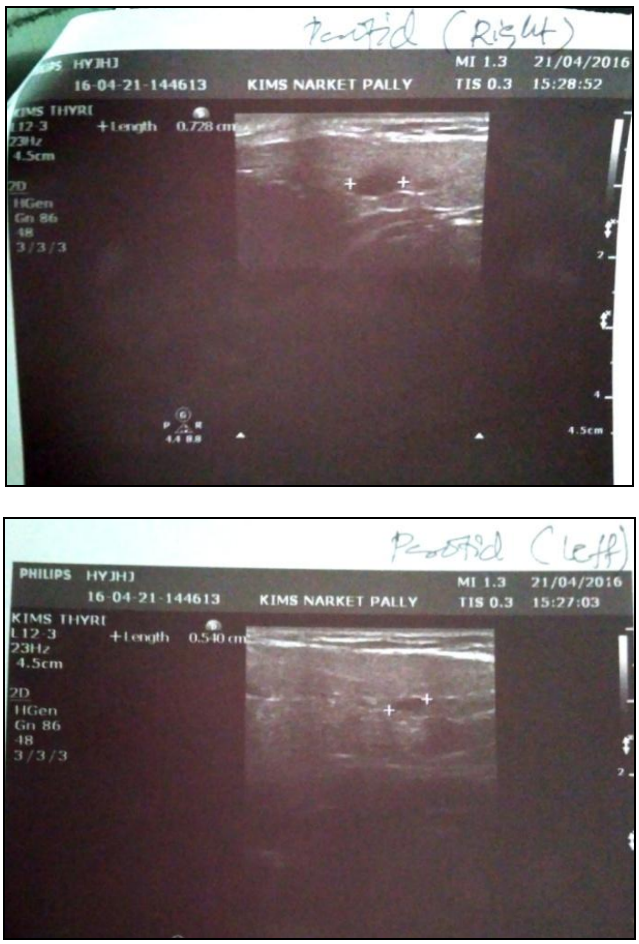

Fig 2: right and left parotid gland showing lymphoepithelial cyst.

Discussion

Diagnostic modalities may be non-invasive and invasive. Non-invasive diagnostic evaluation consists of an ultrasound scan of the parotid gland, computed tomography scanning (CT) and/or magnetic resonance imaging (MRI) in cases of diagnostic ambiguity. Ultrasonography is ideal for evaluating "superficially located anatomic soft tissue entities" such as the parotid gland.[9] Furthermore, its advantages include that it is easy to perform, painless, inexpensive, readily available and obviates radiation exposure to patients.[9] Additionally, ultrasonography allows for evaluation of both cystic and lymphoproliferative lesions of the parotid glands.

In a study by Kabenge *et al.* (2010) [10], four distinctive ultrasound patterns in the parotid glands of HIV-positive patients were described. These include: lymphocytic aggregations, lymphoepithelial cysts (prominent round hypo-echoic areas with well circumscribed margins and internal septa), fatty infiltration (in patients on protease inhibitor therapy) and lymphadenopathy [10]. considering this ultrasound was selected in this study to evaluate parotid gland changes.

Pathogenesis

Parotid gland enlargement is commonly due to the development of BLEC within the parotid gland. To date, the precise etiology of these lesions is unknown and the pathogenesis has prompted much controversy.[5] BLEC is defined as single or multiple cysts within lymph nodes situated mainly along the tail of the parotid gland that have been trapped during parotid gland embryogenesis. It is therefore not surprising that it is this region of the parotid gland that enlarges early on during the course of the disease process. This lymphoid proliferation may result in ductal obstruction and ductal dilatation that mimics a true cyst. Parotid enlargement may also result from proliferation of the glandular epithelium that is trapped within these intra-parotid lymph nodes. HIV has a predilection for lymphoid tissue and elevated concentrations of the virus can be found within these nodes [6, 7].

In a subgroup of HIV-positive patients, a disease process known as "Diffuse infiltrative CD8 lymphocytosis syndrome" has been observed. This entity is characterized by a CD8 lymphocytosis, bilateral parotid swelling, a diffuse visceral CD8 lymphocytic infiltration (usually involving the lung), and cervical lymphadenopathy. An immunogenetically distinctive group (HLA- DR5) is particularly predisposed to this pathology [8].

There is considerable debate as to the terminology used to describe these lesions. The terms include benign lymphoepithelial cysts (BLEC), benign lymphoepithelial lesions (BLEL), cystic BLEL, AIDS-related lymphadenopathy, diffuse infiltrative CD8 lymphocytosis syndrome (DILS), cystic lymphoid hyperplasia and HIV associated salivary gland disease [5].

Prevalence of lymphoepithelial cysts

In our study, all the patients were of no obvious parotid gland swelling was seen. But ultrasonographically LEC was seen in 46% of cases. Comparison with other studies is difficult because most of them performed diagnostic imaging whether ultrasound, CT or MRI for patients only with visible swelling, whereas in our study we carried out ultrasound imaging in a small group of HIV patients without parotid swellings. In other studies, there is less distinction between LECs and other similar-looking

lesions and some authors refer to LECs by different names [11, 12].

Fatty infiltration

2% patients showed FI (lipodystrophy) in the parotid glands. Drug treatment using HAART is effective at reducing salivary gland enlargement. However, the protease inhibitors component of HAART has been shown to cause side-effects of parotid FI, paradoxically manifesting as parotid swelling. The length of time before this side-effect becomes clinically evident is not known [13, 14].

Echogenic foci

Dave *et al.* [15] identified multiple tiny radiopaque dots on non-contrast-enhanced CT scans in the parotids of one patient with bilateral parotid enlargement and interpreted the dots as microcalcifications. Vona *et al.* [16] showed sonograms of lymphoepithelial cysts which contained ‘‘high level echoes in suspension’’. These proved to be crystals of calcium oxalate upon FNAC. In Dave *et al.* ’s article [15] microcalcifications were found in only one child out of the four in their study of patients who had benign LECs and were HIV positive.

In conclusion diagnostic ultrasound is the most appropriate imaging modality to investigate the parotid glands in HIV-positive patients. Even patients with no visible parotid enlargement are likely to have abnormalities that can be detected sonographically. There is a wide spectrum of ultrasound patterns, which can be categorized into four main group. In the present study we have found a high prevalence of lymphoepithelial cysts and lymphocytic aggregations in patients without parotid enlargement, in this small study population it is difficult to assess a prevelance of parotid gland changes due to HAART therapy. Further studies with larger population has to be done to find the association of parotid gland changes due to HAART therapy.

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