Case Report

Benign Lymphoepithelial Cyst of Parotid Glands in HIV-Positive Patient

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Parotid enlargement mostly results from benign lymphoepithelial cysts (BLCs) in HIV-positive patients, as this can often be the first indication of human immunodeficiency virus infection. BLCs develop secondary to a benign lymphoproliferative disease that is not a tumor but HIV-related reaction, yet pathophysiology was still unclear. FNA cytology is considered the basic and minimal invasive diagnostic tool. BLCs can expand and distort the patient's facial appearance. This is a cosmetically deforming disease entity as well as the many treatments that accompany it. Choices of treatment are anti-retroviral therapy, repeated fine-needle aspiration and drainage, radiotherapy, sclerotherapy and surgery. The patient presented in this paper is a surgical case control for our findings upon review of the literature. Based on this case control and our review of the literature, it is concluded that surgical intervention offers the best complete response to the disease and cosmetic result for these patients.

Keywords: *Benign lymphoepithelial cyst, Parotid mass, HIV*

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Parotid mass is common in head and neck tumors. Most parotid masses are benign tumor (60-70%)[1]. In an increasing number of incidence of HIV infection, many HIV-infected patients will present with a neck mass during their illness. The differential diagnosis includes neoplasm, infection, HIV lymphadenopathy and parotid disease. Parotid enlargement mostly results from benign lymphoepithelial cysts (BLCs) that develop secondary to a benign lymphoproliferative disease that pathophysiologically is not a tumor, but an HIV-related reaction known as "Benign lymphoepithelial cyst".

Case Report

A 45-year-old Thai man, presented with a mass at the left cheek, and was referred by a provincial hospital to the plastic outpatient department of Thammasat University Hospital, Thailand. His preoperative laboratory screening anti-HIV was positive. His present illness was a slowly growing mass at the left cheek with no history of pain or discharge (Fig. 1).

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His concerns were cosmetic in nature and malignant awareness. At the hospital, he had undergone two times of FNA for cytology. The patient had been told that the result was negative for malignancy. Laboratory screening anti-HIV was done and revealed positive. The mass had been smaller after the aspirations performed. It had slowly grown up again. For this reason, he was referred.

On physical examination, an enlarged, well-circumscribed, movable left parotid mass measuring 5 centimeters was identified over the mandible angle. There was no facial palsy. On intraoral examination, the mucosa was moist and normal in appearance. No evidence of oral manifestation of HIV was presented. Milking of the left parotid gland produced minimal clear salivary flow through Stensen's orifice. We noted neither abnormalities of the right parotid salivary gland nor cervical lymphadenopathy.

A computerized tomography was obtained a well-defined border mixed enhancing solid and cystic mass 2.3x2.8 centimeters at inferior aspect of superficial lobe of parotid gland (Fig. 2).

Repeated FNA was performed then mild turbid serosanguinous fluid 3 milliliters was sent for official histopathological report and acid-fast bacterial (AFB) stain. Cytological diagnosis was lymphoepithelial lesion and AFB was not found.

Fig. 1 An enlarged, well-circumscribed, movable left parotid mass measuring 5 centimeters was identified over the mandible angle.

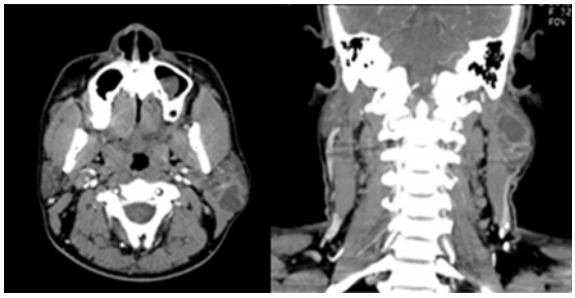

Fig. 2 A computerized tomographic was obtained a well-defined border mixed enhancing solid and cystic mass 2.3x2.8 centimeters at inferior aspect of superficial lobe of parotid gland.

He had no underlying disease or other illness, but anti-HIV was positive from the pre-operative laboratory screening. Standard of care for HIV infection was done. Blood studies revealed CD4 count 264 cell/mm^3 (11.67%). VDRL, HBsAg and Anti-HCV were negative.

Left parotidectomy was performed. Intra-operative finding was the compound cystic mass involved superficial and deep lobe of the left parotid gland attached to sternocleidomastoid and posterior belle of the digastric muscle, but invaded neither nerves

Fig. 3 Gloss pathology showed compound cystic mass.

Fig. 4 Intraoperative finding was left parotid mass involved superficial and deep lobe attached to sternocleidomastoid muscle. No lymph node enlargement.

nor adjacent organs. Lymph nodes were not found (Fig. 3,4). The final operation was total parotidectomy.

A post-operative Jackson-Pratt drain was placed for prophylaxis fluids draining. The length of stay was 5 days. At the first follow-up at seventh post-operative day, the drain was removed. A post-operative complication was the neurapraxia of the marginal mandibular branch and frontal branch of the facial nerve that fully recovered in 2 weeks. The 1-month follow-up on this patient represents with no postoperative morbidity, normal facial nerve function, and a well healed scar. The medical treatments of HIV infection in the perioperative period and in the long term were performed.

Histological findings reveal a cystic space lined by multilayered squamous epithelium with sub-epithelial florid lymphoid hyperplasia (Fig. 5).

Discussion and literature review

Lymphoepithelial cysts are known to arise in the lateral cervical areas, which are referred to as branchial cleft cysts or in the oral mucosa. In addition to these 2 major sites, the parotid gland has been recognize as parotid gland enlargement is reported to occur in approximately 1-10% of HIV-infected patients[2]. Benign lymphoepithelial cysts (BLCs) that develop secondary to a benign lymphoproliferative disease. It is common in adult and children not on ART. This can often be the first indication of human immunodeficiency virus infection.

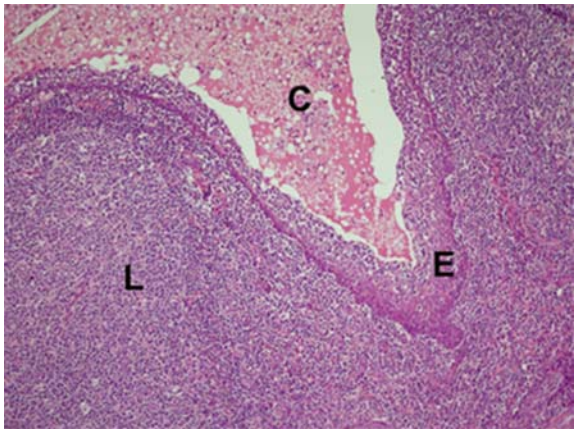

Fig. 5 Histologic section reveals a cystic space (C) lined by multilayered squamous epithelium (E) with sub-epithelial florid lymphoid hyperplasia (L). Proprietary by Kintarak J.

Numerous terms and wide spectrum of disease have been used to describe lymphatic parotid enlargement including; Benign lymphoepithelial lesions (BLEL), Benign lymphoepithelial cysts (BLEC), Cystic BLEL, AIDS-related lymphadenopathy, Diffuse infiltrative lymphocytosis syndrome (DILS), Cystic lymphoid hyperplasia, HIV-associated salivary gland disease[2], and Lymphoepithelial sialadenitis (LESA) of Sjogren syndrome. Therefore, lymphatic parotid enlargement can be both HIV-related and unrelated reaction.

BLEC has two hypothesized etiologic mechanisms. The first pathogenesis is "sialadenitis-based theory" that starts from the dilatation of ducts due to duct epithelial hyperplasia, which might be stimulated by lymphocytic infiltration in focal sialadenitis and consequent cystic enlargement of dilated ductal lumina then the lesion is demarcated from the parotid tissue because of granulation tissue reaction, which may be completed in fibrous capsules[2,3]. The second hypothesized "obstructive theory" is that HIV-related reactive lymphoproliferation and of the intraparotid lymph nodes with interstitial lymphoid infiltrate, causing entrapped lymphoepithelial lesions of striated ducts with basal cell hyperplasia. The frequent progression to a multifocal cystic lymphoepithelial lesion[4-7].

Table 1. Advantages and disadvantages of treatment for benign lymphoepithelial cysts of the parotid gland

	Advantage	Disadvantages
HAART therapy	Noninvasive	Incomplete response
	Standard of care for HIV	
	Not need hospital stay	
FNA drainage	Minimally invasive	Temporaty improvement, high recurrence rate
	Avoids radiation	Multiple treatments
	Not need hospital stay	
Radiation therapy	Noninvasive	Therapeutic doses of radiation (24 Gray)
	Avoids needle stick	Side effects include xerostomia,skin necrosis, mucositis
	Not need hospital stay	Incomplete response
Sclerotherapy	Minimally invasive	Multiple treatments
	Avoids radiation	Varying degrees of drug toxicities rangingfrom rash to pulmonary fibrosis
	Not need hospital stay	Incomplete response
		Fibrosis makes future surgery more difficult
Surgery	Complete response	General anesthesia
	Avoids radiation	In hospital stay
		2-6-hour invasive procedure
		Surgical scar
		Surgical complications; hematoma (7%), facial nerve injury (2.3-6%),
		Frey's syndrome (5%), recurrence (2%) in the remaning parotid tissue

Clinical features are slow growing, soft, cyst-like, painless masses involving the superficial lobe, commonly bilateral and multiple, cervical lymphadenopathy, rarely with facial nerve involvement and can cause gross facial deformities[5,6,8-10]. There are 3% dysplastic changes in a study[3]. In addition, there have been no definite cases of LE carcinomas arising from LE cysts reported in the literature.

Fine needle aspiration (FNA) cytology is considered the basic and minimal invasive diagnostic and therapeutic tool. Characteristic triad of squamous cells, lymphocytes and foamy macrophages[8-10].

Imaging modalities (e.g. ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) are generally not required[8,10].

The differential diagnosis of parotid cysts includes: Branchial cysts, Salivary duct cysts, Traumatic sialocoeles, Sjogren's syndrome, Lymphangiomas, Cryptococcus, polycystic parotid disease, Cystic tumors such as Warthin's, Mucoepidermoid carcinoma and Cystadenocarcinoma, Cystic metastases from cutaneous squamous cellcarcinoma and Melanoma, Hydatid cysts, Tuberculous abscesses, and even possible confusion with a Lipoma[11].

A unilateral, solid mass with involve of the skin, cranial nerve 7, fixed nature should lead to an imaging and FNA to exclude an infection or malignant processTreatment for benign lymphoepithelial cyst is sought mainly for cosmetic reasons[8]. This clinical commentary analyzes the cosmetically deforming disease entity, and the many treatments that accompany it, and includes conservative treat with institution of highly active antiretroviral therapy (HAART), repeated fine-needle aspiration and drainage, radiotherapy, sclerotherapy and surgery[5,8,10,11].

A literature review of the aforementioned treatments for BLEC summarizes the advantages and disadvantages, duration of procedures and the cost of treatment for BLEC[11].

HAART therapy is theorized to correct the root cause of BLEC. This has not been shown to be quantitatively effective in decreasing the size of the lesions.

Repeated fine-needle aspiration and drainage is a popular treatment, which rules out the possibility of another pathologic condition. Cysts can be drained up to twice per month, but there is a 100% recurrence. For radiation therapy, in 1995 and 1999 studies showed not only fewer responses and no long-term local control, but also many side effects of radiation.

Sclerotherapy injections includes multiple sclerotic agents, e.g. sodium morrhuate, doxycycline, ethanol, bleomycin, and OK-432 (picibanil), that easily be done as an outpatient. Need Multiple treatments and there are varying degrees of drug toxicities *e.g.* local edema/erythema, rash, low-grade fever, and Life-threatening irreversible pulmonary fibrosis. Sclerosing agents produce inflammation and fibrosis makes future surgery more difficult.

The role of surgery is now limited to the few cases of diagnostic uncertainty or patients with deforming lesion.

Reservations regarding parotidectomy in HIV-infected patients include the following: immunocompromised patients have a higher rate of postoperative infections, there is an unnecessary risk of HIV transmission imposed on the surgeon and the surgical team, and there could be facial nerve injury.

The medical treatment of HIVpatients in the perioperative period has been developed, and with the advent of viral load measurement, the risks of HIV transmission during surgery have been dramatically reduced. Recent studies show that the postoperative rate of infection in HIV-infected patients is similar to that in the normal population. In the hands of an experienced surgeon, parotid gland surgery for benign disease has been shown to have a permanent paresis rate of 2.3% (one or more branches of the facial nerve), while partial superficial parotidectomy has a permanent paresis rate of 0%[11].

Conclusion

Human immunodeficiency virus testing is recommended for patients with benign lymphoepithelial cysts, as this can often be the first indication of HIV infection.

Fine needle aspiration (FNA), a relatively non-traumatic procedure, could represent both a diagnostic and a therapeutic tool in parotid BLECs. There are many choices of treatment; anti-retroviral therapy, repeated fine-needle aspiration and drainage, radiotherapy, sclerotherapy and surgery. Surgery is the gold standard treatment for BLEC, as evidenced by this literature review and case example.

Potential conflicts of interest

None.

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Lymphoepithelial ของต่อมพาโรติดในผู้ป่วยติดเชื้อเอชไอวี

ณัฏฐาพร ปิยะสาธุกิจ, สุรจิต อาวสกุลฤทธิ, จุฑาทิพย์ ดินทรักษ์

ต่อมพาโรติดโตในผู้ป่วยที่ติดเชื้อเอชไอวีโดยส่วนมากเกิดจากโรคถุงน้ำ lymphoepithelial ซึ่งเป็นอาจพบเป็นอาการและอาการแสดงแรกที่บ่งชี้ถึงการติดเชื้อเอชไอวี พบว่าเกิดจากเซลล์เม็ดเลือดขาว lymphocyte แทรกในต่อมพาโรติดซึ่งเป็นการตอบสองของร่างกายต่อเชื้อเอชไอวี โดยพยาธิกำเนิดยังไม่แน่ชัด การเจาะดูดด้วยเข็มเล็ก และส่งตรวจทางเซลล์วิทยา (FNA) เป็นการส่งตรวจเบื้องต้นที่สามารถให้การวินิจฉัยได้ โรคถุงน้ำ lymphoepithelial สามารถมีขนาดใหญ่และส่งผลให้ผิดรูปของใบหน้า โดยการรักษาเพื่อรักษาโรคและอาการของโรคนั้นมีหลายทางเลือกคือ การใช้ยาต้าน retroviral การเจาะดูดระบายถุงน้ำด้วยเข็มเล็ก (FNA), การใช้รังสีรักษา, การฉีดสารเพื่อให้เกิดการอักเสบในถุงน้ำ (sclerosing therapy), และการผ่าตัดต่อมพาโรติด ในการศึกษานี้เป็นตัวอย่างโรคถุงน้ำ lymphoepithelial ที่ติดเชื้อเอชไอวีและได้รับการรักษาโดยการผ่าตัด และติดตามผลการรักษาในระยะเวลา 1 เดือนหลังการผ่าตัด โดยผลการศึกษาในผู้ป่วยรายนี้ร่วมกับการทบทวนวรรณกรรมสรุปได้ว่าการรักษาโรคถุงน้ำ lymphoepithelial โดยการผ่าตัดต่อมพาโรติดให้ผลดีที่สุดการตอบสนองของโรคต่อการรักษาและความสวยงาม