Clinical Case Report

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Lymphoepithelial carcinoma of the salivary glands

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Abstract

Rationale: Lymphoepithelial carcinoma (LEC) is a rare malignancy with the histopathological feature of undifferentiated carcinoma and an intermixed reactive lymphoplasmacytic infiltration. Although clinically significant because of its malignant nature, it is difficult to make a differential diagnosis by preoperative imaging. Here, we report 3 cases of primary LEC arising in the major salivary glands, which showed unusual imaging features unlike other malignant tumors.

Patient concerns: Our first case is a 44-year-old man with LEC in the right parotid gland, the second case is a 71-year-old woman with LEC in the right submandibular gland, and the third case is a 35-year-old woman with LEC in the right parotid gland. All of the patients presented with a palpable mass of variable duration.

Diagnoses: Computed tomography (CT) scans revealed a relatively well-defined, slightly hyperattenuated exophytic solid mass that had homogeneous well-enhanced regions. Ultrasonography (US) in the first 2 cases showed well-defined, hypoechoic solid masses with posterior enhancement. The CT findings seem to be benign tumors, but US features are compatible with highly cellular and hypervascular tumors.

Interventions: The resection of the involved salivary gland with postoperative radiation therapy was performed.

Outcomes: There was no evidence of recurrence or metastasis after 5 years in all 3 patients.

Lessons: Understanding these unusual imaging findings may be helpful in detecting LEC, and may also help clinicians provide adequate management to patients, such as surgery with adjuvant radiotherapy, because of its malignant entity.

Abbreviations: ADC = apparent diffusion coefficient, CT = computed tomography, DWI = diffusion-weighted imaging, EBER = Epstein-Barr virus-encoded small RNA, EBV = Epstein-Barr virus, FNA = fine-needle aspiration, LEC = lymphoepithelial carcinoma, MR = magnetic resonance, PET-CT = positron emission tomography-computed tomography, RT = radiotherapy, T1W = T1-weighted, T2W = T2-weighted, US = ultrasonography.

Keywords: computed tomography, lymphoepithelial carcinoma, salivary gland, ultrasonography

1. Introduction

Lymphoepithelial carcinoma (LEC) is an uncommon malignant tumor composed of undifferentiated malignant epithelial cells with characteristic lymphoid stroma.[1,2] The most common location of LEC is the nasopharynx. However, it can also occur in other organs including the salivary glands, particularly the parotid and submandibular glands. However, LEC in these glands is very rare, only accounting for 0.4% of the malignant tumors.[1] LEC has a unique ethnic predilection for the Eskimo, Chinese, and Japanese populations,[3] with a significant association with Epstein-Barr virus (EBV).[4] These tumors mainly affect females in the fifth decade of life.[5] Although it is clinically significant because of its malignant entity, it is difficult to make a differential diagnosis by preoperative imaging of a salivary gland mass.

Here, we report 3 rare cases of confirmed LEC originating from the salivary glands and discuss the radiologic features of LEC and several considerations of salivary gland tumors.

2. Case report 1

A 44-year-old man presented with a painless, slowly growing palpable mass in the right preauricular region for 1 year. Upon physical examination, an approximately 3-cm, well-defined mobile mass was found in the right parotid area. Facial nerve function was intact, and there were no palpable enlarged cervical lymph nodes. Otherwise, he had no notable medical history. Contrast-enhanced computed tomography (CT) scans revealed an oval-shaped, well-defined, hyperattenuated exophytic solid mass compared to the parotid gland, which had homogeneous enhancement in the inferior aspect of the right parotid gland. There was no evidence of cystic change or calcification in the mass and no enlarged lymph nodes (Fig. 1A, B). Ultrasonography (US) showed a round, well-defined hypoechoic solid mass with posterior enhancement in the lower portion of the right parotid gland ($1.9 \times 1.7 \times 1.9$ cm, 3.1 mL). Color Doppler images revealed focal increased vascularity in the hypoechoic mass (Fig. 1C). A US-guided fine-needle aspiration (FNA) biopsy was performed, and the histopathological report showed metastatic squamous cell carcinoma. The patient underwent magnetic resonance (MR) imaging; the mass lesion was

Editor: Meihua Zhu.

The authors declare no conflict of interest.

This study was approved by the institutional review board of the Soonchunhyang University Hospital. It has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The institutional review board of this university waived the need to obtain informed consent.

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Medicine (2017) 96:7(e6115)

Received: 14 July 2016 / Received in final form: 4 January 2017 / Accepted: 20 January 2017

http://dx.doi.org/10.1097/MD.0000000000006115

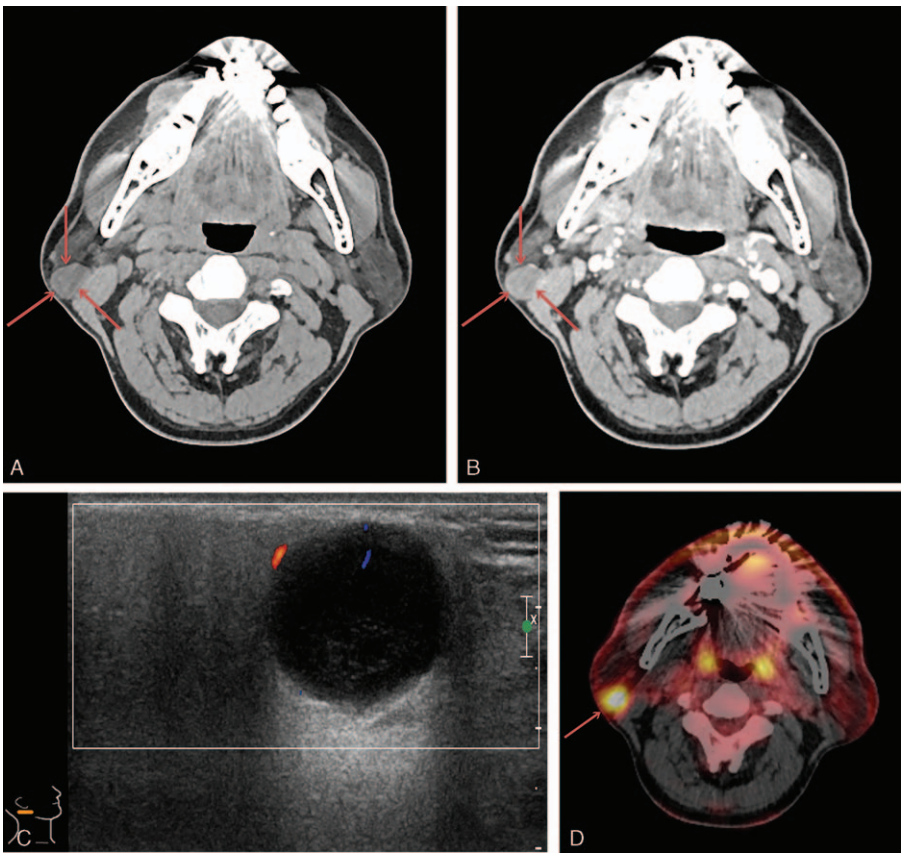

Figure 1. (A) A 44-year-old man presented with a palpable preauricular mass for 1 year. A precontrast computed tomography scan shows a hyperdense homogeneous solid mass compared to the surrounding parotid gland. (B) The mass shows well-defined homogeneous enhancement on a postcontrast scan. (C) Color Doppler ultrasonography shows a well-defined hypoechoic solid mass with posterior enhancement and focal increased vascularity in the hypoechoic mass in the lower portion of the right parotid gland. (D) The mass shows hypermetabolism on a positron emission tomography-computed tomography scan; the maximal SUV was 6.5.

isointense relative to muscle with homogeneous and strong enhancement in T1-weighted (T1W) images, and was hyperintense relative to the parotid gland in T2-weighted (T2W) images. It also showed diffusion restriction in diffusion-weighted imaging (DWI). Because the FNA biopsy revealed metastatic squamous cell carcinoma, a positron emission tomography-computed tomography (PET-CT) scan was performed to evaluate the primary malignancy. There was no evidence of hypermetabolic lesions except for a biopsy-confirmed salivary mass (Fig. 1D). The patient underwent a total right parotidectomy, and the resected parotid gland showed a 2.0×1.7-cm sized well-circumscribed gray-white, round, solid mass. Histologic findings revealed sheets of cohesive tumor nests with dense lymphoid proliferation (Fig. 2A). The tumor cells had enlarged vesicular nuclei with prominent nucleoli and indistinct cell borders. In situ hybridization for EBV, Epstein-Barr virus-encoded small RNA (EBER), was positive in tumor cells (Fig. 2B). The patient was discharged without complication and postoperative radiation therapy was performed. There was no evidence of recurrence or metastasis after 5 years.

3. Case report 2

A 71-year-old woman was admitted with a painful, recently growing palpable mass in the right submandibular region for 1 week. According to the patient, the mass was first detected 3 months ago, and she had not experienced any discomfort associated with the mass at the time. Upon physical examination, an approximate 2-cm, firm, and movable mass was found in the right submandibular area. Examination of the oral cavity, oropharynx, and laryngopharynx found no lesions. The patient had a medical history of insulin-dependent diabetes and hypertension, which had occurred about 4 years before. Contrast-enhanced CT scans showed a lobulated, marginated, well-enhanced exophytic solid mass with an internal cystic change, abutting to the right submandibular gland (Fig. 3A). There were no enlarged lymph nodes. US revealed an approximate 2-cm, well-defined, lobulated hypoechoic solid mass with posterior enhancement, which was abutting to the right submandibular gland. Color Doppler images showed increased vascularity in the hypoechoic mass (Fig. 3B). The patient underwent excision and biopsy with right neck dissection, which was confirmed as LEC on pathology. The patient had no evidence of recurrence or metastasis after 5 years.

4. Case report 3

A 35-year-old healthy woman complained of a palpable and slowly growing mass in the left periauricular region for 3 years. At the time, the patient had no pain and her facial nerve was intact. Physical examination revealed a 2-cm, nontender, and movable mass in the left parotid area. Contrast-enhanced CT scans showed a round, well-defined, hyperdense solid mass with homogeneous enhancement in the superficial lobe of the left parotid gland. There

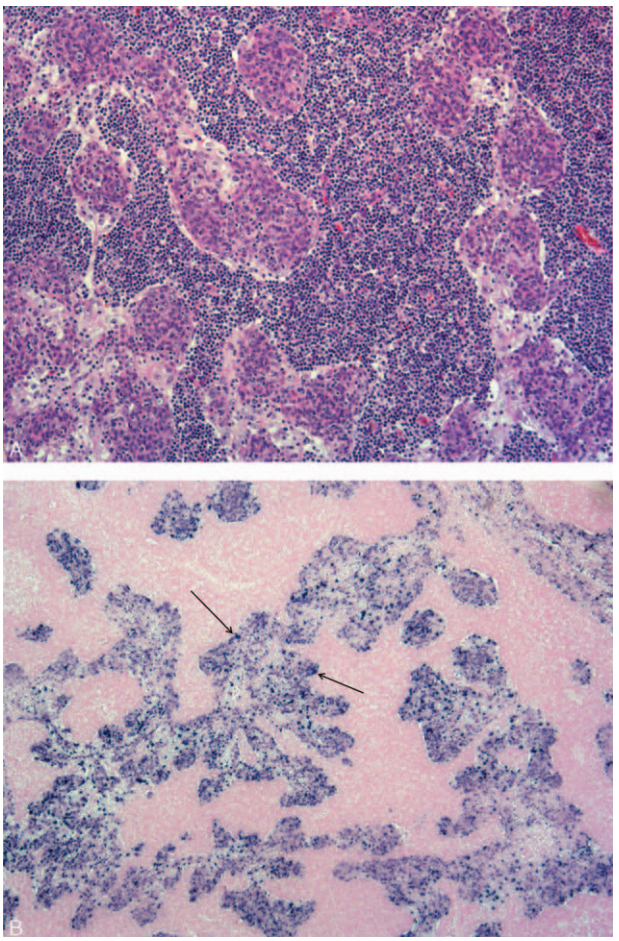

Figure 2. (A) Microscopic findings reveal sheets of cohesive tumor nests with dense lymphoid proliferation (H&E stain, 100×). (B) In situ hybridization for Epstein-Barr virus was positive in tumor cells.

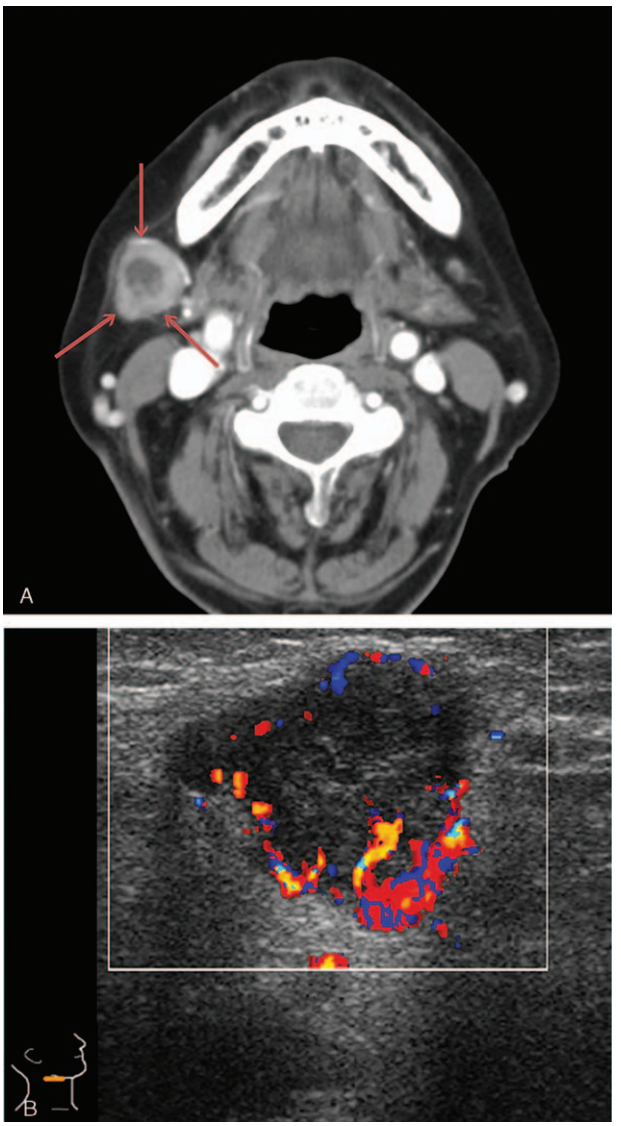

Figure 3. (A) A 71-year-old woman was admitted with a painful, recently growing palpable mass in the right submandibular region for 1 week. A well-enhanced solid mass with an inner cystic change is seen on the enhanced computed tomography scan. (B) Color Doppler ultrasonography shows a well-defined, lobulated hypoechoic solid mass with posterior enhancement and increased vascularity in the hypoechoic mass, abutting to the right submandibular gland.

was no evidence of cystic change or calcification in the mass, and no enlarged lymph nodes (Fig. 4). The patient underwent a left superficial parotidectomy, which confirmed LEC. The patient was discharged without complication. The patient had no evidence of recurrence or metastasis after 5 years.

5. Discussion

Salivary gland tumors are uncommon neoplasms, accounting for <3% of all head and neck tumors.[6] They comprise a diverse group of benign and malignant histologies with a variety of differential diagnoses with different treatments and prognoses. However, FNA cytology can be inconclusive in cases of improper sampling or inaccessible tumor location. Therefore, preoperative imaging plays an important role in the management of salivary gland tumors.

Most salivary gland tumors are benign and 80% occur in the parotid gland. The general rule about salivary gland neoplasms is that the smaller the salivary gland involved, the higher the malignancy rate. Thus, the malignancy rate increases from 20% to 25% in the parotid gland to 40% to 50% in the submandibular gland and to 50% to 81% in the sublingual and minor salivary glands. The most common tumors of the salivary gland are pleomorphic adenomas, and the most frequent malignancy of the parotid gland is mucoepidermoid carcinoma. In the submandibular, sublingual, and minor salivary glands, adenoid cystic carcinoma is the most common malignancy.[7–10] Tumors in these glands are either primary salivary tumors, which arise in lymphatic tissue, or metastases; they rarely originate from other tissues such as blood vessels, nerves, and fat.

Pleomorphic adenoma is the most common salivary gland tumor and represents 70% to 80% of all benign tumors of the major salivary glands. These tumors show typical imaging features of a benign-appearing tumor. Pleomorphic adenomas are typically solitary, ovoid, and well-defined masses that have high attenuation compared to the surrounding parotid parenchyme. In contrast-enhanced CT scans, all of these tumors have variable enhancement. The smaller masses have homogeneous enhancement, and the large masses often have a heterogeneous appearance with internal necrosis, old hemorrhage, cystic changes, and dystrophic calcifications. There are several

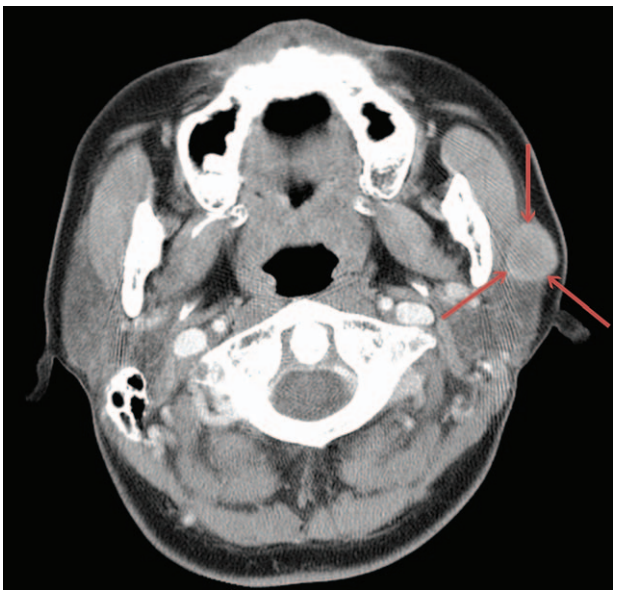

Figure 4. . A 35-year-old healthy woman complained of a palpable and slowly growing mass in the left periauricular region for 3 years. Contrast-enhanced computed tomography scans showed a round, well-defined, hyperdense solid mass with homogeneous enhancement in the superficial lobe of the left parotid gland.

suspicious findings indicative of malignant salivary gland tumors such as irregular tumor margins, extension to adjacent structures, and the presence of metastatic regional lymph nodes. The presence of pain, facial nerve invasion, and rapid tumor growth are also highly suspicious features of malignancies. However, low-grade malignant tumors do not have these features.[11]

Preoperative imaging such as MR imaging, CT, and US has a major role in differentiation of pleomorphic adenoma from other primary malignant tumors, and surgical planning. MR imaging is the method of choice for palpable masses of salivary glands with a strong suspicion of malignancy. On conventional MR imaging, T2 hypointensity and ill-defined margin on postcontrast image of a parotid tumor were proven as useful indicators for malignancy.[12] Recently, new MR techniques such as DWI with apparent diffusion coefficient (ADC) value and proton MR spectroscopy have shown promising results in the differentiation between benign and malignant salivary gland tumors. One report revealed that the mean ADC values of malignant tumors were significantly lower than pleomorphic adenoma and significantly higher than Warthin tumors.[13] Also, CT perfusion, which provides a tissue time-density curve and perfusion data, was useful in the differentiation of benign and malignant tumors in the parotid gland.[14] US is a very sensitive modality in identifying the salivary gland tumors.

LEC is a rare malignancy that is histologically defined as an undifferentiated carcinoma featuring atypical epithelial cells with interstitial infiltrations by lymphocytes and plasma cells.[1,2] The most common location of LEC is the nasopharynx; LEC occurring in the salivary glands is very rare, accounting for only 0.4% of all of the malignant tumors.[1] LEC of the salivary gland was first described by Hilderman et al in 1962, predominantly occurring in the parotid gland with striking geographic and ethnic distribution including the Eskimo, Chinese, and Japanese populations.[3,4] In general, women are more affected than men, and the average age of diagnosis is 40 years.[5] The EBV genome is present in LEC, indicating a strong causal relationship and significant correlation between the virus and carcinoma.[15] However, according to the previous study by Zhan et al[16] with LEC of the major salivary glands from a nonendemic region, the United States, EBV was not detected in these patients of the nonendemic regions. It suggested that the possibility of other pathogenesis involving the carcinogenesis of the LEC. Most patients with LECs had unilateral episodes that manifested as slow-growing, painless masses with variable duration.[1] Owing to the high radiosensitivity of LEC, surgery with radiotherapy (RT) is considered the treatment of choice for this disease, which had the significant impact to improved survival outcomes than surgery alone.[16,17]

LEC mostly affects the parotid gland, whereas involvement of both the submandibular and minor salivary glands is less common. In CT scans, most LECs are solitary, solid, and poorly defined with lobulated contours, homogenous isodensity to slightly low density, less complicated cystic degeneration and calcification, and marked enhancement.[18] LECs are typically isointense on T1W images, and

Table 1

Clinical and imaging features of patients with lymphoepithelial carcinoma of salivary glands.

	Case 1	Case 2	Case 3
Clinical profile			
Sex/age	M/44	F/71	F/35
Chief complaints	Palpable mass	Palpable mass	Palpable mass
Symptom duration	1 y	3 mo	3 y
Epstein-Barr virus on pathology	+	+	+
Imaging characteristics			
Tumor location	Right parotid	Right submandibular	Left parotid
Tumor size, cm	$1.9 \times 1.7 \times 1.9$	$2.2 \times 1.9 \times 2.2$	$1.7 \times 1.5 \times 1.8$
Tumor margin	Well defined, oval	Frank invasion to extraglandular soft tissue	Well defined, round
Inner necrosis	−	+	−
CT scan	Hyperdense compared to salivary gland	Hyperdense	Hyperdense
Enhancement pattern	Homogeneous, well	Well, inner cystic change	Homogeneous, well
Ultrasonography	Hypoechoic solid mass with posterior enhancement	Hypoechoic solid mass with posterior enhancement	Not performed
Color Doppler image	Focal increased vascularity	Focal increased vascularity	Not performed
MR imaging	Isointense on T1WI, hyperintense on T2WI	Not performed	Not performed
PET-CT scan	Hypermetabolic	Not performed	Not performed
Pathologic lymph nodes	−	−	−

+ = present, − = not present, CT = computed tomography, MR magnetic resonance, PET-CT = positron emission tomography-computed tomography, T1WI = T1-weighted image, T2WI = T2-weighted image.

have low signal intensity on T2W images with moderate enhancement on MR images. However, these imaging findings are nonspecific, making it difficult to definitively differentiate from other benign and malignant tumors of the salivary glands. Unlike other malignant salivary tumors, such as mucoepidermoid carcinoma and adenoid cystic carcinoma, cystic degeneration and calcification are rare in LEC and typically show homogeneous attenuation or signal intensity.

In our cases, CT showed well-defined, enhancing, exophytic, homogeneous masses in the salivary glands with internal necrosis in only 1 case. US revealed a hypoechoic solid mass with posterior enhancement and increased vascularity on Color Doppler images in 2 cases. On MR imaging of case 1, the mass lesion was isointense relative to muscle in T1W image, hyperintense relative to the parotid gland in T2W image, and well-defined margin on post contrast T1W image (Table 1). These CT and MR findings seem to be benign tumors, but US features are compatible with highly cellular and hypervascular tumors. When these atypical findings are encountered, an LEC diagnosis should be considered.

In conclusion, LEC represents a rare malignant tumor of the salivary gland, and may be diagnosed when a well-defined, homogeneously attenuated, and relatively significant enhancing tumor is seen in the salivary gland with an exophytic growth pattern, particularly in the parotid gland. Furthermore, US can be helpful for discriminating between highly cellular and hypervascular tumors such as LECs. Additional information including the correlation with different ethnic groups and EBV should be considered. Understanding these unusual imaging findings may be helpful in detecting LEC, and may also help clinicians provide adequate management to patients, such as surgery with adjuvant RT, because of its malignant entity.

Acknowledgement

The authors are not associated with the funding.

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