RESEARCH ARTICLE

Lymphoepithelial carcinoma of salivary glands: CT and MR imaging findings

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Objectives: To depict the CT and MRI characteristics of salivary gland lymphoepithelial carcinoma (LEC) and provide more diagnostic information for this malignancy.

Methods: 103 salivary gland LEC subjects were retrospectively reviewed. The subjects include 35 males with a mean age of 40.8 years and 68 females with a mean age of 49.4 years. Of the 103 subjects, 86 had carcinomas in the parotid gland, 5 in the submandibular gland, 1 in the sublingual gland, 3 in the cheek and 8 in the palate. All subjects underwent routine CT and MRI (plain and contrast-enhanced scans) prior to surgical treatment and histopathological examination.

Results: Based on the pathological outcomes, all the salivary gland LECs were classified into two types from CT and MRI scans: solitary LEC (56 cases, 54.4%) and multiple LEC (47 cases, 45.6%). The latter included solitary salivary gland LEC with extraglandular lymph-node metastases (12 cases), parotid gland LEC with ipsilateral intraglandular lymph-node metastases (11 cases), parotid gland LEC with ipsilateral intra- and extraglandular lymph-node metastases (23 cases) and bilateral parotid gland LEC (1 case). The salivary gland LEC was depicted on CT and MRI scans as a lobular mass in 64 of 104 (61.5%), homogeneous mass in 65 of 104 (62.5%) or enhanced neoplasm in 94 of 104 (90.4%).

Conclusions: Salivary gland LEC has a predilection for females in the fourth to fifth decade of life and the parotid gland. CT and MRI findings between solitary and multiple salivary LECs vary. A majority of multiple parotid gland LECs are characterized by metastasis of ipsilateral intraglandular lymph nodes, which may accompany with or without extraglandular lymph-node metastases.

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Introduction

According to the 2005 World Health Organization classification of salivary gland tumours, lymphoepithelial carcinoma (LEC) is defined as “an undifferentiated carcinoma accompanied by a prominent non-neoplastic lymphoplasmacytic infiltrate”,¹ which replaces a previous subtype termed “undifferentiated carcinoma with lymphoid stroma”. Salivary

gland LEC is considered a rare malignant tumour accounting for less than 1% of all malignant salivary gland tumours, but has a marked racial predilection for Inuit and Southeast Asian populations. An investigation from the endemic area with a large sample (6982 cases) indicated that there was a relatively high incidence of salivary gland LEC (5%) among all the malignant salivary gland tumours.² Therefore, it is meaningful to evaluate this condition for clinical diagnosis and management.

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Table 1 General information of 103 subjects with salivary gland LEC

Location of LEC	Parotid gland	Submandibular gland	Sublingual gland	Palate gland	Buccal gland	Total
No. of cases (%)	86 (83.5%)	5 (4.9%)	1 (1%)	8 (7.8%)	3 (2.9%)	103
No. of males	30	2	1	1	1	35
Mean age (age range) for males (years)	38.4 (16–64)	48 (25–71)	42	62	76	40.8
No. of females	56	3	0	7	2	68
Mean age (age range) for females (years)	47 (11–82)	51.3 (49–53)	0	61.6 (29–82)	71.5 (66–77)	49.4
Male/female	1:1.87	1:1.5	1:0	1:7	1:2	1:1.94
Mean age (range) (years)	44 (11–82)	50 (25–71)	42	61.6 (29–82)	73 (66–77)	46.5
Metastatic lymph nodes (%)	40 (46.5%)	3 (60%)	1 (100%)	2 (25%)	0 (0%)	46 (44.7%)

LEC, lymphoepithelial carcinoma.

The roles of routine CT and MRI examinations in diagnosis of salivary gland tumours have been extensively described. Recently, a few articles described the CT and MRI findings of salivary gland LEC.^{3,4} However, the number of cases from these studies is based on a relatively small sample. To promote the overall evaluation, a supplement for CT and MRI findings of salivary gland LEC on the basis of the relatively large sample is required, especially in minor salivary gland LEC. The objectives of this study are to depict the CT and MRI characteristics of salivary gland LEC, compare the similarities and differences of CT and MRI findings between major and minor salivary LECs and provide more information for diagnosing this disorder.

Methods and Materials

The guidelines of the Helsinki Declaration were obeyed in this research. From March 1999 to December 2015, 103 subjects were surgically-pathologically confirmed to have salivary gland LEC, in whom malignant tumours arising from the nasopharynx and other sites were excluded. All the subjects underwent routine plain and contrast-enhanced CT and MR scans at our institute, including 84 subjects with only CT scan (from 1999 to 2015), 11 subjects with only MRI scan (from 2003 to 2015) and 8 subjects with both. The general information for these 103 subjects is listed in Table 1. A comparison of general information between major and minor salivary gland LECs is shown in Table 2.

CT scans were performed using a Siemens Somatom ART (Siemens Ltd, Medical Engineering Group, Erlangen, Germany) on 10 subjects and 16-section GE LightSpeed® (General Electric Medical Systems, Milwaukee, WI) on the remaining 82 subjects. CT scans were acquired at 130 kV/210 mAs (Somatom ART) and 120 kV/250 mAs (GE LightSpeed). Axial section of 5 mm thickness, reconstructed at 1.25 mm (GE LightSpeed), was carried out using a soft-tissue algorithm. A bolus intravenous injection of 80 ml (injection rate of 1.5–2.0 ml s⁻¹) of a non-ionic contrast medium (iodine 300mg m⁻¹) was administered to all the 92 subjects.

MR scans were performed on a 1.5 T GE Signa Twin-Speed system (General Electric Medical Systems), and a neurovascular array coil was used. Axial plain MR images were obtained using a T_1 weighted spin-echo sequence (TR/TE = 600/11 ms) and a T_2 weighted fast spin-echo sequence (TR/TE = 4700/85 ms) with field of view = 24 cm, acquisition = 3, matrix = 256 × 192, slice thickness = 5 mm and spacing = 1. Coronal MR images were acquired using a T_2 weighted fast spin-echo sequence (TR/TE = 3200/100 ms, field of view = 20 cm, acquisition = 3, matrix = 320 × 160, slice thickness = 5 mm and spacing = 1). An intravenous injection of gadolinium contrast medium (0.1 mmol kg⁻¹ of body weight) was administered to all the 19 subjects. Axial and coronal contrast-enhanced T_1 weighted spin-echo sequence with or without fat suppression were scanned after the intravenous injection of gadolinium contrast medium.

The observed items on CT and MR images include LEC location, size (maximum diameter of the maximum mass on axial or reconstructed coronal images), number (solitary or multiple), shape (irregular, round or oval, lobular), internal structure (homogeneous or heterogeneous attenuation/signal intensity; calcification), and margins (even, uneven, partial even and uneven). The

Table 2 Comparison of general information between major and minor salivary gland LECs

Location of LEC	Major salivary LEC	Minor salivary LEC	Total
No. of cases (%)	92 (89.3%)	11 (10.7%)	103
No. of males	33	2	35
Mean age (age range) for male (years)	39.1 (16–71)	69 (62–76)	40.8
No. of females	59	9	68
Mean age (age range) for female (years)	47.2 (11–82)	63.8 (29–82)	49.4
Male/female	1:1.79	1:4.5	1:1.94
Mean age (range) (years)	44.3 (11–82)	64.7 (29–82)	46.5
Metastatic lymph nodes (%)	44 (47.8%)	2 (18.2%)	46 (44.7%)

LEC, lymphoepithelial carcinoma.

Figure 2 Solitary LEC sited in the right palate (70-year-old female). Axial contrast-enhanced CT image shows a lobular mass with homogeneous enhancement in the right palate (black arrow). Right palate and upper alveolar bone resorption is also found.

enhanced degree of salivary gland LEC after the intravenous administration of contrast medium was classified into “non-enhancement” and “enhancement”. The former was defined as attenuation or signal intensity of neoplasm lower than or similar to that of the adjacent

Figure 1 Solitary LEC sited in the right buccal space (76-year-old male). Axial contrast-enhanced CT image shows a lobular and homogeneous mass with partial even and uneven margins in the right buccal space. The density of the mass is similar to that of the adjacent muscles.

Figure 3 Sublingual gland LEC (right side) with ipsilateral extraglandular lymph-node metastasis (Type 1; 42-year-old male). Axial contrast-enhanced CT image shows a lobular and homogeneous mass with partial even and uneven margins in the right sublingual gland (white arrow). An enlarged lymph node is also found in level II of the ipsilateral neck, and accompanied with adjacent internal jugular vein deformation due to the compression of this metastatic lymph node (black arrow).

muscle, and the latter as greater than that of the adjacent muscle. The homogeneous and/or heterogeneous masses were recorded after the intravenous administration of contrast medium.

On the basis of the surgical and pathological outcomes, the multiple salivary gland LECs were classified into four types on CT and MRI: Type 1, solitary salivary gland LEC with extraglandular lymph-node metastases; Type 2, parotid gland LEC with ipsilateral intraglandular lymph-node metastases; Type 3, parotid gland LEC with ipsilateral both intra and extraglandular lymph-node metastases and Type 4, bilateral parotid gland LECs.

For multiple salivary gland LECs, the maximum mass within the salivary gland neoplasms shown on CT and MRI was recorded. Thus, for one subject with bilateral parotid gland LECs, the CT and MRI findings of the masses located in both sides were separately recorded.

Two experienced radiologists independently interpreted the CT and MR images. Final decisions regarding CT and MRI findings were reached by consensus.

Results

Surgically and pathologically, 56 of 103 subjects (54.4%) were diagnosed as solitary salivary gland LEC (Figures 1 and 2), and 47 of 103 subjects (45.6%) as multiple

Figure 4 Parotid gland LEC (left side) with ipsilateral intraparotid lymph-node metastases (Type 2; 34-year-old female). Coronal contrast-enhanced T_1 weighted image with fat suppression shows a lobular mass (black arrow) and multiple metastatic lymph nodes (white arrows) are shown in the left parotid gland. All the masses appear as homogeneous enhancement.

salivary gland LECs (Figures 3–6). The latter was histopathologically confirmed as salivary gland LEC with cervical lymph-node metastases in 46 subjects (ipsilateral cervical lymphnode in 45 and bilateral in 1), and the remaining 1 as a bilateral parotid gland LEC (Figure 6). In 47 subjects with multiple salivary gland LECs, there were 12 cases to be included in Type 1 (6 in the parotid gland, 3 in the submandibular gland, 1 in the sublingual gland and 2 in the palatine gland) (Figure 3); 11 cases in Type 2 (Figure 4); 23 cases in Type 3 (Figure 5), and 1 case in Type 4 (Figure 6).

Of 87 subjects with the parotid gland LEC, 40 (46.5%) were pathologically confirmed to have metastases to cervical lymph nodes, in which, the intraparotid

lymph-node metastases were identified in 34 subjects (39.1%). The incidence of intraparotid lymph-node metastases was calculated to be 73.9% (34 of 46 subjects). There was only one subject with multiple parotid gland LECs to have the distant metastasis (lung). No patient with salivary gland LEC was pathologically proved to accompany with lymphoepithelial lesion.

The CT and MRI findings of solitary and multiple salivary gland LECs are listed in Tables 3 and 4, respectively. The CT and MRI findings for all the salivary gland LECs are shown in Table 5.

Of the 56 subjects with solitary salivary gland LEC, 9 (16.1%) were identified as having multiple nodules within the parotid gland on CT and MR images. These multiple intraparotid nodules were pathologically found as a primary parotid gland LEC (maximum diameter ranged from 14 to 35 mm) accompanied with reactive lymph nodes (maximum diameter ranged from 5 to 10 mm). The same situation was also found in one subject with bilateral parotid gland LECs (Figure 6).

Discussion

Compared with the non-endemic areas,⁵ the Eastern Chinese population (endemic area) has a higher rate of salivary gland LEC, accounting for 5–9.7% among all the malignant salivary gland tumours.^{2,6} In the two highest endemic areas of salivary gland LEC, North American Inuit and Eastern China, a slight female predominance and higher frequency of parotid gland involvement were noticed.^{2,7} In this series, we find that a majority of salivary gland LECs involve females in the fourth to fifth decade of life, and a minority of salivary gland LECs seem to have a marked predilection for older females.

In the few published articles referring to the CT and MRI findings of salivary gland LEC,^{3,4} the salivary gland LEC was depicted as an intraglandular mass with a lobulated/plaque-like shape and ill- or partially illdefined margins, accompanied by ipsilateral

Figure 5 Parotid gland LEC (left side) with ipsilateral intra and extraglandular lymph-node metastases (Type 3; 43-year-old male). Coronal CT image reconstructed from axial contrast-enhanced CT images (a) and axial plain T_1 weighted image (b) show the multiple and heterogeneous masses with irregular shape and uneven margins in the left parotid gland. Also, the multiple enlarged lymph nodes with central necrosis are found in level II of the neck. Axial contrast-enhanced T_1 weighted image with fat suppression (c) demonstrates the multiple masses with heterogeneous enhancement.

Figure 6 Bilateral parotid gland LECs (Type 4; 42-year-old female). On axial contrast-enhanced CT image (a) and coronal T2 weighted image (b), a lobular mass (right side) and a round (left side) mass with even margins are separately found in bilateral parotid glands (white arrows). Coronal contrast-enhanced T1 weighted image with fat suppression (c) demonstrates both masses with homogeneous enhancement (white arrows). Also, on both coronal MRI images (b), the multiple, small reactive lymph nodes (black arrows), proved by pathological examination, are shown in bilateral parotid glands, respectively.

lymphadenopathy. In this study, the CT and MRI manifestations of most salivary gland LECs can be generally depicted as an enhanced and homogeneous mass with a lobulated shape and even or partial even margins. According to the CT and MRI findings in this series, salivary gland LEC are firstly classified as solitary and multiple types. We consider that the classification is significant for indicating the clinical diagnosis, management and prognosis estimation. Indeed, salivary gland LEC has a propensity to spread to regional cervical lymph nodes.¹ The incidence of metastasis of regional cervical lymph nodes was reported from 10 to 60%.^{3,5,8} Our results indicate that 45% of all the subjects are found to have the metastases of regional cervical lymph nodes. For the type of multiple salivary gland LECs, most of them are appeared as a primary neoplasm accompanied by the cervical lymph-node metastases, which can be further classified as intraglandular and extra-glandular lymph-node metastases in this study. In fact, CT and MRI findings of salivary

gland LEC varies depending on different sites and types of the neoplasm.

Parotid gland LEC

Among the major salivary glands, the parotid gland is affected in approximately 80% of salivary gland LEC cases.¹ Our series indicate that 84% of salivary gland LEC involved the parotid gland. In this study, for the solitary parotid gland LEC, most of them appear as a homogeneous and enhanced mass with even or partial even margins on CT and MRI. The parotid gland LEC with intraglandular and/or extraglandular lymph-node metastases may be either a homogeneous or heterogeneous enhanced mass. To our knowledge, the malignant epithelial tumours originating from the parotid gland are infrequently reported to accompany with the intraparotid lymph-node metastasis except in parotid gland LEC. The lymph-node metastases within the parotid gland are rarely mentioned in the published studies. Recently, Kashiwagi et al⁹ reported

Table 3 CT and MRI findings of 56 patients with solitary salivary gland LEC

Location of LEC	Parotid gland	Submandibular gland	Palate gland	Buccal gland	Total
No. of patients	45	2	6	3	56
Mean maximum diameter of mass (mm) (range)	28.9 (10–66)	47.5 (33–62)	26 (15–39)	27.7 (21–33)	29.2 (10–66)
Irregular	4	0	1	0	5 (8.9%)
Round or oval	15	0	1	1	17 (30.4%)
Lobular	26	2	4	2	34 (60.7%)
Homogeneous	30	1	6	3	40 (71.4%)
Heterogeneous	15	1	0	0	16 (28.6%)
Calcification	6	0	0	0	6 (10.7%)
Enhancement	42	2	3	2	49 (87.5%)
Non-enhancement	3	0	3	1	7 (12.5%)
Even margin	22	0	1	1	24 (42.9%)
Uneven margin	7	1	2	0	10 (17.9%)
Partial even and uneven margins	16	1	3	2	22 (39.3%)

LEC, lymphoepithelial carcinoma.

Table 4 CT and MRI findings of 47 patients (48 sides) with multiple salivary gland LECs

Location of LEC	Type 1	Type 2	Type 3	Type 4	Total
No. of patients	12	11	23	2	48
Mean maximum diameter of mass (mm) (range)	31.2 (14–54)	30.4 (17–40)	41.6 (17–61)	24 (23–25)	35.7 (14–61)
Irregular	3	1	1	0	5 (10.4%)
Round or oval	4	3	4	2	13 (27.1%)
Lobular	5	7	18	0	30 (62.5%)
Homogeneous	8	7	9	1	25 (52.1%)
Heterogeneous	4	4	14	1	23 (47.9%)
Calcification	1	0	1	0	2 (4.2%)
Enhancement	9	11	23	2	45 (93.8%)
Non-enhancement	3	0	0	0	3 (6.2%)
Even margin	4	5	5	2	16 (33.3%)
Uneven margin	4	3	5	0	12 (25%)
Partial even and uneven margins	4	3	13	0	20 (41.7%)

LEC, lymphoepithelial carcinoma; Type 1, solitary salivary gland LEC with extraglandular lymph-node metastasis; Type 2, parotid gland LEC with ipsilateral intraglandular lymph-node metastasis; Type 3, parotid gland LEC with ipsilateral both intra and extraglandular lymph-node metastasis; Type 4: bilateral parotid gland LECs.

the CT and MRI findings of lymphatic metastatic tumours in the parotid gland. However, in their study, there were no any cases with the primary malignancies arising from the parotid gland itself. Anatomically, only the parotid gland contains the lymph nodes

among the salivary glands. In this study, the incidence of intraparotid lymph node metastases approximates to 74% of all the multiple salivary gland LECs. Therefore, we believe that the primary malignancy accompanied by the intraglandular lymph node metastasis may

Table 5 CT and MRI findings of all the 103 patients (104 sides) with salivary gland LEC

Location of LEC	Parotid gland	Submandibular gland	Sublingual gland	Palate gland	Buccal gland	Total
No. of patients	87	5	1	8	3	104
Mean maximum diameter of mass (mm) (range)	33.9 (10–66)	36.5 (25–62)	22	26.1 (15–39)	27.7 (21–33)	33.1 (10–66)
Irregular	7	1	0	2	0	10 (9.6%)
Round or oval	26	0	1	2	1	30 (28.8%)
Lobular	54	4	0	4	2	64 (61.5%)
Homogeneous	50	3	1	8	3	65 (62.5%)
Heterogeneous	37	2	0	0	0	39 (37.5%)
Calcification	8	0	0	0	0	8 (7.7%)
Enhancement	83	5	0	4	2	94 (90.4%)
Non-enhancement	4	0	1	4	1	10 (9.6%)
Even margin	37	0	0	2	1	40 (38.5%)
Uneven margin	17	2	0	3	0	22 (21.2%)
Partial even and uneven margins	33	3	1	3	2	42 (40.4%)
Mandible erosion	1	1	0	0	0	2 (1.9%)
Palatine bone erosion	0	0	0	2	0	2 (1.9%)
Sternocleidomastoid muscle involvement	28	1	0	0	0	29 (27.9%)
Masseter muscle involvement	8	0	0	0	0	8 (7.7%)
Medial pterygoid muscle involvement	3	1	0	0	0	4 (3.8%)
Lateral pterygoid muscle involvement	2	0	0	0	0	2 (1.9%)
Longus capitis muscle involvement	0	0	0	1	0	1 (1%)
Internal jugular vein involvement ^a	5	2	1	1	0	9 (8.7%)

LEC, lymphoepithelial carcinoma.

^aAll of the internal jugular vein involvement shown on CT and MRI result from the metastatic cervical lymph nodes rather than primary salivary gland LEC.

be characteristic of the parotid gland LEC on CT and MRI although this feature is uncommonly seen for all the salivary gland LECs. On the other hand, we find a phenomenon that a primary LEC within the parotid gland may be accompanied by intraglandular reactive lymph nodes. Although we do not know the real reasons and relationship between the LEC and reactive lymph nodes, the phenomenon seems to be easily confused with the parotid gland LEC with metastases of intraglandular lymph nodes on CT and MRI.

Submandibular gland and sublingual gland LEC

The LEC located in the submandibular gland and sublingual gland is rarely reported in the previous investigations. Our observation is that the general CT and MRI findings of both submandibular and sublingual gland LECs are similar to that of some solitary parotid gland LEC, and most of them appear as a lobulated and homogeneous mass with uneven or partial uneven margins. Both submandibular and sublingual gland LECs seem to have a higher incidence of metastatic lymph nodes of neck (60%).

Minor salivary gland LEC

Minor salivary gland LEC is also rarely reported. The LEC from the minor salivary gland may take place in the palate, cheek, and larynx.^{1,2} According to the outcomes of this study, we find that minor salivary gland LEC has the following features on CT and MRI: (1) the palate is the most common site affected by the minor salivary gland LEC; (2) minor salivary gland LEC accompanied by metastasis of cervical lymph nodes seems to be less commonly seen when compared with the major salivary gland LEC; (3) most of minor salivary gland LEC are shown on CT and MRI as a homogeneous mass with lobular shape and (4) the number of non-enhanced LEC in minor salivary gland seems to be greater than that in major salivary gland.

Differential diagnosis

Differential diagnosis varies depending on the location and type of the salivary gland LEC shown on CT and MRI. According to our experiences and knowledge, the solitary major or minor salivary gland LEC with or without metastases of regional cervical lymph

nodes are difficult to differentiate from some benign and/or malignant tumours in the oral-maxillofacial region because of lack of characteristics. Recently, some investigations with diffusion-weighted MRI (DW-MRI) and dynamic contrast-enhanced (DCE) MRI indicated that both methods had a potential or significant role in differentiating benign tumors from malignant tumours in the salivary glands.^{10,11} Therefore, the further study is required to observe if the role is adapted to the solitary salivary gland LEC.

For the multiple LECs within the parotid gland, multiple Warthin tumours and lymphadenopathy (such as non-Hodgkin lymphoma) in the parotid gland may resemble each other on CT and MRI. However, multiple Warthin tumours usually involve the older males and have less extraglandular lymph node involvement. In addition, a bilateral parotid gland involvement by the tumours is more frequently found in multiple Warthin tumours than in LECs. On CT and MRI, most parotid non-Hodgkin lymphomas, especially parotid non-MALT lymphoma, may mainly appear as the multiple homogeneous masses with intra- and extraglandular lymphadenopathy.¹² In this study, about half (48%) of all the patients with multiple salivary gland LECs appear as the heterogeneous enhanced masses (Table 4). Furthermore, an intraglandular lymph node involvement seems to be more common in parotid LEC than in parotid non-Hodgkin lymphoma.

Conclusions

Salivary gland LEC has a predilection for females in the fourth to fifth decade of life and the parotid gland. CT and MRI findings vary between the solitary and multiple salivary gland LECs. The former usually appears as an enhanced and homogeneous mass with a lobulated shape and even or partial even margins. The latter mainly appears as a primary malignancy with metastatic lymph nodes. A majority of multiple parotid gland LECs are characterized by metastases of ipsilateral intraglandular lymph nodes, which may accompany with or without extraglandular lymph-node metastases. Compared to the minor salivary gland LEC, major salivary gland LEC with metastases of cervical lymph nodes seems to be more frequent.

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