Oral Squamous Cell Carcinoma with Metastasis to the Parotid Lymph Node

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Objective: *To increase the awareness of oral squamous cell carcinoma (OSCC) metastasis to the parotid region and the characteristics of these cases, and to evaluate the outcomes and provide treatment suggestions.*

Methods: *A retrospective study was conducted among the OSCC patients with metastasis to the parotid gland at the Peking University School and Hospital of Stomatology from 2000 to 2015. The demographic data and the medical records including primary tumour, treatment protocol, follow-up information and outcomes were collected and analysed.*

Results: *A total of 10 patients with parotid metastasis (out of 1358 OSCC patients) were included in the study. The incidence of parotid metastasis was relatively low (0.74%). All the cases were poorly differentiated (Grade II/III) and the primary sites were in an advanced stage (T3/4). Parotid metastasis occurred frequently following neck dissection and radiotherapy, and the inferior parotid lymph nodes were most commonly involved. Surgery and radiotherapy were mainly salvage protocols for parotid metastasis. The 5-year survival rate of these patients was 38.9% by the Kaplan-Meier method.*

Conclusion: *OSCC has the potential to metastasise into the parotid lymph nodes. The salvage rate and prognosis were relatively poor. Removing of the parotid tail along with the neck dissection is recommended for OSCC patients.*

Key words: *oral squamous cell carcinoma, parotid lymph node, metastasis*

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It is common for head and neck surgeons to find neoplasms in the parotid gland. Most of the masses originated from the parotid gland are primary tumours. However, a wide range of metastatic neoplasms can also present as masses in the parotid gland. Parotid squamous cell carcinomas, which are aggressive malignancies that remain relatively rare, are often presented as metastasis from cutaneous carcinomas of the scalp and face, rather than primary diseases[1-3]. Additionally, primary tumours such as breast carcinomas, prostate carcinomas, and gastrointestinal tumours, which occur outside the head and neck region may also have the ability to metastasise to the parotid gland through the thoracic duct or the Batson's paraspinal venous plexus[4].

Although uncommon, our clinical experience suggested that squamous cell carcinomas from the oral cavity may also have the risk to metastasise to the parotid gland. From the review of current literatures, only a few studies with limited case series reported this phenomenon[4-7]. The purpose of this study was to increase the awareness and reveal the potential of parotid metastasis of oral squamous cell carcinoma (OSCC), describe the characteristic of these cases, evaluate the outcomes and provide treatment suggestions.

Materials and methods

The study population was drawn from data of patients admitted at the Department of Oral and Maxillofacial Surgery, Peking University School and Hospital of Stomatology, from 2000 to 2015. The study protocol was approved by the Institutional Review Board at the

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Table 1 Demographic characteristics and primary tumour features for the case series.

ID	Sex	Age (years)	Primary site	Clinical TNM stage	Primary histological stage	Treatment of primary tumour	Treatment of the neck	pN stage
1	M	53	Left MG	T4N1M0	III	Surg+RT	RND	N1
2	F	68	Left MG	T4N0M0	II	Surg	END	N0
3	M	57	OF	T3N1M0	II	Surg+RT	RND	N1
4	F	46	Right tongue	T4N2M0	III	Surg+RT	RND	N2b
5	F	54	Right MG	T4N1M0	III	Surg+RT	RND	N1
6	M	52	Right MG	T4N2M0	II	Surg+RT	RND	N2b
7	F	57	Left MG	T4N0M0	II	Surg+RT	END	N1
8	F	65	Left BU	T4N2M0	III	Surg+RT	RND	N2
9	F	57	Left BU	T3N1M0	III	Surg+RT	RND	N2b
10	M	69	Left BU	T3N1M0	III	Surg+RT	RND	N1

MG, mandibular gingiva; OF, oral floor; BU, buccal mucosa; TNM, tumour-node-metastasis; Surg, surgery; RT, radiotherapy; RND, radical neck dissection (level I-V); END, elective neck dissection (level I-III).

Peking University School and Hospital of Stomatology. The inclusion criteria were the following: (1) histologically diagnosed with OSCC; (2) no previous treatment; (3) without evidence of distant metastasis at initial stage; (4) the parotid lymph node metastasis confirmed histologically during the follow-up. The exclusion criteria were the following: (1) history of cutaneous head and neck SCC or a secondary primary SCC from mucosa outside of oral cavity; (2) previous radiotherapy or chemotherapy before primary surgery; (3) direct tumour extension to the parotid gland. The medical records of patients were retrieved from the electronic medical record system of the hospital. All the primary tumours were staged with clinical and imaging examinations based on the 2009 Union for International Cancer Control/American Joint Committee on Cancer Staging criteria (7th edition).

In this study, all the patients were initially treated with surgery. The primary sites were radically resected at 1.5 cm margins and the margins were confirmed with frozen section intraoperatively. For patients with clinical positive node (cN+), a radical or modified radical neck dissection was performed simultaneously. For clinically node-negative (cN0) neck, elective level I-III neck dissection was performed in the T2-4 cases, while a 'wait and see' policy was chosen for the T1 patients. Postoperative radiotherapy was routinely suggested for patients with positive lymph nodes. Salvage surgery with or without adjuvant radiotherapy or chemo-radiotherapy was performed when local or regional failure was confirmed. Patients with parotid lymph node metastasis received total or superficial parotidectomy.

Patients were followed-up every 3 months within the first 2 years and every 6 months until the fifth year, and then annually after 5 years. The cut-off date for all the follow-up period among survival patients was 31 December 2018. The demographic characteristics and clinical data including the primary site, tumour-node-metastasis (TNM) staging, histological grade, parotid lymph nodal metastasis, treatment and follow-up outcomes were collected and analysed using SPSS version 19.0 software (SPSS, Chicago, IL, USA). The survival rate was calculated using Kaplan-Meier methods.

Results

A total of 1358 cases of patients confirmed with OSCC were reviewed during the study period. Among this total, 10 patients (four male and six female patients) matched the inclusion criteria, presenting with parotid metastasis during the follow-up. The parotid metastasis rate was 0.74% (10/1358). Patient demographics and primary tumour features for these 10 patients are shown in Table 1. The average age was 57.8 years (ranging from 46 to 69 years). The primary tumour included the mandibular gingiva (n = 5, 50%), buccal mucosa (n = 3, 30%), tongue (n = 1, 10%) and the oral floor (n = 1, 10%). All the cases were classified as T3 (30%) and T4 (70%). Radical neck dissection was performed in eight cases which were evaluated as cN+ neck, and the metastatic lymph nodes were all identified pathologically. The other two

Table 2 Characterisation of parotid metastasis and follow-up outcomes of this series.

ID	Parotid metastasis location	With local recurrence	With regional recurrence	Time of parotid recurrence (months)	Salvage for parotid metastasis	Out-comes	Follow-up time (months)
1	Inferior	Yes	No	5	SP	DOD	5
2	deep lobe	No	Yes	6	TP+RT	DOD	16
3	inferior	No	No	9	SP	ANED	74
4	inferior and deep lobe	No	No	19	TP	ANED	76
5	inferior	No	No	18	SP	DOC	54
6	Inferior	No	Yes	10	SP	DOD	27
7	Inferior	No	Yes	10	SP+RT	DOD	25
8	Inferior	No	No	19	SP	NED	50
9	inferior	No	No	15	SP	ANED	25
10	inferior	No	No	15	SP	ANED	39

SP, superficial parotidectomy; TP, total parotidectomy; RT, radiotherapy; DOC, dead of other cause; DOD, dead of disease; ANED, alive with no evidence of disease.

patients with cN0 neck received elective neck dissection simultaneously with primary tumour resection, and one of them presented with a positive lymph node in level I, pathologically. The primary tumours were all confirmed with grade II OSCC (40%) and grade III (60%), histologically. All the nine patients confirmed with pN+ received postoperative radiotherapy.

During the follow-up period, all the patients presented with metastasis in parotid region. The mean time point for parotid metastasis occurrence after the primary surgery was 12.6 months (ranged from 5 to 19 months; Table 2). Metastasis to the inferior lymph nodes in the parotid tail was observed in eight cases, to the lymph node of deep lobe in one case, and to both inferior and deep lymph nodes in another case. In one patient, the parotid metastasis occurred with simultaneous local recurrence. In another two cases, the parotid metastasis was observed after regional failure and neck dissection in contralateral side.

Salvage therapy mainly included surgery and radiotherapy. Eight patients received superficial parotidectomy and two patients received total parotidectomy. Three of them underwent additional salvage radiotherapy after surgery (Table 2).

The average follow-up period was 39.1 ± 23.9 months after the salvage therapy of the parotid region. Until the final visit, four patients died of disease, one patient died of lung disease, and the other five patients were still alive and disease-free (Table 2). According to the Kaplan-Meier survival curve, the 5-year survival rate of this case series was 38.9% (Fig 1).

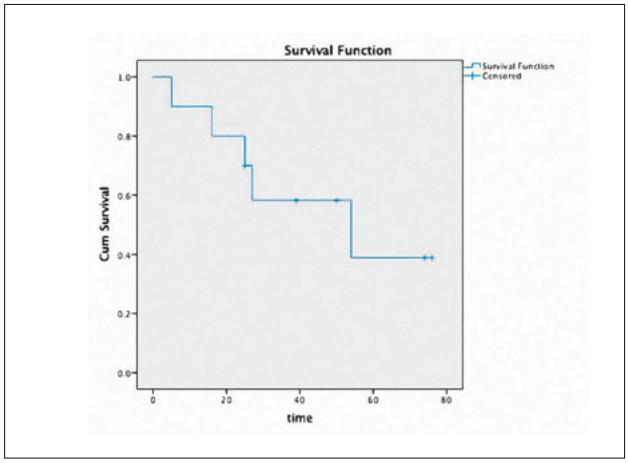

Fig 1 Kaplan-Meier survival curve for OSCC patients with parotid metastasis

Discussion

Although most of the tumours found in the parotid gland are primary epithelial tumours, lymphatic metastatic neoplasms can also present in the parotid gland, considering the embryological development of this gland[4-5]. The parotid lymphatic system mainly collects the drainage from the cutaneous sites of the head and neck such as the parietal scalp, the ipsilateral forehead, and the posterior cheek and auricle, and drains to the deep cervical lymph nodes of the upper neck[8-9]. These sites have been identified as the 'storm area' and it is well recognised that malignant tumours such as malignant melanomas

and cutaneous SCCs in this area are at high risk for metastasising to the parotid lymph nodes[10].

For oral cancer, the normal lymphatic drainage route is to the neck area from level I to V. Although the frequency is extremely low, several studies with small case series have reported the potential of OSCC to metastasise into the parotid region. In a very early stage, Ord et al[5] reported two cases of OSCC metastasis into the parotid gland. Yu and Ma[11] also reported three cases of parotid metastasis from SCC of the oral cavity. Recently, Olsen et al[7] presented 12 cases of oral and oropharyngeal SCCs with metastasis into the parotid gland, and only seven of them were originated from the oral cavity. The authors suggested removing the inferior parotid lymph nodes when treating OSCC cases with substantial cervical metastasis. Furthermore, Liao et al[12] assessed outcomes following recurrence of oral SCCs at unusual sites, including the parotid region, and demonstrated that cases of parotid metastasis usually indicated poor prognosis.

The present study represents so far the largest sample size of OSCC that metastasises into the parotid region. In our series of patients with parotid metastasis, the mandibular gingiva and buccal mucosa were the most common primary sites (80%). Based on the lymphatic anatomy, the lymph from the mandibular gingiva and buccal mucosa may drain to the submandibular and submental lymph networks, which are the junctional lymph node areas between the jugular lymph system and the buccal, facial, and parotid lymphatic systems[5,13]. Thus, the structure of the lymphatic drainage in this area may confer a relatively high risk for metastasis of tumours in the mandibular gingiva and buccal mucosa into the parotid region. In this series, all of the cases were in an advanced stage (T3/4), and histologically diagnosed as grade II/III. Identifying the relationship between parotid metastasis and the characteristics of the primary tumour is difficult based on a series of only 10 patients; nevertheless, the possibility that OSCC with advanced stage and poor differentiation may present a high risk of metastasis into the parotid region should be considered.

Anatomically, parotid lymph nodes can be divided into two groups. The first group, which comprises the superficial lymph nodes that are located at the surface of the parotid fascia and the gland, can be primarily divided into preauricular and infraauricular nodes. The second group comprises the deep or intraparotid lymph nodes located within the parotid parenchyma[8,14]. In the present series, the metastatic masses presented in the parotid tail in 9/10 cases, which indicates a likely involvement of the inferior parotid lymph node. In the Olsen et al[7] study, which assessed 12 cases of oral and oropharynx SCCs with metastasis into the parotid gland, the inferior parotid lymph nodes were involved in 4/7 cases of OSCCs and in 5/5 cases of oropharynx SCC. Since the parotid tail was the most commonly affected region, we strongly suggest the evaluation and resection of the parotid tail when performing neck dissection.

The parotid tumours in all the patients presented as a delayed metastasis in the present study, which is in agreement with literature[1,2,5,7,12]. Before the metastasis presented in the parotid area, nearly all the patients received neck dissection, and most of them (90%) received postoperative radiotherapy. Parotid metastasis occurred synchronously with local recurrence only in one case and occurred with contralateral neck failure in another three cases. Meanwhile, it was notable that the time point of parotid failure presented within 2 years and half of them (5/10) even within 1 year in the present study. Thus, we suspected that these nodal diseases may have resulted from unrecognised occult metastasis at the time of initial tumour presentation. Based on the above findings, we suggest that, in addition to the oral cavity and neck, the parotid region should be taken into consideration during the postoperative follow-up of OSCC patients.

The delayed metastasis to the parotid region after neck dissection and radiotherapy indicated that the parotid metastasis of oral SCC may result from retrograde or aberrant lymphatic drainage, possibly due to a disruption in normal lymphatic drainage due to neck dissection. Fisch[13] and Pisani et al[14] reported that both radiotherapy and surgery treatments induce frank changes in the normal patterns of cervical lymph flow. The calibre and number of lymphatic vessels as well as the size and number of lymphatic nodes are markedly reduced following radiation of the neck area. Furthermore, this intervention also perturbs the sequence of filling of the cervical lymphatic system. Histological findings show that a complete block in the cervical lymph flow was found at the junctional area level. However, collateral circulation can slowly develop. Two alternate routes were observed: a submental diversion through pre-existing channels after unilateral neck dissection, and a retrograde flow to the subcutaneous and dermal lymphatic networks after bilateral neck dissection or radiation[13-14]. These phenomena may explain why parotid metastasis may occur after neck dissection or radiation. Surgical treatment to address metastasis into parotid lymph nodes still remains controversial. Some authors suggest a superficial parotidectomy while others recommend total parotidectomy[1-5,7,11-12]. In the present series, superficial parotidectomy was performed in eight patients, and

one of them received additional radiotherapy. Another two patients underwent total parotidectomy because of deep lobe invasion. Four patients died of the disease during the follow-up, another patient died of systematic disease without recurrence of the tumour, and the other five patients remained alive without disease at the last follow-up. The 5-year survival rate was 38.9%, which was similar to the overall survival rate of OSCC patients with neck metastasis[15-16]. It was difficult to draw a conclusion on survival for OSCC patients with parotid metastasis, considering the limited size of the sample and the few published studies. However, the data and trend of the survival curve still may indicate poor prognosis of these patients.

Based on the present series and the literature review, we suggest superficial or total parotidectomy for OSCC patients with parotid metastasis. In addition, considering that the inferior parotid lymph nodes were most likely involved, removing the parotid tail synchronously with neck dissection, is strongly recommended.

Conclusion

The OSCC has the potential and risk to metastasise into the parotid region, and the inferior parotid lymph nodes are most commonly involved. Parotid metastasis is likely to occur in patients who have undergone neck dissection and radiotherapy previously and may be caused by reflux or retrograde movement of the lymph. Evaluation of the parotid region should be performed carefully by clinical and radiographic examination of OSCC patients at initial presentation and during the follow-up period. Resection of the parotid tail is suggested during neck dissection. Superficial or total parotidectomy is recommended for parotid salvage. The OSCC patients with parotid metastasis indicate poor prognosis. Rather than descriptive studies, more prospective and comparable studies with larger sample size are still required to draw a reliable conclusion.

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Conflicts of interest

The authors reported no conflicts of interest related to this study.

Author contribution

Dr Wen Bo ZHANG designed the study, collected clinical data and prepared the manuscript; Drs Yang WANG, Chi MAO, Chuan Bin GUO and Dr Guang Yan YU contributed to the clinical data of patients; Dr Xin PENG designed the study and revised the manuscript.

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