A case of metastasis of small cell lung cancer to the parotid gland: a case report and literature review

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Abstract
Small cell lung cancer metastasizing to the parotid gland is very rare and only a few cases have been reported. A 64-year-old man presented with a painless mass and peripheral facial paralysis. Neck ultrasound identified a solid mass in the right parotid gland with enlargement of the lymph nodes in the gland and the right submandibular lymph nodes. Lung computed tomography imaging demonstrated abnormalities in the upper and middle lobes of the right lung and intermediate bronchus, with obstructive pneumonia, as well as enlargement of the right hilar and mediastinal lymph nodes. Postoperative histopathological analysis identified small cell carcinoma in the right parotid gland with involvement of the right neck lymph nodes (one of eight). Bronchoscopy was performed and immunohistochemical analysis of the specimen demonstrated possible metastasis of small cell lung cancer to the parotid gland. From postoperative day 15, the patient started to undergo six cycles of an adjuvant chemotherapy regimen. No complications of the chemotherapy regimen were observed after three cycles. Treatment and follow-up are ongoing.

Keywords
Parotid gland tumour, small cell cancer, lung cancer, metastasis

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Introduction

Primary parotid tumours in adults are mostly benign pleomorphic adenomas. Malignant lesions are uncommon, but include predominantly mucoepidermoid carcinomas, adenocystic carcinomas and malignant mixed carcinoma. Small cell carcinoma histology of parotid tumours is rarely seen, accounting for only 1.7% of parotid gland tumours, with only a few cases so far reported. This current report presents a rare case of small cell parotid gland cancer metastasized from the lung that was diagnosed in a 64-year-old man. Furthermore, the report describes the examination and treatment plan; and provides a literature review of the current standard of care.

Case report

In October 2018, a 64-year-old man presented at the Department of Otolaryngology, Head and Neck Surgery, First Hospital of Jilin University, Changchun, Jilin Province, China with a painless mass below the right ear and complained of peripheral facial paralysis for a month. A physical examination found a 2.0 × 2.0 cm mass, with poor mobility, in the right parotid region. The accompanied peripheral facial paralysis on the right side was classified as House-Brackmann Grade III. Neck ultrasound identified a solid mass in the right parotid gland with enlargement of the lymph nodes in the gland and the right submandibular lymph nodes. Lung computed tomography (CT) demonstrated abnormalities in the upper and middle lobes of the right lung and intermediate bronchus, with obstructive pneumonia, as well as enlargement of the right hilar and mediastinal lymph nodes. The patient showed no symptoms of coughing, expectoration or haemoptysis.

The patient insisted on confirming the malignancy of the solid mass in the right parotid gland but refused to undergo preoperative needle biopsy. Intraoperative pathology confirmed a malignant tumour with metastatic potential. Thus, the right parotid gland and facial nerve were resected and selective neck dissection performed. Postoperative histopathological analysis demonstrated small cell carcinoma in the right parotid gland (Figure 2a) with involvement of the right neck lymph nodes (one of eight). Bronchoscopy was performed and the pathological results were small cell carcinoma (Figure 2b).

Figure 1. Coronal (a), lung window (b) and mediastinal window (c) computed tomography images of a 64-year-old man who presented with a painless mass below the right ear and complained of peripheral facial paralysis for a month. The images show abnormalities in the upper and middle lobes of the right lung and intermediate bronchus and obstructive pneumonia. Enlargement of the right hilar and mediastinal lymph nodes, indicated by black and white arrows, is also visible.
Immunohistochemical analysis of the post-operative pathological specimen indicated positive staining for pan-cytokeratin, CD56, chromaffin granule protein A, synapsin (Syn) and thyroid transcription factor-1 (TTF-1) (Figure 3), partial positive staining of Ki-67 and cytokeratin 7, and negative staining for CD99, cytokeratin 5/6 and common leukocyte antigen (LCA). Immunohistochemical analysis of the bronchoscopy pathological specimen demonstrated positivity of pan-cytokeratin, CD56, Syn, TTF-1, partial positivity of Ki-67, but no staining of P40, cytokeratin 20, cytokeratin 5/6, vimentin and LCA, suggesting possible metastasis of small cell lung cancer to the parotid gland. Positron emission tomography (PET)/CT identified a hypermetabolic lesion in the right upper and middle lobes of lung and intermediate bronchus (Figure 4), suggesting possible central lung cancer with distal obstruction and inflammation. Multiple lymph nodes were involved, and localized peritoneal thickening with hypermetabolism was observed under the right lobe of the liver, suggesting possible liver metastasis. Although hyperplasia, calcification and a
hypermetabolic area were observed in the prostate under PET/CT, analysis of prostate-specific antigen in the serum and magnetic resonance imaging (MRI) showed no lesion.

The patient recovered well after the surgery and was scored 1 on the Eastern Cooperative Oncology Group performance scale. From postoperative day 15, the patient started to undergo six cycles of adjuvant chemotherapy with a combination of cisplatin + etoposide: days 1–3, 75 mg/m$^2$ cisplatin intravenously + 100 mg/m$^2$ etoposide intravenously; day 4, 100 mg/m$^2$ etoposide intravenously; day 5, 50 mg/m$^2$ etoposide intravenously; and the cycle was repeated every 20 days. Supportive therapy was also provided. No complications of the chemotherapy were observed after three cycles, treatment and follow-up are ongoing. Ethical approval was not required for this case report. The patient provided written informed consent for the publication of their data.

Discussion

Small cell carcinoma accounts for 15% of malignant tumours originated from the bronchus and 25% of all lung cancer.\textsuperscript{1} It is usually associated with a high degree of malignancy and is frequently accompanied by paraneoplastic syndromes.\textsuperscript{8} The highly vascularized microenvironment in the lung facilitates cancer cell extravasation thereby making possible distant metastases, which are commonly seen in the mediastinum, supraclavicular lymph nodes, liver, bone, adrenal gland and brain.\textsuperscript{1,9} Small cell carcinomas in the parotid glands rarely originate locally,\textsuperscript{10} and are more often metastatic tumours from other organs such as the lung.\textsuperscript{11} Distant metastasis to the parotid gland is a very rare clinical event. To the best of our knowledge, only six cases have been reported (Table 1).\textsuperscript{1,3–7} Previous observations in cases with metastatic lung small cell carcinoma to parotid glands have shown that these patients rarely live longer than 10 months,\textsuperscript{1,7} the median survival of small cell lung cancer patients,\textsuperscript{1} suggesting a poor prognosis for these patients.

Comprehensive physical examination, imaging and histopathology are required in the diagnosis. Although solid masses with poor mobility but high growth rate are usually associated with a high degree of malignancy, the decisive diagnosis relies on needle and excisional biopsies. It is also of importance to perform chest X-rays, CT and ultrasound to identify the primary lesion. In addition, metastasis of small cell lung cancer, which is predominantly through haematogenous dissemination,\textsuperscript{12} to the parotid gland suggests an advanced stage of lung cancer, so whole body PET/CT is necessary to track remote metastasis.
Table 1. Previous case reports of metastasis of small cell lung cancer to the parotid gland.1,3–7

| Case | Author            | Sex | Age, years | Nerve palsy | Examination & primary lesions | Other examinations & primary lesions | Other systemic metastases | Treatment | Survival                  |
|------|-------------------|-----|------------|-------------|-----------------------------|-------------------------------------|---------------------------|-----------|---------------------------|
| 1    | Ulubas et al.1    | M   | 59         | No          | Thoracic CT; right main bronchus | Bronchoscopy, bone scintigraphy | Bone metastases            | Chemotherapy and supportive therapy | Died 10 months after the diagnosis |
| 2    | Boeger et al.3    | M   | 54         | No          | Chest X-rays and CT; left lung | Bronchoscopy | No          | Total parotidectomy with facial nerve preservation | Not mentioned |
| 3    | Borg4             | M   | 72         | No          | CT; left apical lung         | Bronchoscopy | No          | Radiotherapy               | Alive 3 years later without evidence of disease recurrence |
| 4    | Hisa and Tatemoto5 | M   | 61         | No          | CT; right main bronchus      | Bronchoscopy | Brain metastases | Left superficial parotidectomy and right superficial parotidectomy, chemotherapy | Died 17 months after the diagnosis |
| 5    | Shalowitz et al.6 | M   | 54         | Left side facial weakness | Chest X-rays and CT; pleural surface of the left lower lung | Bronchoscopy | No          | Chemotherapy and radiotherapy | Living at the time of the report |
| 6    | Shi et al.7       | M   | 61         | No          | Chest X-rays and CT; right upper lobe | Bronchoscopy | No          | Partial parotidectomy and facial nerve dissection, chemotherapy and radiotherapy | Not mentioned |

CT, computed tomography.
The treatment of metastatic parotid tumour is a matter of debate. In our view, total or partial parotidectomy with consideration for neck dissection, followed by postoperative chemotherapy should be included in the treatment regimen, because small cell lung cancer is sensitive to chemotherapy. If facial paralysis occurs, the facial nerve loses its reserved value. Before surgery, the current patient was advised to undergo facial nerve graft at the same time, but the patient refused. Follow-up showed that the patient did not undergo any kind of secondary facial reconstruction. A previous case report suggested that neck dissection may be unnecessary because the metastasis is more likely to be caused by haematogenous dissemination. In contrast, in our opinion, selective neck dissection can minimize the risk of recurrence and metastasis to some extent. In this current case, a total parotidectomy with facial nerve resection was undertaken, with selective neck dissection, followed by adjuvant chemotherapy. Chemotherapy combining cisplatin and etoposide was undertaken in this current case study, considering the sensitivity of small cell lung cancer to these drugs. No obvious complication was observed after three cycles of treatment and no disease progression has been observed during follow-up.

In conclusion, metastasis of small cell lung cancer to the parotid gland is rare and associated with poor clinical outcomes. Physical examination, diagnostic imaging, such as chest X-ray, CT and MRI, and histopathological analyses are required for a definitive diagnosis. Currently, it is mainly managed by surgery and chemotherapy, but the long-term efficacy remains to be characterized.

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Authors’ contributions
Yu Cui, Xiang-Yan Cui and Yu Wu collaborated in the conception and design of the study. Yu Cui, Xiang-Yan Cui and Yu Wu acquired the data. Yu Cui, Zhan-Peng Zhu and Wan-Zhong Yin performed the data analysis and interpretation. All authors were involved in writing the manuscript. All authors read and approved the final manuscript.

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The authors declare that there are no conflicts of interest.

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