Case Report

Coughing up – Small cell carcinoma lung with gingival metastasis

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Abstract
Small cell lung cancer (SCLC) is known for its metastatic potential. The most common sites are liver, adrenal, bone and brain. We report a case of a 37 year old female patient, diagnosed with SCLC, presenting with gingival metastasis, an unusual metastatic site. Radiation therapy to the metastatic lesion to a dose of 20 Gray in 5 fractions over 5 days was delivered which achieved haemostasis and good palliation. However, the patient expired in 2 months owing to systemic metastasis.

Introduction
Small cell lung cancer (SCLC) is an aggressive subtype of lung cancer known for its metastatic potential [1]. Around 70% of SCLC presents with extensive disease. With combination chemotherapy, about 20% achieve a complete response with a median survival of 7 months. However, only 2% are alive at 5 years [2]. The most common sites of metastasis of SCLC are liver, adrenals, bone and brain. Metastasis to gingiva and hard palate is rare. Cases of lung cancer metastasizing to these sites have been reported [3–7] and in one case metastasis to gingiva was the presenting feature [8]. Herein, we report a case of extensive stage SCLC treated with chemotherapy and radiation therapy presenting with metastasis to gingiva. This unusual site of metastasis was a cause of bleeding, thus requiring palliation.

Case history
A thirty-eight year old housewife presented with dry cough, progressive dyspnoea and chest pain for two months. There was no fever, haemoptysis, weight loss, seizures or any medical
co-morbidity. She did not have any history of smoking or alcohol intake. Her performance status was good and systemic examination did not reveal any abnormalities. Chest X-ray showed a mediastinal mass and contrast enhanced computed tomography (CECT) showed a $7.1 \times 7.0 \times 4.6$ cm mass in left peri-hilar region with necrosis and calcification encasing the great vessels (Fig. 1). In view of her young age and non-smoker status, a DOTANOC scan was done suspecting bronchial carcinoid. However no uptake was noted. Biopsy revealed a malignant small round cell tumour with areas of necrosis. Synaptophysin, chromogranin and cytokeratin were positive on immunohistochemistry (Fig. 2) with MIB-1 labelling index greater than 90%. Whole body Positron Emission Tomography (PET) CT revealed an additional asymptomatic brain metastasis. The patient was diagnosed as small cell carcinoma lung and staged as T4N1M1b according to the seventh American Joint Committee on Cancer (AJCC) recommendations [9].

In view of good performance status whole brain irradiation to a dose of 30 Gray (Gy) in 10 fractions over 2 weeks was delivered. Subsequently she received 6 cycles of chemotherapy with cisplatin and etoposide. A response assessment PET CT showed no change in the size of lung mass. However the previously noted brain metastasis was non 18-Fluorodeoxyglucose avid. Following this she was treated with radiation therapy (RT) to a dose of 20 Gy in five fractions over five days to the lung mass. After one month of RT she presented to our clinic with a single episode of bleeding (10–15 ml) from oral cavity. Detailed physical and local examination showed two ulcero-proliferative lesions – one $4 \times 2$ cm in the upper gingiva posterior to the first molar and one $1 \times 1$ cm lesion in hard palate (Fig. 3).

The blood counts were within normal limits. A course of antibiotics and anti-fungals showed no improvement. CT face and neck showed a mass in the upper gingiva, causing destruction of alveolus and extending to adjacent hard palate and buccal mucosa (Fig. 4). Biopsy revealed it to be a small cell carcinoma. The immuno-histochemical markers were similar to the one reported from the lung primary thus linking it to be metastatic from the lung (Fig. 5A–E).

The patient received palliative RT, 20 Gy in five fractions over five days to the metastatic site. At one month follow up she had partial regression of the lesion and did not report any further episodes of bleeding from oral cavity.

Unfortunately, she developed jaundice at the next visit and imaging showed multiple liver metastases. She was offered best supportive care as performance status was not suitable for further cancer directed therapy. She expired at home two months post detection of the oral cavity ulcers.

Discussion

Though small cell lung cancer is notorious for hematogenous dissemination, oral cavity is a rare site for metastasis. If
metastasis from any primary cancer is detected in oral cavity, the most common primary is lung cancer. Previously reported literature describes metastasis in oral cavity from lung to mandibular bone, tongue, gingiva and tonsil [10]. Metastasis to oral cavity generally signifies widespread systemic disease. Median survival after discovery of oral metastasis is dismal and is often limited to few months [10]. Till date around 20 cases of lung cancer metastasizing to gingiva have been reported in literature. Oral metastasis can present as either rapidly growing masses or ulcero-proliferative lesions [6]. A review of 17 cases of oral metastasis from lung primary by Huang et al. revealed undifferentiated carcinoma to be the most common histology followed by large cell carcinoma, adenocarcinoma, small cell carcinoma and squamous cell carcinoma in that order [6]. In this case, an ulcero-proliferative lesion was observed, which also caused erosion of the alveolus and the pterygoid plates. Though not immediately life threatening, oral cavity lesions can be troublesome as they interfere with nutrition and thus quality of life.

The pathogenesis of metastasis is complicated. The presence of chronic inflammation in gingiva has been postulated as a cause. Fragmented basement membranes in the vessels and cytokines around the site of inflammation may act as a homing trigger for the metastatic clone [11].

The current case was treated according to National Comprehensive Cancer Network (NCCN) guidelines, which advocate combination chemotherapy with cisplatin/carboplatin and etoposide/irinotecan and cranial irradiation. Treatment of gingival metastasis is controversial. Both systemic chemotherapy and radiotherapy has been used. Surgical excision can also be tried to improve nutrition and hygiene or control bleeding [6]. In this case, the lesion presented as an ulcer with bleeding; hence radiotherapy was delivered for haemostasis and palliation. Since it is rare for lung cancer to metastasize to the oral cavity, a variety of differential diagnoses are entertained. They include pyogenic granuloma, dental abscess, neutropenic ulcer and second primary malignancy in oral cavity. However metastasis from the primary tumour should be always considered in a known case of lung cancer and a detailed evaluation with histopathological examination is mandatory. Small cell lung cancer is very sensitive to radiation treatment and therefore is very effective in achieving haemostasis and palliation.

Conflict of interest

The authors have no conflict of interest to report.

Figure 4  CT image of the same lesion – showing soft tissue mass in the region of left alveolus causing destruction of bone and eroding the pterygoid plates.

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Figure 5  A Sections from the oral cavity mass show a similar tumour as in Fig. 2 (H&E, ×400). B: The tumour cells show 'dot like' immunopositivity for pan-cytokeratin (IHC, ×400). C: The Ki-67 labelling index is approximately 90% (IHC, ×400). D: Tumour cells show diffuse cytoplasmic positivity for synaptophysin (IHC, ×400). E: Tumour cells show nuclear immunopositivity for Thyroid Transcription factor-1. (IHC, ×400).
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