

Peer-reviewed article, submitted February 2025, accepted November 2025

# A case report of metastatic small cell lung cancer presenting as a radiolucent lesion in the mandible

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## Abstract

Small cell lung cancer (SCLC) is an aggressive and uncommon type of lung cancer with a tendency to metastasise. Despite this, metastasis of SCLC to the oral cavity is rarely reported in the English literature. Here we describe a case of a 76-year-old male with a radiolucent lesion of the left mandible associated with lingual expansion. He had a history of end-stage SCLC with brain metastases. A biopsy of the mandibular lesion confirmed a diagnosis of poorly differentiated carcinoma which was consistent with a distant metastasis of SCLC. In addition, immunohistochemical staining of the biopsy tissue was positive for INSM1, a chemo refractive marker, indicating the lesion may have been responsive to chemotherapy. The patient subsequently received palliative radiotherapy and passed away three months after the initial consult. This case is a rare presentation of SCLC metastasising to the oral cavity and, given its benign radiographic appearance, highlights the importance for clinicians to take a thorough medical history and a low threshold to biopsy suspect lesions. Furthermore, early diagnosis of oral metastases can improve the quality of life of patients, as treatment can commence earlier, emphasising the importance to educate patients with a history of aggressive cancer, and to routinely examine them.

## Introduction

Metastatic cancer in the oral cavity is rare, with the mandible being the more common site for distant metastases followed by oral soft tissues (Hirshberg *et al.*, 2008). In the male population the most common primary site for metastatic disease in the oral cavity is the lung (Hirshberg *et al.*, 2008). One type of aggressive lung cancer is small cell lung cancer (SCLC) which has the capability to metastasise early and is strongly associated with smoking. (Rudin *et al.*, 2021).

Here we describe a rare presentation of SCLC metastases to the mandible. Initially the patient presented to a general dental practice and was subsequently referred to a specialist Oral and Maxillofacial Surgery unit for further investigation and biopsy. This case highlights the importance of a thorough medical history, and is a timely reminder of the importance of investigating suspicious radiolucent lesions in the maxillofacial region.

## Case

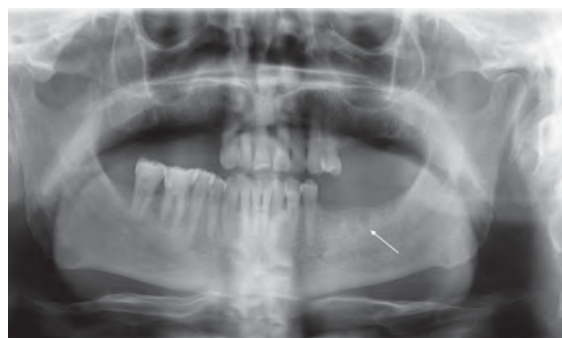
A 76-year-old male was referred by a general dentist for a radiolucent lesion of the left mandible. The patient had end stage SCLC with multiple brain metastases diagnosed in 2018. As such, he was treated with chemoradiation to the right chest. In 2021, SCLC reoccurrence in the right chest was diagnosed and subsequently completed further radiotherapy followed by chemotherapy (carboplatin and etoposide). Furthermore, he had basal squamous carcinoma of the skin which had metastasised to the left shoulder in 2023 and was managed palliatively with radiotherapy. In addition, the patient had a history of atrial fibrillation, pulmonary embolism, depression, chronic obstructive pulmonary disease (COPD) and hearing impairment. His medication at the time of examination was morphine, rivaroxaban, dexamethasone, mirtazapine, temazepam and salbutamol. He was a smoker of unknown pack year history and denied regular alcohol consumption. The patient provided informed consent for all stages of treatment and for publication of their health information.

The lesion was an expansile mass on the lingual surface of the left mandible, which had been gradually increasing in size over a three-month period, and subsequently became painful. The patient did not report any paraesthesia. The lesion was adjacent to an edentulous space in the left mandible, with no recent history of extractions.

On examination, there was tenderness on palpation of the ipsilateral left submandibular lymph nodes, but with no extraoral swelling. Intraoral examination noted a firm, lower left hand side lingual lesion with no ulceration, exposed bone or bleeding. An area of soft tissue mobility was noted over the lesion. The OPG showed a radiolucency in the left mandible (Figure 1), with the radiology report not drawing any suspicion to the radiolucent area in Q3. Further CBCT imaging showed a 4.5 x 4.7mm radiolucent defect on the left-hand side lingual aspect of the mandible (Figure 2A, 2B).

An incisional biopsy of the left-hand side lingual aspect of the posterior mandible, with histological examination displaying submucosal deposits of tumour comprising sheets and islands of cells with scant cytoplasm, hyperchromatic nuclei and absent nucleoli with evidence of nuclear moulding and extensive crush artefact (Figure 3A, 3B). In addition, there was notable necrosis and apoptotic debris. The cells were positive for TTF-1 with focal staining of CK7 and scattered positive cells with INSM1 and Synaptophysin

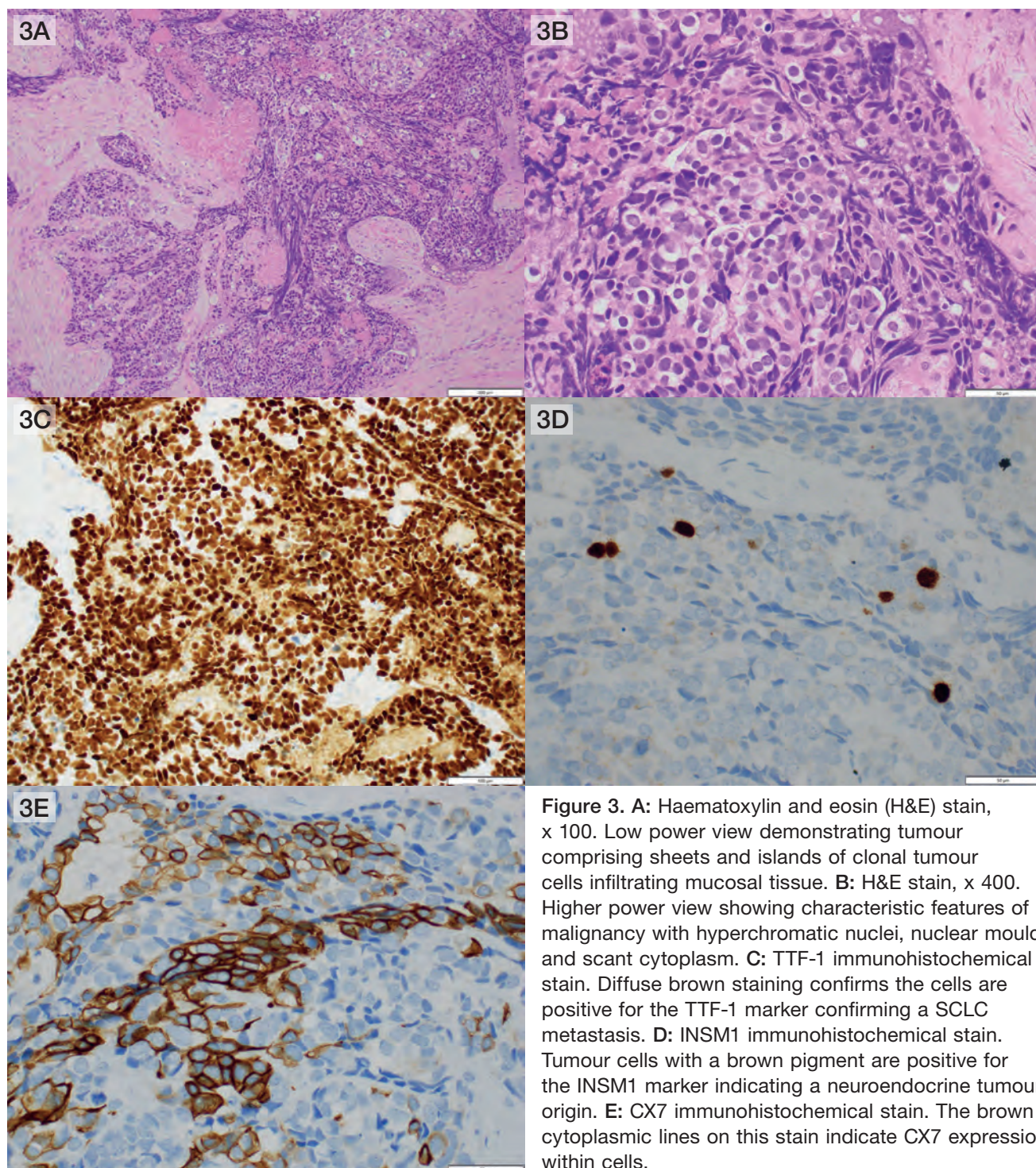




**Figure 1.** Orthopantomogram image (OPG) of mandible, showing a radiolucency in the left mandible.



**Figure 2.** Cone Beam Computed Tomography image (CBCT) of mandible, showing a 4.5 x 4.7mm radiolucent defect on the left-hand side lingual aspect.



**Figure 3.** **A:** Haematoxylin and eosin (H&E) stain, x 100. Low power view demonstrating tumour comprising sheets and islands of clonal tumour cells infiltrating mucosal tissue. **B:** H&E stain, x 400. Higher power view showing characteristic features of malignancy with hyperchromatic nuclei, nuclear moulding and scant cytoplasm. **C:** TTF-1 immunohistochemical stain. Diffuse brown staining confirms the cells are positive for the TTF-1 marker confirming a SCLC metastasis. **D:** INSM1 immunohistochemical stain. Tumour cells with a brown pigment are positive for the INSM1 marker indicating a neuroendocrine tumour origin. **E:** CX7 immunohistochemical stain. The brown cytoplasmic lines on this stain indicate CX7 expression within cells.



(Figure 3C, 3D, 3E). The sample was negative to CK20, chromogranin and p40.

The histopathological diagnosis was a poorly differentiated carcinoma. Given the patient's history of end-stage SCLC, the lesion was diagnosed as a distant metastasis of SCLC.

The patient was referred for palliative radiotherapy of the oral metastasis, where he passed away 3 months post presentation.

## Discussion

Although lung cancer is the leading cause of cancer-related death in Australia, accounting for 8856 deaths alone in 2023, metastasis to the oral cavity is rare (Health & Welfare, 2024; Moraes *et al.*, 2017). SCLC represents 13% of newly diagnosed lung cancers worldwide and has a predilection to metastasise early (Wang *et al.*, 2022). However, the mandible is one of the most infrequent secondary sites for SCLC reported in the literature (Moraes *et al.*, 2017).

A literature search was conducted through the PubMed database utilising the keywords "small cell lung cancer" and "mandible". This search returned 29 articles. Articles were excluded if they did not detail the type of lung cancer (ie. no diagnosis of SCLC) or were not written in English. Of the initial 29 articles, three met the screening criteria. Screening the reference lists of these articles identified three additional relevant publications, yielding a total of six articles describing cases of small cell lung cancer metastasising to the oral cavity (Table 1).

The first known case was described by Svirsky in 1989 in a 62 year old male with a history of smoking (Svirsky *et al.*, 1989). Our case also had a history of smoking, which is a known risk factor for development of SCLC and

hence subsequent metastases (Bircan *et al.*, 2008; Svirsky *et al.*, 1989).

Moraes *et al.* in 2017 described a case of a 66 year old male presenting with odontogenic pain in the right hand side mandible, with radiographic features of a residual cyst (Moraes *et al.*, 2017). This presentation was similar to our case, highlighting the ability for oral metastases to appear radiographically benign highlighting the importance of clinical examination with radiographic findings. Similar to our case, immunohistochemical testing was for the TTF-1 marker (Moraes *et al.*, 2017). TTF-1 is a neuroendocrine marker, which is expressed in most SCLC cases, however it does not offer significant prognostic value unless paired with a Circulating Tumour Cells analysis (Messaritakis *et al.*, 2017).

In 2004, Zachariades *et al.* described a case of a 50 year old male with left hand side mandibular swelling which developed the complications of hypesthesia and a displaced pathological mandibular fracture secondary to SCLC metastasis (Zachariades *et al.*, 2004). Our case did not demonstrate the associated advanced sequelae as described by Zachariades *et al.* However, it highlights that sequelae arising from undiagnosed oral metastases can be detrimental for a patient's quality of life.

Outside of the oral cavity, the cases reported in the literature have detailed metastases to the brain, liver and bone (Bircan *et al.*, 2008; Svirsky *et al.*, 1989; Zachariades *et al.*, 2004). Our case only demonstrated metastases to the brain which was previously defined prior to presentation.

Capodiferro *et al.* conducted a retrospective review over 30 years of the number of lung metastasis to the head and neck region (Capodiferro *et al.*, 2023). Out of the 112 cases of lung cancer patients, only 21 were noted to have

**Table 1.** Literature review with documented SCLC metastases to the Oral Cavity

Author	Year	Age (Yrs)	Sex	Smoking status	Location	Other Metastases	Histology
Moraes	2017	66	M	Unknown	Mandible	Nil Prior	Basophilic irregular cells with scant cytoplasm and hyperchromatic nuclei with crushing artifacts. Positive for Cytokeratin 7, Chromogranin A, TTF-1
Maschino (Maschino <i>et al.</i> , 2013)	2013	79	M	Unknown	Maxillary Gingiva	Other metastases noted – unknown location	Unknown
Bircan	2008	53	M	50PYH	Soft tissue, Mandible	Liver	Small tumour cells with ill-defined cell borders, hyperchromatic nuclei and crush artifact. Immunohistochemistry positive for Synaptophysin Pan CK
Lim (Lim <i>et al.</i> , 2006)	2006	N/A	N/A	N/A	2 cases of unknown site	N/A	N/A
Zachariades	2004	50	M	Unknown	Mandible	Brain	Carcinoma cells in fibrous stroma with hyperchromatic nuclei. Nil immunohistochemistry
Svirsky	1989	62	M	60PYH	Soft Tissue, Mandible	Liver, Spleen	Basophilic nuclei with finely dispersed nuclear chromatin. Small cell islands were noted



metastasised to the head and neck region, of which 5 of the 21 were from SCLC metastasising to the tongue, maxillary gingiva, parotid gland and submandibular lymph nodes.

The histological description of SCLC in the literature is described as “scant cytoplasm, ill-defined cell borders, granular nuclear chromatin and absent or inconspicuous nucleoli” (Rudin *et al.*, 2021; van Meerbeeck *et al.*, 2011). From review of our histological slides, the case fits this definition of a poorly differentiated carcinoma. Notably, our case was positive for INSM1, a neuroendocrine marker. The literature suggests that INSM1 is not chemorefractive, implying the SCLC could have responded in a favourable manner if diagnosed earlier (McColl *et al.*, 2017; Xu *et al.*, 2022).

From review of our case and the literature, the frequency of SCLC metastases to the oral cavity is rare and indicative of end stage progression of SCLC (Hirshberg *et al.*, 2008). The symptoms of an oral cavity metastasis are vague and appear to mimic other more common odontogenic pathologies, most notably periapical disease or a recent extraction socket, which are of a benign nature. SCLC has a poor long term prognosis with patients having a life expectancy of approximately seven months post diagnosis (Rudin *et al.*, 2021; van Meerbeeck *et al.*, 2011). Hence early diagnosis and management is vital, including in the palliative setting, to ensure patients have a reduced morbidity associated with metastases. Given dentists are

the first line for inspecting changes in the oral mucosa, the case highlights the importance to take and review a comprehensive medical history, clinical examination and radiographic assessment. A broad differential diagnoses is critical to avoid misdiagnoses, given the benign appearance of malignant pathologies and a low threshold to biopsy. Our case is the first reported in the English literature of an SCLC metastases that was INSM1 positive which could have been responsive to earlier chemotherapy, potentially improving the patient's end stage quality of life. As such, it highlights the importance of routine dental screening and educating patients regarding signs and symptoms of changes in the oral cavity to ensure such presentations can be diagnosed at the earliest stage possible.

### Author contributions

All authors contributed to conception and design of the work, data collection, analysis and interpretation, drafting and critical revision of the article, and final approval of the version to be published.

### Conflicts of interest

The authors declare no conflicts of interest.

### Acknowledgements

The authors thank the patient for being willing to share details of their case.

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