



## A Rare Submandibular Gland Metastasis from Small Cell Neuroendocrine Carcinoma of the Lung: Which is Better Therapy? Case Report

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### Introduction

Small Cell Lung Carcinoma (SCLC) is usually of pulmonary origin, and only in 5% of cases it is extrapulmonary, mostly located in the head and neck. It is sensitive to chemotherapy. However, due to its aggressiveness, distant metastases are commonly found at the time of diagnosis in more than 50% of cases. In particular, the lymphatic spread mostly involves the mediastinal and the supraclavicular nodes while the hematogenous spread affects the liver, bone, skull and adrenal glands. Less than 2% of the secondary lesions occur in the salivary glands [1,2], mostly through the hematogenous route, and only 3 cases of SCLC metastases of the submandibular gland are described [3-5].

This report presents a rare case of SCLC metastases to the submandibular gland diagnosed in a 63-year-old man. The diagnostic work-up and the treatment plan are described.

### Case Presentation

A 63-year-old man presented a mass in the right submandibular region. It was 3-cm in diameter, bulky, slightly displaceable, and well demarcated. Bilaterally, the facial nerve was intact. At the endoscopic examination, the oropharynx was not involved. There were no palpable cervical lymph nodes.

The patient had a positive history for smoking (20 cigarettes per day) and myocardial infarction. He was affected by type 2 diabetes, hypertension and heart failure with FE 35%. The patient also described a high-grade SCLC of the lower lobe of left lung. The patient underwent two cycle of Radiotherapy (RT) (60 Gy + 20Gy).

At one month follow-up, the CT scan revealed the presence of a heterogenous 2 cm mass with regular margins and necrotic areas in the context of the right submandibular gland (Figure 1, 2). However, nor cervical or mediastinal lymphadenopathy were associated to it.

PET/CT examination showed increased 18F-FDG uptake of the left lung and of the right submandibular site (Suv 26)

Two weeks later, the FNA examination of the submandibular lesion reported a SCLC metastasis. The mass was strongly positive for CD56, and synaptophysin, CK, and TTF-1.

The patient refused the surgery and he was referred to the oncologic follow-up. Topotecan was then administered to the patient as a first step in the second-line systemic therapy. Three months later, an interval CT scan showed a considerable reduction in the size of his submandibular gland tumor.

The patient is currently in follow-up.

### Discussion

SCLC metastasis of the salivary glands is an extremely rare condition [2]: The parotid gland is the most common site involved, followed by the submandibular gland [1].

The small cell neuroendocrine carcinoma of the submandibular gland presents as an asymptomatic palpable mass, that may be accompanied by pain, paresthesia, and facial nerve palsy [1,2]. SCLC of salivary glands are high-grade malignant tumors characterized by local infiltration with an early angiolymphatic and perineural invasion, and frequent regional and distant metastases

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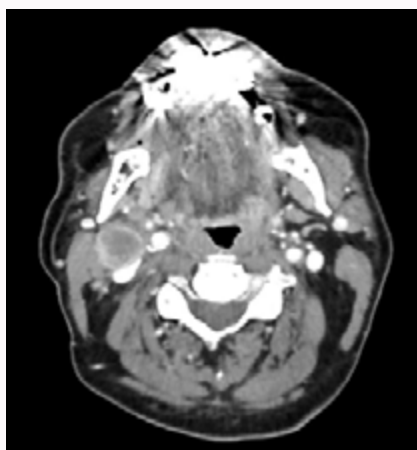
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**Figure 1:** CT scans demonstrate a 6.0 cm × 3.5cm sized mass in the left lobe (lingula).



**Figure 2:** CT heterogeneous enhanced, approximately 2 cm sized mass with central necrotic lesion and regular margin in the left submandibular gland.

[6].

The definitive diagnosis of the small cell neuroendocrine carcinoma of the submandibular gland obviously requires a biopsy, with particular attention to the immunohistochemistry. The FNA is fundamental in the diagnostic work-up: This tumor expresses chromogranin, synaptophysin, CD57, CD56 and neurofilaments; and most of them are cytokeratin's positive with perinuclear pattern, and negative to S-100 and HMB45 [7,8]. Total body CT scan, brain Magnetic Resonance Imaging (MRI), and Positron Emission Tomography (PET) scans must be performed to distinguish between primary and metastatic SCLC [6].

The treatment of small cell neuroendocrine carcinoma of the submandibular gland has not been established yet [2,6,9]. When it is a primary tumor of the gland, the surgical excision with adjuvant

chemo- or radiation therapy can be usually considered as an effective treatment. While the chemotherapy is the first treatment choice for metastatic cancer and recurrences [10]. The median overall survival for patients with metastatic small cell lung carcinoma receiving standard chemotherapy is in the range of 9 to 11 months [9].

Surgery and postoperative radiation therapy could improve local control, but they do not change the long-term survival [9,10]. The tumor size is the most important prognostic factor: If it is greater than 4 cm the prognosis is unfavorable. Other negative prognostic factors include aging, distant metastases, and CK20- negative tumors [8]. The presence of numerous neuroendocrine markers is associated with better prognosis.

The submandibular gland SCLC metastases should be considered in the differential diagnosis of submandibular gland's neoplasms. FNA is quick, little-invasive, and accurate to get a reliable diagnosis. Systemic therapy is still considered the best treatment for those patients with a good performance status in order to enhance the quality of life and lengthen the overall survival.

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