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Case report

# Primary small cell carcinoma of the larynx. Survival time of 47 months. Case report



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## ABSTRACT

Small cell carcinoma (SCC) of the larynx is a rare type of neuroendocrine carcinoma (NEC), few cases of which have been described in the literature. The prognosis for this type of carcinoma is poor, with a survival time typically not exceeding two years. We describe the case of a 54-year-old male patient with a primary tumor in the right ventricular band and a biopsy compatible with SCC. The patient underwent radiotherapy (RT) and concomitant chemotherapy (QT) and, after a relapse at 17 months, underwent total laryngectomy with bilateral neck dissection. The survival time was 47 months. Further studies are required to elucidate the possible causes of the better prognosis in some cases.

## 1. Introduction

NEC arise in neuroendocrine cells and may be either neural or epithelial in origin. The WHO has characterized neuroendocrine tumor of the larynx into four types: typical carcinoid tumor, atypical carcinoid tumor, small-cell neuroendocrine tumor, and paraganglioma. SCC is defined as tumor cells with small size (generally less than the diameter of 3 small resting lymphocytes), scant cytoplasm, high cell proliferation (Ki-67), and frequent necrosis [1–4].

Certain bibliographies may refer to another group of epithelial carcinomas, known as combined SCC, associated with squamous carcinoma or adenocarcinoma, only 14 cases of which have been described in the literature [5].

The first case of NEC was published by Goldman et al., in 1969 [6] and was an AC. The first authors to describe a case of small cell carcinoma of the larynx (SCCL) were Olofsson and Van Nostram in 1972, the second being described by Ferlito in 1974 [7,8].

NEC are rare, the atypical type being more frequent and the carcinoid type being less frequent. Five hundred cases of primary NEC of the larynx have been reported in the literature [9,10], of which 160 cases were classified as SCC [11,12].

The commonest site for NEC is the gastrointestinal tract (70%), followed by the respiratory tract (25%). They occur rarely in the skin,

paranasal sinuses, nasal cavity, genitourinary tract, salivary glands or larynx [2,7]. NEC account for less than 1% of neoplasms arising in the larynx [7]. The prognosis is related with the level of differentiation, being worse for the least differentiated types [1,2].

The treatment of choice for C or AC is surgery, whereas RT and QT seem to be the treatment of choice for SCCL. Surgery offers little hope and is reserved for cases of relapse after RT and QT. SSCL has the worst prognosis, the 5-year survival rate is 48% and 16% for two years and 5% for five years [7,9].

The incidence of SCC has increased in recent decades, although it still remains rare. In 1972 just two cases were reported [7,8]. In 1983, increased to 43 [13] and in 1985 the number of cases rose to 58 <sup>14</sup>. Prevalence increased thereafter, with 160 cases being described in 2004 [11] and 183 in 2015 [15]. Also in 2015, the University of Wisconsin published a case study of 298 patients with SCCL identified from the US National Cancer Database [16]. In the past two years, the incidence of small cell carcinoma of the larynx has doubled. The reasons for the increase in prevalence over the past 45 years, and particularly in the past two years, require further study.

#### 2. Presentation of case

We present the case of a male patient, aged 54 years, smoker of one

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Fig. 1. Cervical CT. Tumor in the right hemilarynx, without cervical adenopathy.

packet a day. He presented with dysphonia as his only symptom in November 2013. Fibroscopy revealed paralysis of the right vocal fold and an edematous lesion of the right ventricular band. No cervical lymphadenopathies were present in the physical examination.

A cervical computed tomography (CT) scan revealed a mass of  $32 \times 18 \times 29$  mm in the right ventricular band, vocal fold and parapharyngeal space, as well as obliteration of the retropharyngeal fat plane. No cervical lymphadenopathies were observed. (Fig. 1).

Biopsy revealed a squamous layer with a proliferation of small cells in the subepithelial tissue, with a predominantly solid pattern organized into trabeculae. The neoplastic cells had low cytoplasm levels and shaped nuclei with marginated, salt-and-pepper chromatin, with no evident nucleolus. Necrosis, apoptotic bodies and abundant mitosis were also observed (Fig. 2). SCC was diagnosed.

Immunohistochemistry of SSC requires neuroendocrine markers

positive (CD56, synaptophysin and chromogranin A), epithelial cell markers positive; negative for p53 and p63 (squamous cell carcinoma is positive), and positive Ki-67 proliferation in 75% of tumorous cells (Fig. 3).

PET/CT ruled out metastasis (cT3N0M0). After assessment by the Head and Neck Tumors Committee of our Health Area, RT plus concomitant QT was agreed. In 2014, prophylactic percutaneous endoscopic gastrostomy was inserted (as per the current protocols of our Medical Oncology Unit) [16], completing RT up to a total dose of 54 Gy on bilateral cervicals II-III-VI and 66 Gy on the larynx. The patient underwent four cycles of concomitant cisplatin plus etoposide, between 20 January 2014 and 24 March 2014. Re-assessment with PET/CT and fibroscopy (no paralysis of the right vocal fold and no edematous lesion of the right ventricular band) showed a complete clinical response.

Our Head and Neck Cancer Unit, using multidisciplinary otorhinolaryngology and oncology testing, maintaining complete remission according to fibroscopy and CT, evaluated the patient every month for 11 months.

In December 2014, a chest CT scan was ordered, showing a nodule in the left lower lobe (LLL). Core needle biopsy was compatible with SCC, although fibrosopy remained clear of relapse of the larynx and a PET/CT scan showed no metastasis. RT (55 Gy) was completed on LLL by mid-January 2015.

Fibroscopy examination in April 2015 showed paralysis of the right hemilarynx with edema of the right aryepiglottic fold and arytenoid. Cervical CT and biopsies were compatible with SCCL, and a PET/CT scan suggested a small lesion (solitary metastasis) in the right upper lobe (RUL). After assessment by the Head and Neck Tumors Committee, in June 2015 a total laryngectomy was performed with bilateral neck dissection, pectoralis major flap reconstruction and insertion of a voice prosthesis. RT was applied to the new pulmonary lesion, followed by four cycles of carboplatin plus etoposide between August and November 2015.

After a neoplasia-free interval of four months, a PET/CT scan showed lesions compatible with malignancy at the base of the tongue, right cervical lymph node, right paratracheal stripe and both lung roots. Fine needle aspiration confirmed SCC metastasis.

This relapse was not considered to be treatable by radical means, so in May 2016 weekly palliative treatment was begun with gemcitabine/ irinotecan, temozolomide, carboplatin/etoposide and praclitaxel, the final cycle being administered on June 1 2017.

The patient died in November 2017. Loco-regional disease was the cause of the death.



Fig. 2. Right arytenoid cartilage, coated in squamous epithelium with pseudoepitheliomatous hyperplasia and stroma infiltrated by a neoplastic mass. (A). Haematoxylin and eosin (H&E) stain  $(5 \times)$  showing small cells, solid pattern (B). H&E stain  $(20 \times)$ .

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