Small Cell Neuroendocrine Carcinoma of the Larynx: A Rare and Aggressive Tumor – Case Report and Literature Review

Abstract

Introduction: Small cell neuroendocrine carcinomas (SCNECs) of the larynx are extremely rare, accounting for approximately 0.6% of all laryngeal malignancies. They display an aggressive clinical course and are associated with a poor prognosis.
Case presentation: We report the case of a 58-year-old man with a history of heavy smoking (30 pack-years) who presented with a progressive left lateral cervical mass over one year. Clinical examination revealed cachexia (ECOG 2), a 10 cm left cervical mass, and a tracheostomy. CT imaging demonstrated a left glotto-supraglottic mass invading adjacent structures, with ipsilateral necrotic jugulocarotid lymphadenopathy. Direct laryngoscopy confirmed involvement of the left hemilarynx. Histology and immunohistochemistry showed SCNEC (CK+, chromogranin+, synaptophysin+, TTF1−, rare p40 expression). Staged as T2N1M0, the patient received two cycles of cisplatin–etoposide chemotherapy. The clinical course was marked by severe dysphagia, rapid deterioration, and afebrile neutropenia, requiring hospitalization. The patient died the following day from cardiopulmonary arrest.
Conclusion: This case highlights the rarity, aggressiveness, and poor prognosis of laryngeal SCNEC, underscoring the need for early diagnosis and prompt multidisciplinary management.

Keywords: Larynx; Neuroendocrine carcinoma; Small cell; Rare; Prognosis.

Introduction

Neuroendocrine tumors (NETs) of the larynx are rare, representing approximately 0.6% of laryngeal neoplasms [1]. In 2007, around 500 cases had been reported in the literature [2]. They belong to a heterogeneous group of tumors that can affect various organs, particularly the gastrointestinal tract and bronchial tree. According to the WHO 2005 classification, five histological subtypes are recognized, including small cell neuroendocrine carcinoma (SCNEC), which is most commonly described in the lung. Extrapulmonary SCNEC accounts for less than 5% of cases, with the gastrointestinal tract and bronchopulmonary system being the most common sites [3].
Although SCNECs are generally chemo- and radiosensitive, they tend to show rapid locoregional progression and early distant metastasis, resulting in poor survival rates.

Case Presentation

General data: A 58-year-old man with a history of heavy smoking (30 pack-years) presented with a progressively enlarging left lateral cervical mass evolving over one year.

Clinical presentation: Symptoms began with a cervical swelling that gradually increased in size. Four months before admission, the patient underwent a tracheostomy and biopsies in a

private clinic, followed by referral for radiotherapy. On examination, he appeared cachectic (ECOG 2), tracheostomized, with a 10 cm left cervical mass showing overlying inflammatory changes.

Investigations:

- **Imaging:** Cervico-thoraco-abdomino-pelvic CT revealed a necrotic left glotto-supraglottic tumor invading the aryepiglottic fold, epiglottis, left paraglottic space, piriform sinus, and parapharyngeal space, with massively necrotic ipsilateral jugulocarotid lymph nodes. Stage: T2N1M0.
- **Endoscopy:** Direct laryngoscopy demonstrated a tumor involving the left vocal cord, ventricular band, vallecula, anterior commissure, and left piriform sinus, with spared subglottic level and contralateral structures.
- **Histopathology and immunohistochemistry:** Small cell neuroendocrine carcinoma strongly expressing cytokeratin, chromogranin, and synaptophysin, negative for TTF1, and with rare p40 expression.

Management and outcome: Multidisciplinary tumor board recommended concomitant chemoradiotherapy. However, due to intolerance to the supine position, only cisplatin–etoposide chemotherapy was initiated. After two cycles, the patient developed total aphagia, rapid functional decline, and afebrile neutropenia, requiring hospitalization. He died the following day from cardiopulmonary arrest.

Discussion

Epidemiology and clinical presentation: Laryngeal neuroendocrine carcinomas are rare, with SCNEC being exceptional. The mean age of onset is in the sixth decade, with a male predominance and strong association with tobacco use [4]. Clinical presentation is often late and non-specific, including dysphonia, dyspnea, dysphagia, and cervical lymphadenopathy, as seen in our patient.

Histopathologic and immunohistochemical diagnosis: Diagnosis relies on histology supported by immunohistochemistry to differentiate SCNEC from other laryngeal malignancies such as poorly differentiated squamous cell carcinoma or lymphoma. Commonly expressed markers include cytokeratin, chromogranin, synaptophysin, and CD56 [5]. In our case, the immunoprofile (CK+, chromogranin+, synaptophysin+, TTF1−, rare p40) was consistent with a primary laryngeal origin rather than metastatic pulmonary disease.

Differential diagnosis: Includes other neuroendocrine carcinomas of the larynx (typical and atypical carcinoid), poorly differentiated squamous cell carcinoma, metastatic pulmonary SCNEC, and certain lymphomas [6].

Treatment: No standardized protocol exists for laryngeal SCNEC due to its rarity. Management is generally extrapolated from pulmonary SCNEC, with cisplatin–etoposide chemotherapy, with or without radiotherapy, considered standard [7]. Surgery is rarely indicated due to the early systemic nature of the disease. In our case, radiotherapy could not be performed, and chemotherapy alone yielded poor tolerance and rapid decline.

Prognosis: Laryngeal SCNEC carries a poor prognosis, with 5-year survival rates below 20% [8] due to the high frequency of early metastases, even in cases with initial treatment response. Our patient's rapid deterioration and death reflect the aggressive nature of the disease.

Future perspectives:

- **Immunotherapy** with anti–PD-1/PD-L1 agents, as used in pulmonary SCNEC [9].
- **Molecular profiling** (TP53 mutations, RB1 alterations) for targeted therapies [10].
- **Adaptive radiotherapy** for frail patients.

Conclusion

Laryngeal SCNEC, though potentially sensitive to chemo- and radiotherapy, remains associated with poor outcomes. Given its rarity, reporting such cases is essential to improve understanding, facilitate early diagnosis, and optimize treatment strategies.

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