Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/21532
DOI URL: http://dx.doi.org/10.21474/IJAR01/21532

RESEARCH ARTICLE

SMALL CELL NEUROENDOCRINE CARCINOMA OF THE LARYNX: A RARE AND AGGRESSIVE TUMOR – CASE REPORT AND LITERATURE REVIEW

O.El Meliani , H. Majd , M.T. Saoudi, K. Maadin, N.Demnati Sadki, L. Amaadour, K. Oualla, Z. Benbrahim, S. Arifi and N. Mellas

Manuscript Info

Manuscript History
Received: 07 June 2025
Final Accepted: 9 July 2025
Published: August 2025

Key words:-
Larynx; Neuroendocrine carcinoma; Small cell;Rare;Case report; Chemotherapy; Prognosis.

Abstract

Introduction: Small cell neuroendocrine carcinomas (SCNECs) of the larynx are extremely rare, representing approximately 0.6% of all laryn geal malignancies. They follow an aggressive clinical course and are a sociated with a poor prognosis.
Case presentation: We report the case of a 58 year old man with a hist ory of heavy smoking(30 packyears)who presented with a progress ve l eft lateral cervical mass over one year.Clinical examination revealed ca chexia (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.Dire ct laryngoscopy confirmed involvement of the left hemilarynx.Histolog y and immunohistochemistry showed SCNEC(CK+, chromogranin+,sy naptophysin+,TTF1−,rare p40 expression). The disease was staged T2 N1M0. The patient received two cycles of cisplatin etoposide chemothe rapy.The clinical course was marked by severe dysphagia, rapid deterio ration, 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, emphasizing the importance for early d iagnosis and prompt multidisciplinary management.

Introduction:-

Neuroendocrine tumors (NETs) of the larynx are rare, accounting for approximately 0.6% of all laryngeal neoplasms [1]. By 2007, about 500 cases had been reported in the literature [2]. These tumors form a heterogeneous group thatcan arise in several organs, most commonly in the gastrointestinal tract and the bronchial tree. According to the WHO 2005 classification, five histological subtypes are recognized, including small cell neuroendocrine carcinoma (SCNEC), which is most frequently described in the lung. Extrapulmonary SCNEC accounts for fewer than 5% of cases, with the gastrointestinal tract and bronchopulmonary system being the most common sites [3].

Although SCNECs are generally sensitive to chemotherapy and radiotherapy, they typically exhibit rapid locoregional progression and early distant metastasis, resulting in poor survival rates.

Corresponding Author:-O.El Meliani , H. Majd

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: The disease began with a cervical swelling that gradually increased in size. Four months before admission, he underwent a tracheostomy and biopsies in a private clinic, after which he was referred for radiotherapy. On examination, he appeared cachectic (ECOG performance status 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:** Findings were consistent with small cell neuroendocrine carcinoma, strongly expressing cytokeratin, chromogranin, and synaptophysin, negative for TTF-1, 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 followingdayfromcardiopulmonaryarrest.

Discussion:-

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

Histopathologic and immunohistochemical diagnosis: Diagnosis relies on histology supported by immunohistochemistry to distinguish 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+, TTF-1−, rare p40 expression) supported a primary laryngeal origin rather than metastatic pulmonary disease.

Differential diagnosis: Other entities to be considered include typical and atypical carcinoid tumors, 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 given the early systemic nature of the disease. In our patient, radiotherapy could not be performed, and chemotherapy alone was poorly tolerated, resulting in rapid decline.

Prognosis: Laryngeal SCNEC carries a poor prognosis, with 5-year survival rates below 20% [8], reflecting the high frequency of early metastases despite initial treatment response. Our patient's rapid deterioration and death highlight the aggressive natural history of this malignancy.

Future perspectives: Given the dismal prognosis of laryngeal SCNEC, there is an urgent need to explore novel therapeutic strategies beyond the conventional cisplatin–etoposide regimen. Current perspectives include:

- **Immunotherapy**: Immune checkpoint inhibitors targeting the PD-1/PD-L1 axis have demonstrated significant benefit in small cell lung cancer (SCLC). Agents such as atezolizumab and durvalumab, when combined with chemotherapy, improved overall survival in extensive-stage SCLC [9]. Extrapolation of these results suggests potential benefit in extrapulmonary SCNEC, including laryngeal cases, although dedicated studies are lacking.

- **Clinical trials:** Given the rarity of the disease, inclusion of patients with laryngeal SCNEC in basket trials or rare tumor consortia is strongly encouraged. Ongoing studies evaluating immune checkpoint inhibitors, novel cytotoxic combinations, and bispecific antibodies in extrapulmonary neuroendocrine carcinomas may open new therapeutic avenues.
- **Molecular profiling and targeted therapies:** Genomic analyses of SCNEC frequently reveal alterations in *TP53* and *RB1*, as well as MYC amplifications [10]. Next-generation sequencing in laryngeal SCNEC may identify targetable mutations or allow inclusion in precision medicine programs.
- **Radiotherapy innovations:** Adaptive and intensity-modulated radiotherapy may be particularly relevant for frail patients unable to tolerate standard regimens, potentially reducing toxicity while maintaining efficacy.

Overall, multidisciplinary collaboration and integration into clinical research programs are essential to improve outcomes in this rare and aggressive malignancy.

Conclusion:-

Laryngeal small cell neuroendocrine carcinoma, although potentially sensitive to chemotherapy and radiotherapy, remains associated with extremely poor outcomes. Its rarity and aggressiveness underscore the importance of early diagnosis and timely multidisciplinary management. Reporting such cases contributes to a better understanding of the disease, facilitates earlier recognition, and may help optimize therapeutic strategies in the future.

Références:-

1. Ferlito A, et al. Neuroendocrine neoplasms of the larynx: An overview. Head Neck. 2016;38 Suppl1:E2259–E2266.
2. Woodruff JM, et al. Small cell carcinoma of the larynx: A clinicopathologic study of 13 cases. Cancer. 1985;55(8):1956–1963.
3. Barnes L, et al. Pathology and Genetics of Head and Neck Tumours. WHO Classification of Tumours. IARC Press, 2005.
4. Renner G. Small cell carcinoma of the head and neck: a review. SeminOncol. 2007;34(1):3–14.
5. van der Laan TP, et al. Primary small cell carcinoma of the larynx: A case series and review of the literature. Eur Arch Otorhinolaryngol. 2015;272(8):2171–2178.
6. Ferlito A, et al. Primary and secondary small cell carcinoma of the larynx: Review of the literature. Ann OtolRhinolLaryngol. 1985;94(6 Pt 1):591–596.
7. Baugh RF, et al. Primary small cell carcinoma of the larynx. Ann OtolRhinolLaryngol. 1986;95(2 Pt 1):166–170.
8. Baugh RF, Wolf GT. The treatment of small cell carcinoma of the larynx. Otolaryngol Head Neck Surg. 1986;94(2):174–178.
9. Horn L, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med. 2018;379:2220-2229.
10. George J, et al. Comprehensive genomic profiles of small cell lung cancer. Nature. 2015;524(7563):47-53.