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Laryngeal Small Cell Neuroendocrine Carcinoma: Case Report and Literature Review

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Abstract **Case Report**

Neuroendocrine malignancy of the larynx are rare but represents the first nonsquamous tumor in this localization. The World Health Organization (WHO) classifies these tumors into 3 groups: typical carcinoid, atypical carcinoid tumor, and small cell neuroendocrine carcinoma (SmCC). SmCC have an aggressive natural history characterized by widespread metastasis. Treatment is based on concomitant or sequential chemoradiation. We report herein the case of a 69 years old men, who presented with laryngeal small cell neuroendocrine carcinoma revealed by progressive dysphonia and cervical lymphadenopathy. The diagnosis was confirmed by biopsy and histopathological study. Pre-treatment workup was negative for metastatic disease. He has received chemotherapy based on etoposide and cisplatin followed by chemoradiation. The evolution was marked by the development of metachronous lung metastasis. Unfortunately, the patient passed away during a chemotherapy-induced myelosuppression after the first palliative chemotherapy cure.

Keywords: Small cell neuroendocrine tumors, larynx, histology, management.

INTRODUCTION

Laryngeal neuroendocrine carcinomas are heterogeneous neoplasms characterized by neuroendocrine differentiation [1]. Small cell neuroendocrine of the larynx is a rare entity, relatively aggressive and has a greater propensity for regional and distant failure, leading to a worse prognosis [2]. Its management has not been standardized but is extrapolated from experience and published evidence for small cell lung cancer (SCLC) because of their similar clinical and pathological features [3].

We report a case of a primary laryngeal small cell neuroendocrine carcinoma in 69 years old man while discussing epidemiology, diagnosis and treatment of this rare and aggressive entity.

CASE REPORT

A 62 years-old Arabic man with no significant past medical history presented to our department with progressive worsening dysphonia and more lately dyspnea.

He has a 40 year history of smoking one pack a day and moderate alcohol consumption.

Physical exam found a right cervical bulky adenopathies of 11 cm in diameter on the right and two other left sided cervical lymphadenopathies of 3cm and 2cm (figure 1).

Fig. 1: Right cervical bulky adenopathies

Indirect laryngoscopy revealed a Left Hemi-laryngeal tissue process (glottic and supra- glottic levels) infiltrating the anterior commissure.

The biopsy with histological examination confirmed the diagnosis of small cell neuroendocrine carcinoma.

A cervical computed tomography (CT) scan showed bulky mass of vocal cord measuring 20cm in its greater diameter, locally advanced, with multiple bilateral cervical and spinal lymph nodes (figure 2).

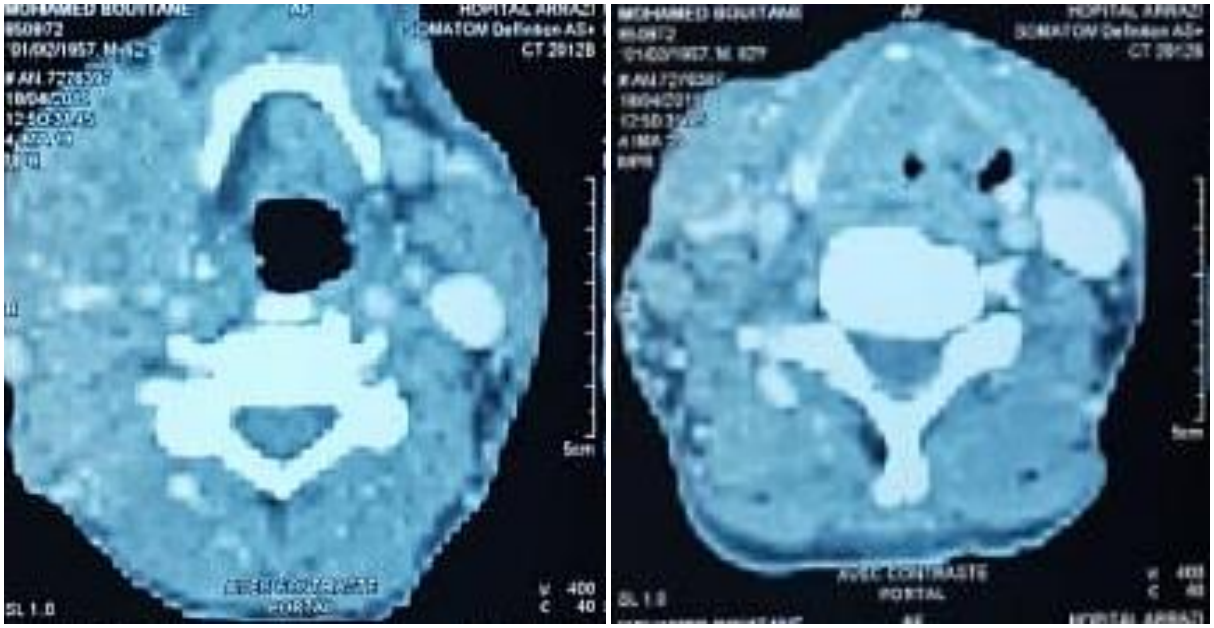

Figure 2: Axial CT scan of the larynx showing a voluminous mass of the vocal cords locally advanced with multiple bilateral cervical lymph nodes

Pre-therapeutic Workup included a thoracic and abdominal CT scan with an octreo-scan, showed no metastatic spread. The tumor was classified cT3N3Mo.

The patient had received three cycles of cisplatin and etoposide-based chemotherapy. Clinical evaluation after third cycle was marked by regression of tumor volume (figure 3).

This chemotherapy was followed by a combination of concomitant radiochemotherapy at a dose of 70 Gy on the tumour and its lymph node extensions, delivered at 2 Gy per fraction in 7 weeks without treatment interruption. Standard RC3D technique was used for treatment with acceptable G2 toxicity.

Figure 3: Regression of lymph node volume after third chemotherapy cure

At the 6th month imaging control, the patient presented with metachronous lung metastasis. Palliative chemotherapy has been indicated. Unfortunately, the patient presented a bone marrow aplasia leading to his death.

DISCUSSION

Epidemiology:

Neuroendocrine neoplasms of the larynx are rare, but represent most common nonsquamous tumor in this organ, accounting for approximately less than 1% of all laryngeal neoplasms [4].

The WHO classification 2017 of head and neck has described 4 subtypes:

- Well-differentiated (WD-NEC),
- Moderately-differentiated (MD-NEC), and
- Poorly-differentiated (PD-NEC) with small cell and large cell sub-types.

A primary small cell neuroendocrine carcinoma of the larynx is quite rare, it represents about 0.5 per cent of all laryngeal cancers [2]. The first case was reported by Olofsson and van Nostrand in 1972.

Median age at presentation is 60 years (range 31–81). Most patients affected are male (sex ratio: 3/1) and smokers (91%).

Diagnosis and Workup:

Clinically, symptoms vary according to the site and extent of the disease [2]. The most common revealing symptom is dysphonia with cervical lymphadenopathy. Some series reported an incidence of cervical lymphadenopathy of 54% to 93% of patients [5, 6].

Imaging plays a crucial role not only in the initial diagnosis but also in long term follow-up of laryngeal small cell neuroendocrine carcinoma.

Endoscopy classically reveals a sub-mucosal tumor and may vary in size from 0.5 cm to 5 cm [7]. The disease can develop in any subsite of larynx, but the supraglottic one is the most commonly affected [8].

Computed tomography is the gold standard imaging modality, it allows good assessment of loco regional extension of tumor especially regional lymphadenopathy. Thoracoabdominal CT and octreoscan are recommended to assess distant metastasis.

Histopathology:

Histologically, the tumors can be divided into 3 types of cell: oat cell, intermediate, and combined. They are characterized by small, dark nuclei with finely granular, salt-and-pepper chromatin, and inconspicuous nucleoli [9]. Cell necrosis and mitotic activity are frequent [7].

Immunohistochemistry can be used in the diagnosis of SCNC of the larynx. The tumors will stain positive for typical neuroendocrine markers, such as chromogranin, synaptophysin, NSE, CD56, CD57, and neuropeptides. Tumor cells can express cytokeratins, epithelial membrane antigen, carcinoembryonic antigen, calcitonin, somatostatin, adrenocorticotropic hormone, bombesin, and serotonin [10]. In addition SCNC may be positive for TTF-1 [11].

Pathological differential diagnosis include some rare cases of sarcoma, such as extraskeletal Ewing/peripheral neuroectodermal tumor, Merkel cell carcinoma, and olfactory neuroblastoma [10].

Treatment and Prognosis:

A correct diagnosis and comprehensive staging are essential for choosing the most appropriate therapeutic approach.

Giving the rarity of this entity, there are no consensus guidelines, and management has mainly been extrapolated from small cell lung cancer because of their similar clinic-pathological features.

In general, radical surgery is not usually the primary treatment; it is known to be associated to poor outcome, with a high risk of distant metastasis and local recurrence [2].

The treatment of choice is concurrent or sequential chemoradiotherapy, it yielded the best 5-year DSS for small cell neuroendocrine carcinoma in the larynx compared with other modalities (30.8% vs 12.9%, P = .001) [12].

In a study of extrapulmonary small cell carcinoma, Galanis *et al.*, reported a higher response rate to platinum-based chemotherapy (72 per cent, with a median survival time of 8.5 months) compared to a doxorubicin-based regimen (57 per cent, with a median survival time of 4.5 months) for extensive or recurrent extrapulmonary small cell carcinomas [13].

Barker *et al.*, [14] reported in a series of 23 patients with non-metastatic, non-sinonasal neuroendocrine carcinomas that the use of cisplatin and etoposide combination chemotherapy doubled the overall two-year survival rate compared with that achieved with local therapy only (68 per cent vs 30 per cent, p= 0.003). It also significantly reduced the rate of two-year distant metastasis from 79 per cent to 39 percent.

Retrospective series analysis conclude to the importance of the addition of combination chemotherapy to local treatment in improving the distant and local prognosis [2].

The authors also advocated the use of sequential chemoradiotherapy and consideration of prophylactic cranial irradiation because of the large incidence of intracranial metastases (25 per cent and 44 per cent after two and five years, respectively) [2].

The prognosis of small cell neuroendocrine carcinoma of the larynx is very poor [15]. Early metastases are exceedingly common and over 90% of patients with laryngeal small cell neuroendocrine carcinoma developing metastatic disease [16]. The most common sites of metastatic spread are the cervical lymph nodes, liver, lung, bone, and bone marrow. It has been reported that patients with metastatic disease have poor median survival of 10.0 months and 2-year OS of 15.7% [17].

CONCLUSION

Laryngeal small cell neuroendocrine tumor is a rare and uncommon entity, characterized by its aggressiveness and poor prognosis. Its management has not been standardized. Concomitant or sequential chemo radiation with etoposide-cisplatin regimen is the mainstay treatment.

Conflict of Interest: The authors declare no conflict of interest.

Informed Consent: The patient's informed consent to the publication of their data has been obtained.

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BIBLIOGRAPHY

1. Carolina, S., & Alfio, F. (2019). Update on Neuroendocrine Carcinomas of the Larynx. *Am J Clin Pathol*, *XX*, 1–15 DOI: 10.1093/AJCP/AQZ106
2. Iqbal, M. S., Paleri, V., Moor, J., Dobrowsky, W., Kelly, C., & Kovarik, J. (2015). Small cell neuroendocrine carcinoma of larynx: case series and literature review. *The Journal of Laryngology & Otology*, *129*(9), 910-915.
3. Wakasaki, T., Yasumatsu, R., Masuda, M., Matsuo, M., Tamae, A., Kubo, K., ... & Nakagawa, T. (2019). Small cell carcinoma in the head and neck. *Annals of Otology, Rhinology & Laryngology*, *128*(11), 1006-1012. DOI: 10.1177/0003489419853601
4. Angouridakis, N., Goudakos, J., Karayannopoulou, G., Triaridis, S., Nikolaou, A., & Markou, K. (2013). Primary neuroendocrine neoplasms of the larynx. A series of 4 cases reported and a review of the literature. *Head & Neck*, *35*(6), E187-E193. (wileyonlinelibrary.com). DOI 10.1002/hed.22955
5. Moisa, I. I. (1991). Neuroendocrine tumors of the larynx. *Head & neck*, *13*(6), 498-508.
6. Mills, S. E., Cooper, P. H., Garland, T. A., & Johns, M. E. (1983). Small cell undifferentiated carcinoma of the larynx: Report of two patients and review of 13 additional cases. *Cancer*, *51*(1), 116-120.
7. Ferlito, A., Silver, C. E., Bradford, C. R., & Rinaldo, A. (2009). Neuroendocrine neoplasms of the larynx: an overview. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck*, *31*(12), 1634-1646. (www.interscience.wiley.com). DOI: 10.1002/hed.21162
8. Mikić, A., Zvrko, E., Trivić, A., Stefanović, D., & Golubović, M. (2012). Small cell neuroendocrine tumor of the larynx–a small case series. *Collegium antropologicum*, *36*(2), 201-204.
9. Lewis Jr, J. S., Ferlito, A., Gnepp, D. R., Rinaldo, A., Devaney, K. O., Silver, C. E., & Travis, W. D. (2011). Terminology and classification of neuroendocrine neoplasms of the larynx. *The Laryngoscope*, *121*(6), 1187-1193.
10. Hunt, J. L., Ferlito, A., Hellquist, H., Rinaldo, A., Skálová, A., Slootweg, P. J., ... & Cardesa, A. (2017). Differential diagnosis in neuroendocrine neoplasms of the larynx. *Advances in anatomic pathology*, *24*(3), 161-168.
11. Ferlito, A., Silver, C. E., Bradford, C. R., & Rinaldo, A. (2009). Neuroendocrine neoplasms of the larynx: an overview. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck*, *31*(12), 1634-1646.
12. van der Laan, T. P., Plaat, B. E., van der Laan, B. F., & Halmos, G. B. (2015). Clinical recommendations on the treatment of neuroendocrine carcinoma of the larynx: A meta-analysis of 436 reported cases. *Head & neck*, *37*(5), 707-715.
13. Galanis, E., Frytak, S., & Lloyd, R. V. (1997). Extrapulmonary small cell carcinoma. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *79*(9), 1729-1736.
14. Barker Jr, J. L., Glisson, B. S., Garden, A. S., El-Naggar, A. K., Morrison, W. H., Ang, K. K., ... & Rosenthal, D. I. (2003). Management of nonsinonasal neuroendocrine carcinomas of the head and neck. *Cancer*, *98*(11), 2322-2328.
15. Ferlito, A., & Rinaldo, A. (2003). Small cell neuroendocrine carcinoma of the larynx: a preventable and frustrating disease with a highly aggressive lethal behavior. *ORL*, *65*(3), 131-133.
16. Gnepp, D. R., Ferlito, A., & Hyams, V. (1983). Primary anaplastic small cell (oat cell) carcinoma of the larynx. Review of the literature and report of 18 cases. *Cancer*, *51*(9), 1731-1745.
17. Pointer, K. B., Ko, H. C., Brower, J. V., Witek, M. E., Kimple, R. J., Lloyd, R. V., ... & Baschnagel, A. M. (2017). Small cell carcinoma of the head and neck: an analysis of the National Cancer Database. *Oral oncology*, *69*, 92-98.