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Case report

The small cell carcinoma neuroendocrine type of the larynx—Case report

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ABSTRACT

Introduction: Extrapulmonary small cell carcinoma neuroendocrine type (ESCCNET) is a rare tumor (2.5%–4.0% of all small cell carcinomas), and during the past 30 years, only 160 cases of primary small cell carcinoma of the larynx have been reported worldwide.

Aim: To report a rare case of small cell carcinoma of the larynx, in a 54-year-old man, including diagnostic work-up, and treatment with chemotherapy (CHT) and radiotherapy (RT), compromised by the patient's nonadherence, and to spread awareness of the need of further research, focused on new therapeutic strategies, in patients with ESCCNET.

Case study: The patient underwent induction CHT based on cisplatin and etoposide. Partial remission was obtained after the 3rd cycle of CHT, confirmed by the CT scan. The patient refused further CHT. He underwent RT. The residual larynx tumor and elective nodal volume were irradiated. A follow-up laryngological examination and control CT scan, performed two months after the completion of RT, showed a complete remission. Eight months later brain CT revealed multiple metastases. Palliative cranial irradiation and CHT were applied. The patient died in October 2011.

Results and discussion: ESCCNET, an unusual neoplasm, accounting for 0.5% of all laryngeal carcinomas, is most commonly located in the supraglottic region. In contrast to squamous cell carcinoma of the larynx, a single modality therapy is not advised for ESCCNET, because these tumors are biologically aggressive, and at least 73% of patients have distant metastases. Therefore, RT and CHT in concomitant or sequential fashion offer the best chance of survival. However, in the presented case, the recommended therapy was not fully implemented, due to the patient's noncompliance.

Conclusions: This report underscores the need for thorough, systemic diagnostic work-up, and emphasizes that the combination of RT and CHT remains the treatment of choice for ESCCNET (while surgery is reserved for persistent and recurrent disease). In addition, it points out that the new therapeutic strategies to improve survival in ESCCNET are needed, such as a prophylactic cranial irradiation that could be explored in future clinical trials.

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1. Introduction

Extrapulmonary small cell carcinoma (EPSCC) neuroendocrine type (EPSCCNET) has been recognized as a clinicopathological entity distinct from the small cell lung carcinoma (SCLC).¹ Galanis et al. reported a series of 81 patients with EPSCC, treated in Mayo

clinic, in whom the carcinoma originated from the: gastrointestinal tract – in 36%, head and neck – in 17%, genitourinary tract – in 15%, and gynecologic organs – in 12% of cases. A careful assessment, with the brain MRI and bone scan is also required in this type of carcinoma.² Small cell carcinoma was first described in the larynx by Olofsson and van Nostrand in 1972.³ During the past 30 years, about 160 cases of primary small cell carcinoma of the larynx have been reported worldwide. These tumors are very rare, and can occur in multiple sites, in the head and neck area.⁴ The most common symptoms of laryngeal small cell carcinoma

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neuroendocrine type (SCCNET) are hoarseness, dysphagia and dyspnea.^{5,6} This neoplasm is characterized by a rapid growth, aggressive metastatic potential, and deeply invasive tumor infiltration. Therefore, a full metastatic workup is extremely important. Two thirds of patients die from the widespread metastases.⁷

Advanced local disease is generally found at an initial physical examination, including cervical lymph nodes metastases that are present in 50% of patients.^{8,9}

Radiotherapy (RT) or surgery should be combined with systemic chemotherapy (CHT) as primary treatment options.^{10,11} CHT is the treatment of choice for relapse or metastases, and for the extensive stages of malignancy. Platinum- or adriamycin-based regimens are the most common protocols, with a response rate from 30% to 90%. Brain metastases are less common in EPSCCNET, comparing to SCLC. Prophylactic cranial irradiation has been suggested for complete response in SCLC. However, there are still insufficient data to suggest it for EPSCCNET.² Reported 3-year, and 5-year survival rates for patients with EPSCCNET are 30%, and 11%–13%, respectively.⁴ Median survival is 8–16 months. EPSCCNET that originates from gynecologic organs, and the head and neck has more favorable outcomes, probably because of the early detection, and intensive treatment applied to these areas.^{2,12} Combined treatment (RT and CHT) modality has been reported to be an independent predictor of survival, according to one study.¹³ However, in another study, no better survival benefit of the combined over the single treatment was shown.¹⁴ To further explore this topic, and to establish the treatment guidelines, prospective trials are warranted, in patients with EPSCCNET.^{2,14}

In this report, we describe an unusual case of metastatic small cell carcinoma of the larynx, in which the diagnostic, and therapeutic aspects (including nonadherence to treatment) have been discussed.

2. Aim

The aim of this work is to report a rare case of small cell carcinoma of the larynx, in a 54-year-old man, including diagnostic work-up, and treatment with CHT and RT (compromised by the patient's nonadherence to the concomitant RT-CHT, after an initial remission), and to spread an awareness of the need for further research, focused on novel therapeutic strategies, in patients with ESCCNET.

3. Case study

A 54-year-old male was admitted to the Otolaryngological Department of Medical University of Łódź, Barlicki University Hospital of Łódź, in March 2010, with a 3-month history of

worsening hoarseness. He has been complaining about mild dyspnoea, and progressive dysphagia, for at least 3 months. There was no history of weight loss. He was an occasional alcohol user, and has been smoking 1–2 packs of cigarettes per day, for 25 years. He had no positive history of any malignancy in the family.

The CT scan of the neck, and laryngoscopy revealed a large mass of the larynx (42 × 40 × 30 mm) with fixation of hemilarynx, invading epiglottis on the right side, both arytenoids, right aryepiglottic fold, right ventricular and vocal fold, with the tumor extension into the subglottic area. There was no lymphadenopathy on the CT scan (Fig. 1). No distant metastases were identified by radiology tests. A biopsy of laryngeal mass revealed small cell carcinoma, with a positive reaction for neuroendocrine markers (chromogranin and synaptophysin) (Fig. 2). The cancer clinical stage was classified as cT3N0M0.

A tracheostomy was placed, and the patient underwent induction CHT, based on cisplatin 30 mg/m² and etoposide 120 mg/m², every 21 days. Partial remission around 60% was obtained after the 3rd cycle of CHT, confirmed both by the laryngeal examination, and CT scan (Fig. 3). Since the patient refused further CHT, RT remained the only modality to use.

The patient started RT in June 2010. The residual larynx tumor was irradiated to 70 Gy in 35 fractions; elective nodal volume was irradiated to 50 Gy in 25 fractions. A follow-up laryngological examination, and control CT scan, performed two months after the completion of RT, showed a complete remission.

In February 2011, the patient presented with neurological symptoms, suggesting a disease dissemination to the brain. Brain CT revealed multiple metastases. Palliative cranial irradiation and CHT were applied. Easy fatigue, headaches, and spontaneous vomiting started in mid September 2011. At that time, the brain CT showed progression of metastases. The patient died in October 2011.

4. Results and discussion

The EPSCCNET represents a rare, distinct type of primary laryngeal neuroendocrine tumor that is characterized by a very aggressive course. The most frequent localization of small cell larynx carcinoma is the supraglottic subsite. About 90% of patients develop distant metastases with predilection to lymph nodes, bones, liver, brain, and skin. Therefore, this malignancy must be regarded as a systemic disease. Detailed radiology studies, including brain CT scan, should be performed before initiation of the treatment.¹⁵ The combination of RT and CHT remains the treatment of choice. Surgical procedures are not recommended as the initial treatment. However, they are best reserved for persistent and recurrent disease, at the primary site (e.g., neck area). It should be emphasized that the presence of metastases, and the treatment

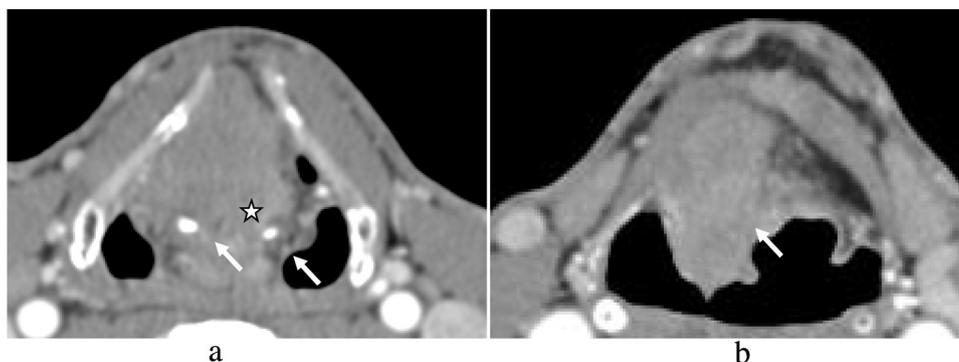


Fig. 1. Slightly and homogeneously enhanced tumor (star) obstructing the larynx, involving arytenoids (arrows) (a), and epiglottis on the right side (arrow) (b) at the axial contrast-enhanced CT scan.

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