

## Case Report

# Primary combined squamous and small cell carcinoma of the larynx: a case report and review of the literature

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**Abstract:** Primary combined squamous and small cell carcinoma is a rare type of laryngeal carcinoma, and only 18 cases have been reported in the literature. Here we report a 70-year-old male patient presenting with transglottic carcinoma, which was composed of both small cell carcinoma and squamous cell. The patient underwent total laryngectomy with bilateral modified neck dissection and consolidation radiotherapy. We found metastasis in right adrenal gland 16 months after initial diagnosis and the patient died of multi-organ metastase in abdomen. Therefore, this type of laryngeal carcinoma might be a great aggressive tumor. More rational treatment regimen and molecule-targeted drugs to such carcinoma should be developed in the future.

**Keywords:** Combined small cell carcinoma, larynx, treatment, prognosis

### Introduction

Squamous cell carcinoma is the most common histological type of laryngeal carcinoma [1]. Small cell carcinoma, accounting for only 0.5 percent of laryngeal carcinomas, is often related to smoking and alcohol abuse [2]. When small cell carcinoma is associated with a squamous component, this tumor is referred to as combined carcinoma [3]. Because of its low incidence, such combined carcinoma is reported unusual. Here we report an additional case of primary combined squamous and small cell carcinoma of the larynx.

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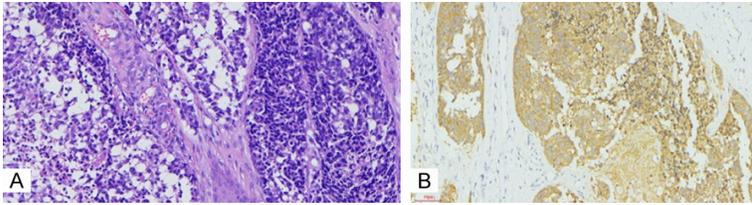
A 70-year-old male patient presented with one-month history of worsening hoarseness, progressive dysphagia with solids, no exact history of weight loss. There was no obvious lymph node at both sides of neck and supraclavicular regions. His medical history of ankylosing spondylitis was more than ten years. He had been smoking two packs of tobacco per day for more than fifty years, with no history of alcohol consumption, with no malignancy history in his family.

On laryngoscope examination, a cauliflower tumor, originating in right laryngeal ventricle,

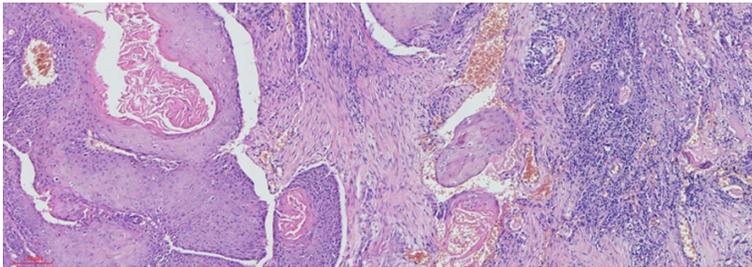
extended inferiorly to anterior commissure and crossed the midline to left vocal cord. The mobility of right vocal cord was obviously impaired. The contrast-enhanced CT scan showed an irregular mass from right laryngeal ventricle crossing midline to left vocal cord, no exact metastatic node noted in both sides of neck. There was no distant metastasis found on the chest roentgenogram, abdominal sonogram and ECT (emission computed tomography).

This patient underwent total laryngectomy with bilateral modified neck dissection and consolidation radiotherapy (60 Gy delivered on the larynx and 50 Gy delivered on the cervical lymph node regions). The frozen sections on all the surgical margins were reported negative for tumor and negative for vascular metastasis. Biopsy of the tumor mass was composed of both small cell carcinoma (**Figure 1**) and squamous cell carcinoma (**Figure 2**), small cell carcinoma lateralized to right side and squamous cell carcinoma to left vocal cord. We found metastasis in right adrenal gland 16 months after initial diagnosis and the patient died of multi-organ metastasis in abdomen. Because an autopsy or a biopsy was not conducted, we could not determine the exact pathological type of metastatic organs.

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**Figure 1.** A. Small cell carcinoma component showing invasive growth of tumor cells, medium size, deep staining, unclear nucleus and scant cytoplasm (HE  $\times 200$ ). B. Strong synaptophysin immunoreactive in the small cell carcinoma component and neuroendocrine granules seen in the cytoplasm of small cell (synaptophysin  $\times 200$ ).



**Figure 2.** The tumor showing infiltrative growth of well-differentiated squamous cells, gathered into nest, cell cone could be seen (HE  $\times 100$ ).

### Discussion

Combined small cell carcinoma consists of small cell carcinoma with a component of squamous cell carcinoma or adenocarcinoma [4]. Primary combined squamous and small cell carcinoma, often leading to early regional and distal metastasis, is a rare type of laryngeal carcinoma, and only 18 cases have been reported in the literature to date. The clinical features of those reported patients are summarized in **Table 1**. Most of these patients are males with fifth to seventh decade. They often have a long history of smoking, and present with symptoms including hoarseness of voice, sore throat, dysphagia or a palpable neck mass. The most common site of the larynx is the supraglottic region. The most common sites of metastatic spread of this aggressive neoplasm are cervical lymph nodes, liver, lung, bones and bone marrow and the 2-year survival was reported just 8.5% [5].

Combined squamous and small cell carcinoma of the larynx, first reported by Ferlito in 1985 [6], has its own histological and biological behavior features. Accurate and detailed examination of laryngeal specimens is necessary for appropriate treatment plan, as well as progno-

sis. In our case, the palpable tumor mass involved in right ventricle which was immunoreactive with synaptophysin and chromogranin had a histological appearance of small cell carcinoma, the neoplasm involved in left vocal cord in which cell cone could be seen in hematoxylin and eosin stain had a histological appearance of well-differentiated squamous cell carcinoma. The histological differences of laryngeal tumor in two sides of larynx may be attributed to the larynx is a highly compartmentalized organ in which right and left halves are physically and anatomically separated from each other [7].

Combined squamous and small cell carcinoma of the larynx constitutes a real challenge for clinicians because each

treatment modality of small cell carcinoma and squamous cell carcinoma must be integrated. As in published reports [8], therapeutic managements included surgery, radiotherapy, chemotherapy or some combinations of these modalities, but guideline of systemic therapy strategy for such type carcinoma of larynx has not been established [9]. In our case, we performed total laryngectomy with bilateral modified node dissection and consolidation radiation therapy. Although local region was well controlled, we still found distance metastasis in right adrenal gland, which was first reported in such type of laryngeal carcinoma. Then we offered a platinum-based chemotherapy regimen [10] to the patient. Considering great side effects of chemotherapy and patient's poor physical condition, his family members rejected our suggestion. At last, the patient died of multi-organ metastasis in abdomen. So combined squamous and small cell carcinoma of the larynx could be considered as a systemic disease which needs systemic chemotherapy to eliminate distance metastasis, and molecule-targeted drugs to such carcinoma should be developed in the future.

In conclusion, primary combined squamous and small cell carcinoma of the larynx is a great

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**Table 1.** Clinical features of reported cases of combined carcinoma of the larynx

Case No.	Source	Age/sex	Site	Positive lymph nodes	Distance metastasis	Therapy	Follow-up
1.	Eusebi et al, 1978	63/M	R supraglottis and glottis	+	-	HL+RND	DOD, at 24 mon
2.	Mills et al, 1983	49/M	R supraglottis and glottis	+	-	TLP+RND+RT+R thy lobectomy	NED, at 6 mon
3.	Ferlito et al, 1985	50/M	L hemilarynx	+	NA	TLP+LRND+RT	DOD, at 14 mon
4.	Ferlito et al, 1985	54/M	Glottis and subglottis	-	-	TL+RND+RT	NED, at 42 mon
5.	Ferlito et al, 1985	47/M	R supraglottis and glottis	+	Lung, bone and brain	RT+Che	DOD, at 48 mon
6.	Ferlito et al, 1985	45/M	R supraglottis and glottis	+	-	RT+Che	DOD, at 21 mon
7.	Ferlito et al, 1985	56/M	Epiglottis	-	-	RT+Che	NED, at 77 mon
8.	Gnepp et al, 1983	57/M	R glottis	+	+	TLP+RT+RRND	DOD, at 3.5 mon
9.	Chen et al, 1986	56/M	R supraglottis	-	-	SL+RRND+Che	AWD, at 13 mon
10.	Chen et al, 1986	55/M	R hemilarynx L supraglottis	+	Bone and lung	TL+RRND+RT+Che	DOD, at 9 mon
11.	Cosby et al, 1988	56/M	L supraglottis	+	-	TL+LRND+Che	Lost to follow up
12.	Gianoli et al, 1992	83/M	R supraglottis	-	-	TL+MND	NED, at 8 mon
13.	Yucel et al, 2000	32/M	Supraglottis	+	-	SL+MND+RT+Che	AWD, at 12 mon
14.	Jaiswal et al, 2004	41/M	L glottis	NA	-	RT+Che	NED, at 8 mon
15.	Barbeaux et, 2006	61/M	R glottis	NA	NA	RT+TL+RND+Che	AWRR, at 44 mon
16.	Barbeaux et, 2006	54/M	L subglottis	-	Lung, bone, peritoneum	RT+Che	AWD, at 36 mon
17.	Gitika et al, 2011	59/M	R supraglottis, epiglottis and glottis, L glottis	+	NA	TL+BMND+R thy lobectomy	Lost to follow up
18.	Our case	70/M	R supraglottis and glottis, L glottis	-	R adrenal gland and abdominal organs	TL+BMND+RT	DOD, at 16 mon

R: right; L: left; M: male; F: female; HL: hemilaryngectomy; TL: total laryngectomy; SL: supralaryngectomy; RND: radical neck dissection; RRND: right radical neck dissection; LRND: left radical neck dissection; MND: modified neck dissection; BMND: bilateral modified neck dissection; thy: thyroid gland; RT: radiotherapy; Che: chemotherapy; NED: no evidence of disease; AWD: alive with disease; AWRR: alive with recurrent relapses; DOD: died of disease; mon: months; NA: not available.

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aggressive tumor often leading to local and/or distance metastasis. More rational treatment regimen and molecule-targeted drugs to such carcinoma should be developed in the future.

### Disclosure of conflict of interest

None.

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