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Case Report

Primary small cell cancer of cervical trachea: a case report and literature review

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Abstract: Primary small cell carcinoma of trachea is even more uncommon and only a few cases have been reported. Our search revealed only 90 cases in the English-language literatures. Case report: we report a case of cervical tracheal small cell cancer. A 67-year-old male presented with over 2-month history of cough and dyspnea. CT and MRI revealed a 1.0 cm × 2.5 cm intraluminal, irregular soft tissue mass in the upper trachea, approximately 2.5 cm below the glottis. A bronchoscopic examination disclosed a large tumor in the cervical trachea and the lesion occupied more than 60% of the tracheal lumen. Cytological examination suggested some poorly differentiated carcinoma cells. The patient received concurrent chemoradiotherapyand did not perform surgery. One week after CCR, the patient occurred difficulty in breath and tracheal stent was implanted. The symptom was improved markedly. Four days after implant of tracheal stent, the patient presented irritable cough and hemoptysis. The amount of bleeding was about 300 ml. The hemorrhage stopped by treatment of vasoconstrictor and fresh plasma. However, two days later, hemoptysis was continuing even if treatment of vasoconstrictor and fresh plasma. The patient and relatives waived the further therapies. The patient died of massive hemoptysis one week out of hospital. Conclusions: The tracheal small cell cancer is rare. The optimal treatment is unclear. In general, the strategy is introduced concurrent chemoradiotherapy following as small cell lung cancer. In cervical trachea, we suggest that surgical resection should be performed followed by postoperative adjuvant therapy.

Keywords: Primary small cell carcinoma, trachea, treatment, incidence

Introduction

Primary tracheal malignant tumor is uncommon. The incidence is about 0.1 in every 100,000 persons per year, corresponding to approximately 0.2% of all tumors of the respiratory tract and to 0.02% to 0.04% of all malignant tumors [1]. Squamous cell carcinoma is the predominant histology of the trachea (50% of all primary tracheal carcinoma), and the second most frequent histology is adenoid cystic carcinoma (16% of all primary tracheal carcinoma), however, primary neuroendocrine carcinoma (PNC) of trachea is rare (9.7% of all primary tracheal carcinoma) [2]. Among PNC, carcinoid is the most common type of neuroedocrine carcinoma [3-7]. Primary small cell carcinoma of trachea is even more uncommon and only a few cases have been reported [2, 7-9].

Since there are no significant symptoms in early stage of tracheal primary small cell cancer, it is always misdiagnosed [10]. Owing to the rarity of primary small cell cancer of trachea, the natural history and optimal treatment remains unclear. Herein, we reported a rare case of primary small cell cancer in the cervical trachea, along with a review of the relevant English-literature.

Case Report

A 67-year-old male presented with over 2-month history of cough and dyspnea. He denied dysphagia, bloody phlegm, fever and weight loss. He was significant history of smoking (one pack of cigarettes per day for 50 years) and alcohol consumption (200 ml white spirit per day for 50 years). He had alcoholic liver cirrhosis 9 years ago and hypertension 1 year ago. He was diagnosed as chronic bronchitis in a local hospital. The patient received antibiotic, antiasthma treatment. His symptoms were not improved. He was admitted to our emergency room.

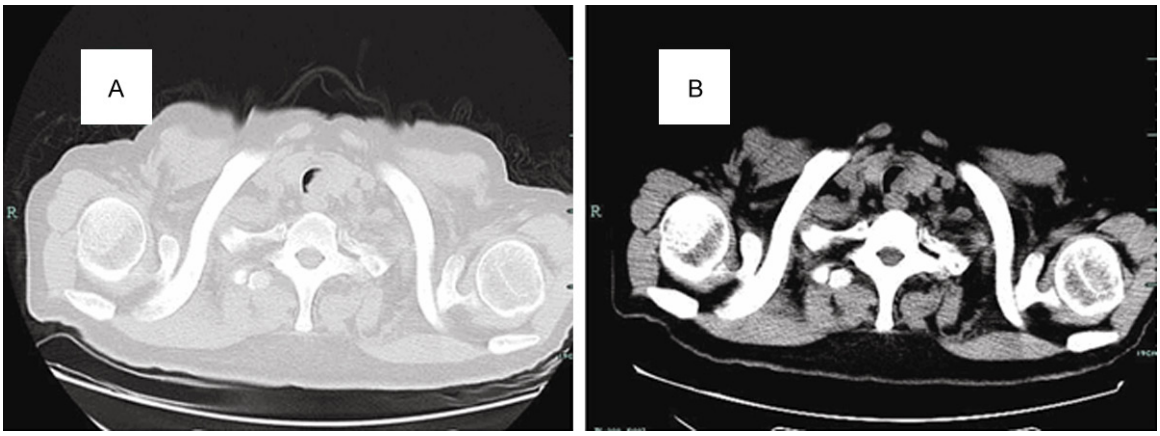

Figure 1. CT revealed a 1.0 cm × 2.5 cm intraluminal, irregular soft tissue mass in the upper trachea, approximately 2.5 cm below the glottis. A. Soft tissue window; B. Bone window.

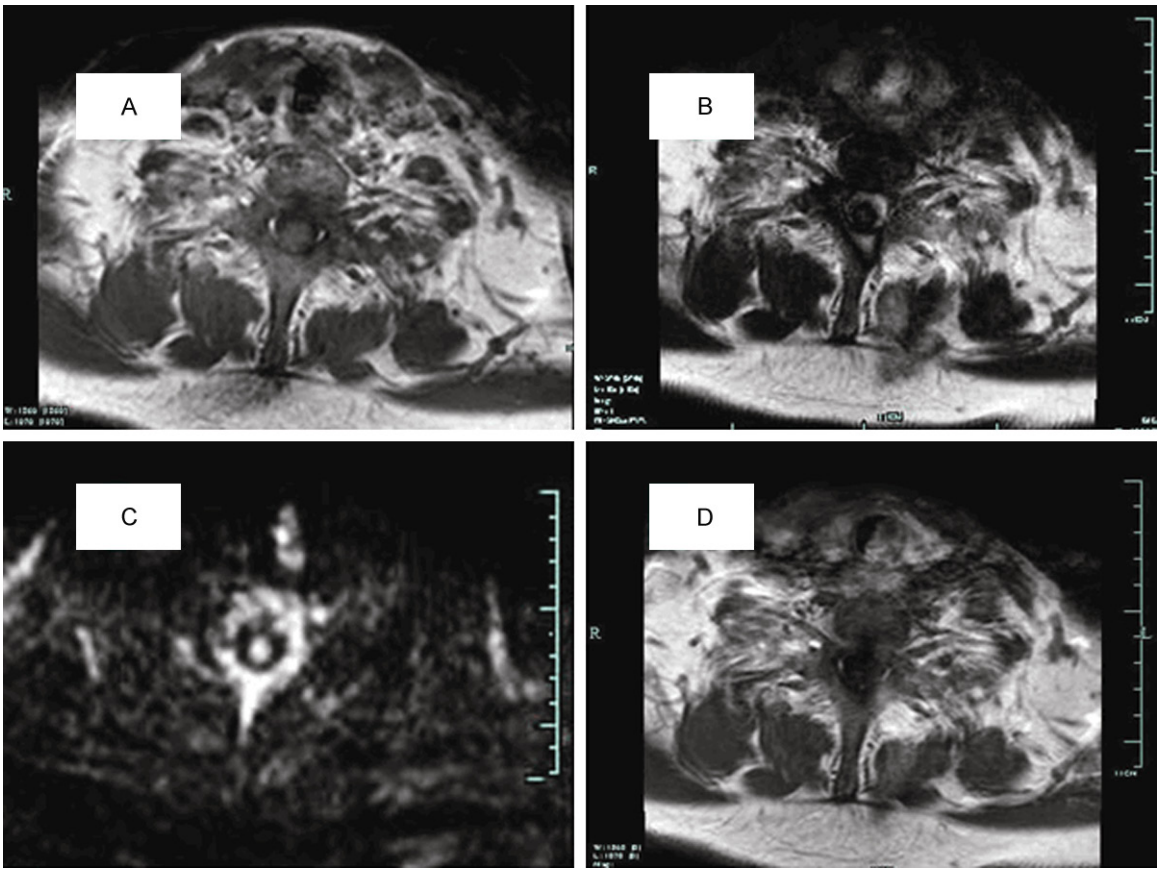

Figure 2. MRI of neck revealed that a 1.0 cm × 2.5 cm irregular mass in the cervical trachea, approximately 2.5 cm below the glottis. The T1 (A)- and T2 (B)-weighted signals were hyperintense. DWI suggested hyperintense lesions (C), contrast-enhanced T1-weighted images revealed heterogenous enhancement (D).

Physical examination revealed second degree of laryngeal obstruction.

Neck and chest computed tomography (CT) revealed a 1.0 cm × 2.5 cm intraluminal, irregular soft tissue mass in the upper trachea, approximately 2.5 cm below the glottis (**Figure 1**). Magnetic resonance image (MRI) of neck revealed that a 1.0 cm × 2.5 cm irregular mass in the cervical trachea, approximately 2.5 cm

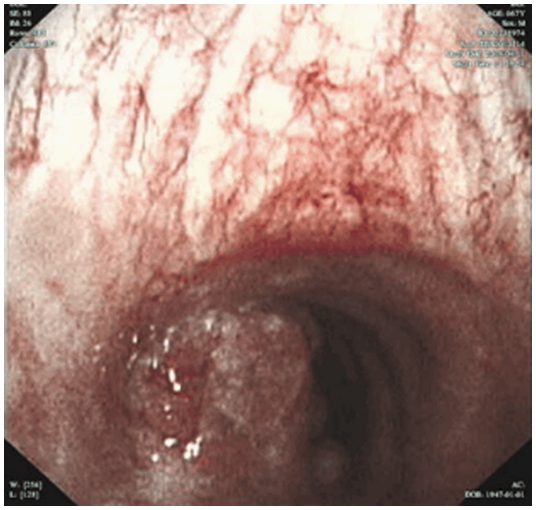

Figure 3. A bronchoscopic examination disclosed a large tumor in the cervical trachea and the lesion occupied more than 60% of the tracheal lumen.

below the glottis. The T1- and T2-weighted signals were hyperintense. Diffusion-weighted imaging (DWI) suggested hyperintense lesions, and contrast-enhanced T1-weighted images revealed heterogenous enhancement (**Figure 2**). The patient was referred our department to receive surgery. A bronchoscopic examination disclosed a large tumor in the cervical trachea and the lesion occupied more than 60% of the tracheal lumen (**Figure 3**). Cytological examination suggested some poorly differentiated carcinoma cells. Biopsy revealed that the lesions were composed of sheet of poorly differentiated atypical cells. Immunohistochemical results revealed that the neoplastic cells were positive for cytokeratins, synaptophysin, and chromogranin, and negative for neuron-specific enolase, vimentin, desmin, and S-100 (**Figure 4**). The diagnosis was small cell carcinoma.

The patient received concurrent chemoradiotherapy (CCR) and did not perform surgery. One week after CCR, the patient occurred difficulty in breath and tracheal stent was implanted. The symptom was improved markedly. Four days after implant of tracheal stent, the patient presented irritable cough and hemoptysis. The amount of bleeding was about 300 ml. The hemorrhage stopped by treatment of vasoconstrictor and fresh plasma. However, two days later, hemoptysis was continuing even if treatment of vasoconstrictor and fresh plasma. The patient and relatives waived the further therapies. The patient died of massive hemoptysis one week out of hospital.

Discussion

The most common histology type of tracheal cancer is squamous-cell carcinoma (SCC), followed by adenoid cystic carcinoma (ACC) [2]. Neuroendocine in the trachea is rare. According World health organization (WHO) 2005, neuroendocrine carcinoma of the hypopharynx, larynx and trachea are divided into four main entities: carcinoid, atypical carcinoid, small cell carcinoma and combined small cell carcinoma (neuroendocrine type with non-small cell carcinoma) [11]. The most common of neuroendocrine carcinoma of is carcinoid. The carcinoid and atypical carcinoid have low malignancy and comparatively good prognosis, most patients need total resection, and the carcinoid tumor of 5-year survival rate is 95%, which has less distant metastasis than atypical carcinoid. The optimal treatment of tracheal carcinoid is surgery [5].

However, small cell carcinoma is rare in the trachea and it is reported either as part of large experiences or separate case reports. The natural history and optimal treatment remains unclear. These cases were always located at lower trachea. The mass of tracheal cancer locating at cervical trachea is uncommon. The tumor of the present patient located at cervical trachea.

Early symptoms as our present case were always not significant and non-specific. The symptoms included cough, repeated episodic stridor, chest distress, polypnea, hemoptysis, cyanosis and dyspnea [10]. Therefore, the misdiagnosis and missed diagnosis rates are relatively high. The initial diagnosis was always chronic bronchitis or asthma or COPD. Thus, a number of patients with primary tracheal cancers may always present with advanced disease and beyond the window of curative treatment [12]. Airway obstruction is often advanced and life-threatening at the time of diagnosis [10-14].

The stage and treatment of primary small cell cancer is always followed as small cell lung cancer (SCLC) TNM stage and therapeutic strategy [13]. Heikal reported a case of small cell cancer presenting as a tracheal polyp. However, the

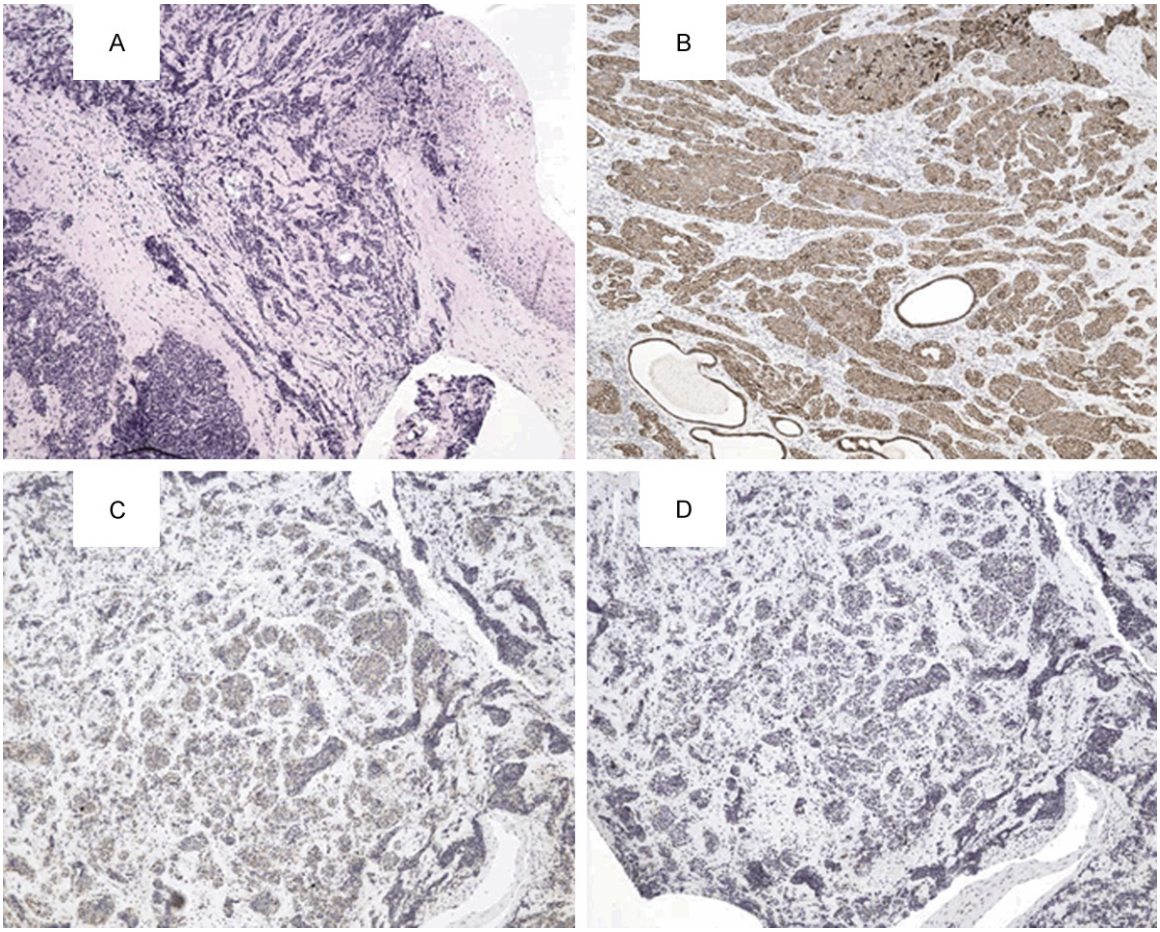

Figure 4. Biopsy revealed that the lesions were composed of sheet of poorly differentiated atypical cells (A). Immunohistochemical results revealed that the neoplastic cells were positive for cytokeratins (B), synaptophysin (C), and chromogranin (D).

patient had lung small cell cancer 5 years ago [13]. They reviewed literatures from 1969 to 2011 and found only 74 cases (4.2%) of small cell cancer of 1747 primary tracheal cancers from 23 English-literatures [13]. Based on Heikal's review, we further reviewed tracheal small cell cancers in the English-literature. We found at least 19 additional cases of tracheal small cell cancer (**Table 1**). In this review, the incidence of small cell cancer of trachea was about 4.3% (90/2090). In 2010, Honings et al found that the incidence was 7.4% (74/997) [14]. However, the incidence was over-estimated. Honings et al found some metastatic tumors from adjacent organs or mediastinal lymph nodes invading to the wall of the trachea misclassified as primary tracheal cancers through an expert audit of tracheal carcinomas registered from 2000 to 2005 with the Netherlands Cancer Registry (NCR) [9]. They audited their previous study and the high rate of small cell cancer (11.0%) may be overestimated due to metastatic lesions from peripheral bronchial carcinoma misclassified as primary small cell tracheal cancer [9, 15]. Thus, it is very important for differentiating tracheal small cell cancer from metastasis of pulmonary small cell cancer via workup including chest imaging (CT), sputum cytology, bronchoscopy, PET/CT, or biopsy.

Thotathil et al reported 15 cases of primary malignant tumors of the trachea; 1 of them (7%) was small cell cancer. The patient received cisplatinum, etoposide and 50 Gy radiation and the patient died 28 months after treatment [16]. Honings et al reported 50 cases of primary tracheal cancers; 1 of them was small cell cancer [9]. Lan et al reported a case of small cell cancer of trachea presenting as acute dys-

Table 1. Primary small cell cancers in English-language literatures

Authors	Year	No. Cases	SCC N (%)	ACC N (%)	SCLC N (%)
Chao[20]	1998	42	28 (66.7)	3 (7.1)	2 (4.8)
Mornex[21]	1998	106	70 (66.0)	4 (3.8)	2 (1.9)
Thotathil[16]	2003	15	6 (40.0)	4 (26.7)	1 (6.7)
Honings[9]	2009	50	27 (54.0)	13 (26.0)	1 (2.0)
Lan[17]	2010	1	0	0	1 (100)
Hetnał[18]	2010	50	24 (48.0)	5 (10.0)	4 (8.0)
Xie[19]	2012	78	33 (42.3)	12 (15.4)	7 (9.0)
Luo[22]	2014	1	0	0	1 (100)
Reviewof Heikal[13]	2012	1747	853 (48.8)	407 (23.3)	71 (4.1)
total		2090	1041 (49.8)	448 (21.4)	90 (4.3)

pnea [17]. The patient received concurrent chemradiotherapy (25 mg/m^2 of cisplatin, 100 mg/m^2 of etoposide and 60Gy irradiation). The patient was alive without evidence of recurrence one year after treatment [17]. Hetnał et al reported 50 cases of primary tracheal cancers, 4 of them (8%) were small cell cancer. They found that the overall survival (OS) of adenoid cystic cancer was better than other histopathologic types. The 5-year OS in the following treatment modalities were: surgery followed by radiotherapy (66%), radiotherapy (16%), chemoradiotherapy (0%), and symptomatic treatment (0%) [18]. Urdaneta et al reported 578 cases of primary tracheal carcinoma using Surveillance, Epidemiology and End Results (SEER) database between 1973 and 2004 [2]. 56 of them were neuroendocrine carcinoma including small cell cancer [2]. They recommended complete surgical resection was the primary treatment of tracheal tumors. There was a poor 5-year overall survival of 27.1% in their series and they found that early diagnosis was the most important issue for better overall survival [2]. Xie and colleagues reported that 78 patients with primary tracheal cancers using SEER database between 1988 and 2007; 7 (9.0%) of them had small cell cancer. All these patients were received radiotherapy (RT). They found that RT may be of benefit to survival of patients with tracheal cancer, in particular those with squamous cell cancer, and other histopathologic type including small cell caner although the limitation of cases [19]. Chao et al [20] and Mornex et al [21] had similar results. Luo et al reported a case of synchronous primary small cell cancer of trachea and squamous cell carcinoma in situ of esophagus. The patient received CCR and no recurrence 12 months after treatment [22].

The treatment of our present case was introduced concurrent chemoradiotherapy based therapeutic strategy of SCLC. However, the patient occurred difficulty in breath and tracheal stent was implanted. The patient died of massive hemoptysis. From the result of our case, we suggest that the treatment of cervical tracheal cancer should be surgical resection and postoperative chemotherapy. We infer that massive hemooptysis should be avoided and the life may be prolonged. In 2009, Honing et al had suggested that incorrect diagnosis and undertreatment were common in primary rare tracheal caners [9]. They inferred that more patients may be selected for surgical resection improving outcome [9]. Yasumatsu et al suggested that these were two different small cell cancers between extrapulmonary and pulmonary and there were different clinical characteristics and risk factors for development of these two entities. They suggested that different therapeutic strategies should be applied in these two diseases [23]. Therefore, further prospective multicentre studies need to better understand of tracheal small cell cancer and treatment modalities.

In conclusion, tracheal small cell cancer is rare. The optimal treatment is unclear. In general, the strategy is introduced concurrent chemoradiotherapy following as small cell lung cancer. In cervical trachea, we suggest that surgical resection should be performed followed by postoperative adjuvant therapy.

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Disclosure of conflict of interest

None.

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