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# A Rare Case of Multiple Secondary Endotracheal Metastasis From Early Stage Small Cell Cancer

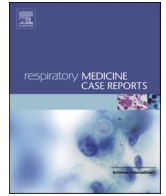
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## Case report

## A rare case of multiple secondary endotracheal metastasis from early stage small cell cancer

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## ABSTRACT

**Introduction:** Small Cell Lung Cancer (SCLC) is an aggressive malignancy with poor prognosis that accounts for 10% of all clinical lung cancer. SCLC commonly metastasizes to the mediastinum, liver, bone, adrenals, and the brain but secondary endotracheal metastasis is an especially rare occurrence. We discuss the case of a 74-year-old male with principal complaint of cough, wheezing and hemoptysis found to have secondary endotracheal lesions on bronchoscopy.

**Case report:** A 74-year-old male, former smoker with a past medical history of pulmonary embolism, bullous emphysema, and limited stage small cell lung cancer with wedge resection and chemotherapy 3 years ago presented with cough, wheezing, weight loss and intermittent hemoptysis ongoing for few weeks. CT scan of the chest showed multiple polypoid masses arising in the anterior wall of the trachea. He underwent bronchoscopy with biopsy. Pathology was consistent with small-cell lung cancer.

**Conclusion:** Secondary tracheal metastasis from early stage small cell cancer is a rare occurrence. The likelihood of tracheal metastasis of lung cancer is amplified when an endotracheal nodule or eccentric thickening of the tracheal wall is seen on CT of patients with high suspicion. It is important for clinicians to suspect endotracheal lesions when a patient presents with recurrent respiratory complaints despite stable surveillance CT scan of chest in patients with history of lung cancer.

## 1. Introduction

Lung cancer is among the most common tumor types; it represents 13% of newly diagnosed cancers worldwide. Small Cell Lung Cancer is an aggressive malignancy with a poor prognosis that accounts for 10% of all clinical lung cancer [1]. It is characterized by a high growth fraction, rapid doubling time and early establishment of widespread metastatic lesions [2]. By the time of diagnosis, 60–70% have extensive local and metastatic disease. SCLC commonly metastasizes to the mediastinum, liver, bone, adrenals, and the brain but secondary endotracheal metastasis is an especially rare occurrence [3]. There have only been 3 cases described in the literature. We discuss the case of 74-year-old male with a principal complaint of cough, wheezing and hemoptysis found to have secondary endotracheal lesions on bronchoscopy with prior history of chemotherapy and left upper lobectomy for small cell lung cancer.

## 2. Case report

A 74-year-old male with 37-pack year smoking history presented to the clinic with complaints of intermittent hemoptysis, wheezing cough, and 35-pound weight loss. He has a past medical history of pulmonary embolism on anticoagulation, bullous emphysema, asbestos exposure and diagnosis of limited small cell lung cancer (2 cm in greatest dimension, Stage IB high grade neuroendocrine carcinoma, T2a, N0 M0, positive visceral pleural invasion, negative margins with 0/26 lymph node showing no metastasis) 3 years ago treated with left thoracotomy and left upper lobectomy along with adjuvant chemotherapy (Cisplatin and Etoposide) and prophylactic cranial irradiation (PCI).

He responded well and was symptom free for 3 years. He had surveillance CT scan of the chest 1 year back which showed stable multiple lung nodules and new 1.5 cm stellate nodule in the right upper lobe and a slight enlargement of 8 mm nodule in the posterior right lower lobe. He

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also had a follow up positron emission tomography (PET) scan that showed an area in the right upper lobe with standardized uptake value (SUV) of 2.2 which might harbor multiple dysplastic nodules but were not large enough for biopsy. Patient underwent Navigational bronchoscopy and pathology was inconclusive. Patient presented to the primary care physician 6 months later with 3-week history of new onset cough, wheezing and 10 lb weight loss. The cough was productive with intermittent bloody sputum associated with nasal congestion and post-nasal drip. He denied chest pain, chills, fever, headaches, heartburn, myalgias, rash, rhinorrhea, sore throat, shortness of breath and night sweats. Patient was on anticoagulation with rivaroxaban, which was continued since he had history of pulmonary embolism. He was treated for upper respiratory infection with oral antibiotics. Patient had 2 admissions to the hospital in 1-month duration for exacerbation of chronic obstructive pulmonary disease and had another CT scan of Chest on his second admission. It revealed a polypoid mass in the anterior wall of upper trachea suspicious for malignant lesion with a 2nd mass also arising from anterior wall suspicious for malignancy vs. adherent debris (Fig. 1). It also revealed new mild adenopathy on the right side, 6 mm nodule in the left lower lobe, prominent peribronchial thickening in the left lower lobe (Fig. 1). Patient underwent bronchoscopy (Fig. 2) that showed two tracheal polyps/lesions causing up to 50% tracheal obstruction. Biopsies were taken and pathology was consistent with small-cell lung cancer (Figs. 3–5). Patient was referred to Interventional Pulmonology and he underwent rigid bronchoscopy with tumor debulking along with cauterization of the two-polypoid lesions. Patient's clinical symptoms including cough and wheezing improved with plans to proceed with definitive treatment, including chemoradiotherapy.

### 3. Discussion

Secondary tracheal tumors are defined as tumors in, but not of the trachea. They are extra-tracheal metastasis that comprises a wide spectrum of tumor histologies and stages [4].

Tracheal metastases have been reported from malignancies of breast, renal, thyroid, skin and colorectal involvement [5]. However, there are

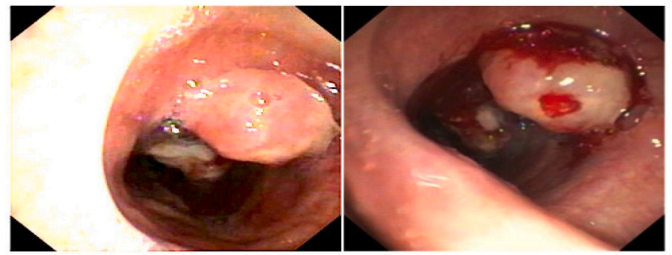


Fig. 2. Multiple polypoid mass noted in the trachea with pre and post biopsies.

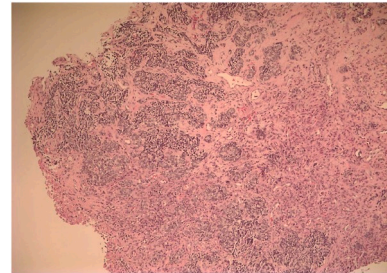


Fig. 3. Small cell carcinoma infiltrating tracheal mucosa; H&E stain, 100X magnification.

no population-based data for these tumors [4]. A study by Marchioni et al. found 4% of endobronchial biopsies for suspected malignancy showed endobronchial metastasis from extra pulmonary tumor. In their series, 30% of breast cancers, 24% of colorectal, 14% of renal cancers, 6% of gastric cancers and 4.5% of prostate cancers and melanoma showed evidence of metastasis [6]. Others have cited an incidence of endotracheal or endobronchial metastasis of non-pulmonary malignancies in the range of approximately 2%–50% [7]. There is wide variation in incidence depending on the criteria being used; however, by all regards, airway metastasis from lung cancers is extremely rare. In a study by Chong et al., only 0.44% (6/1372) of surgically resected

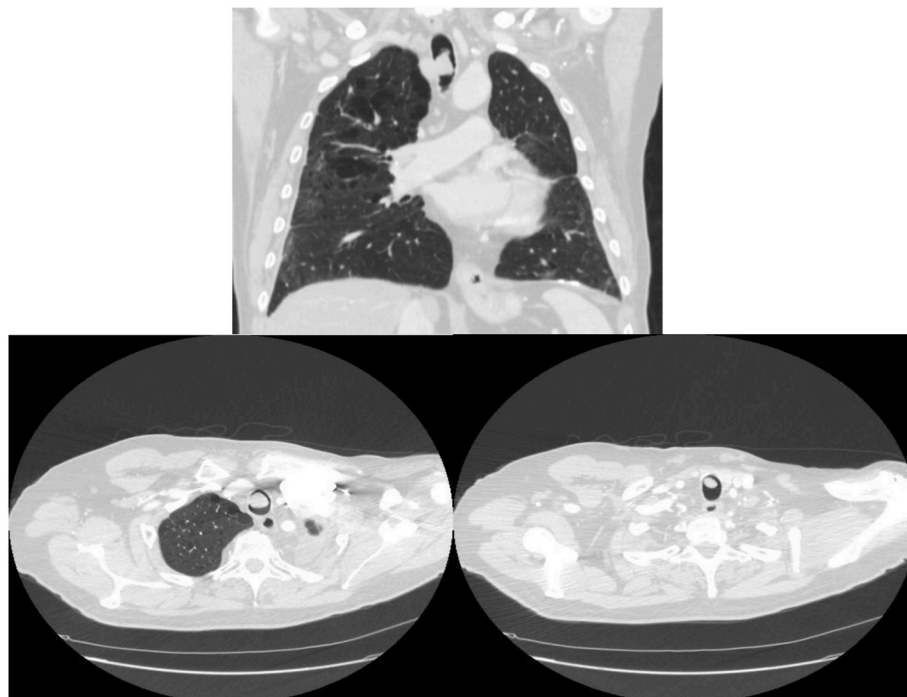
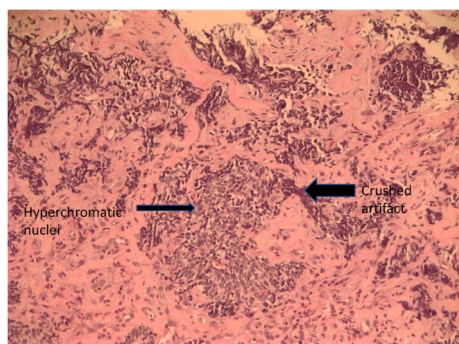
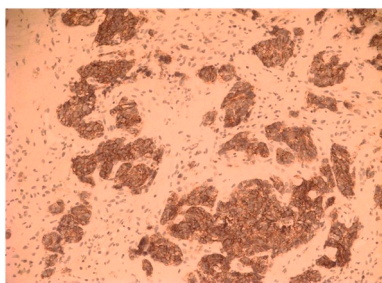


Fig. 1. Coronal and Axial views show 2 polypoid lesions in the trachea.



**Fig. 4.** Hyperchromatic, small round blue cells with crush artifact typical of small cell carcinoma; H & E stain; 200X magnification. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 5.** Positive CD56 immunohistochemical stain demonstrating neuroendocrine differentiation; 200X magnification.

non-small cell lung cancers showed evidence of tracheal metastasis, while 0.77% (5/647) in squamous cell carcinomas, 0.18% (1/552) in adenocarcinomas and none in small cell lung cancer in their series [5].

There are four postulated mechanisms for tracheal metastasis, numbered from type I to IV. These mechanisms were first described by Kiryku et al. Type 1 tracheal metastasis are due to direct metastasis to the bronchus, type 2 are due to direct bronchial invasion by a parenchymal lesion, type 3 are due to bronchial invasion by mediastinal or hilar lymph node metastasis; and finally type 4 are due to a peripheral lesion extending along the proximal bronchus [8]. In Chong et al. study, all tracheal tumor cells involved the submucosal layer, and some tracheal tumor cells were found within the submucosal lymphatic vessels presenting as tumor emboli [5]. In our case, type 1 pattern is the likely mechanism. The natural behavior of small cell lung cancers to invade through lymphatics and perivascular space makes this the most likely mechanisms. Interestingly, Chong et al. proposed an idea of direct implantation via endoscopy, which although possible, is less likely in our situation. There was evidence of endobronchial polyps prior to any bronchoscopy.

The symptoms associated with endotracheal and endobronchial metastases regardless of its primary site are similar to those associated with primary endotracheal and endobronchial tumors. The clinical presentation of tracheal neoplastic obstruction depends on the size of the luminal component. Tracheal tumors large enough to cause symptoms often obstruct half of the airway or decrease the diameter of the tracheal lumen. Obstruction to a tracheal diameter.

<8 mm may result in dyspnea on exertion, whereas an airway of less than 5 mm typically results in dyspnea at rest. In addition to dyspnea, patients may also commonly present with cough, hemoptysis, wheeze, or stridor. Dysphagia is typically rare. Hoarseness may be present when tumors originate close to or within the subglottic space [9]. In a study, based on the presence of symptoms, the leading symptoms were dyspnea (31.8%), neck mass (19.5%), voice change or hoarseness (15.0%), and

hemoptysis (13.7%), while 4.8% were asymptomatic. Early symptoms for the present case were nonspecific and included symptoms of cough, hemoptysis, wheezing, and dyspnea. Lines were further blurred as he had a history of bullous emphysema, pulmonary embolism with chronic anticoagulation use, coronary artery disease. He had several confounding factors to make the diagnosis a challenge.

Imaging is of the utmost importance in surveillance for lung cancer and although rare, there are possible patterns, which can allow for earlier diagnosis. Chong et al. noticed in their series, tracheal metastasis of non-small cell lung cancer showed a predilection for the upper trachea. Similarly, in our case, the polypoid mass and endotracheal lesions were located in the upper trachea. Also, these endotracheal nodules were often confused for phlegm in the tracheal tree. Chong et al. have proposed imaging criteria to distinguish an endotracheal nodule from phlegm [5] termed “mucoïd pseudotumor”. In our case, there was similar confusion as the second nodule was also thought to be due to mucoïd collection. Protocols looking for change or progression in nodule after coughing is a possible suggestion that could better delineate a lesion that would need more attention.

Endotracheal and endobronchial metastases from non-pulmonary malignancies report median recurrence intervals of 50.4–65.3 months. The recurrence interval was 8–52 months (mean,  $25.8 \pm 17.4$  months) after their initial operation for pulmonary. These long rate permits time for possible early intervention and therefore, the added importance of evaluating endotracheal lesions before further dissemination.

Treatment options for airway malignancies depend on the extent of disease. Local treatments include photodynamic and endobronchial brachytherapy, although supporting data is lacking. Interventional pulmonary procedures including tumor debulking, balloon dilatation, and stent placement may be helpful in select cases, but, are not well studied in this population of SCLC patients because of the limited number of cases. The current overall role of surgery for SCLC remains controversial, especially with the question of lymph node involvement [3]. In this case, he developed obstructive symptoms with >50% obstruction of the lumen. Removal was completed with rigid bronchoscopy and tumor debulking with electro cauterization with overall great response.

#### 4. Conclusion

Secondary tracheal metastasis from early stage small cell cancer is an extremely rare occurrence. Early Symptoms for the present case were nonspecific that combined with medical history of pulmonary embolism, bullous emphysema, and diagnosis of limited small cell lung cancer made the diagnosis a challenge. The likelihood of tracheal metastasis of lung cancer may be indicated when an endotracheal nodule or eccentric thickening of the tracheal wall is seen on CT of patients with surgically resected lung cancer.

#### Declaration of competing interest

No financial interest or any conflict of interest exist.

#### CRediT authorship contribution statement

**S. Karakattu:** Writing - review & editing, Writing - original draft, Conceptualization, Methodology. **J. Yorke:** Writing - original draft. **T. Hoskere:** Data curation. **L. Stewart:** Visualization, Validation, Data curation. **W. ElMinaoui:** Supervision.

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#### ABBREVIATIONS

*SCLC*: Small cell lung cancer LUL Left upper lung  
*PCI*: Prophylactic cranial irradiation CT computerized tomography  
*PET*: Positron emission tomography  
*COPD*: Chronic Obstructive Pulmonary Disease PE Pulmonary embolism