# Solitary Primary Tracheal Small-Cell Lung Cancer Causing Acute Respiratory Failure: Diagnosis and Treatment

Chou-Chin Lan MD, Mei-Chen Yang MD, Chih-Hsin Lee MD,
Shiu-Feng Huang MD, and Yao-Kuang Wu MD

**Small-cell lung cancer often presents as an extensive cancer, and rarely as a solitary tracheal tumor. We report a 41-year-old male smoker with dyspnea and wheezing that was initially diagnosed as asthma and treated with bronchodilators. He was later intubated for acute respiratory failure, and computed tomography revealed a tracheal mass. Solitary primary small-cell lung cancer was diagnosed via bronchoscopic biopsy. The patient received bronchoscopic electro-surgery and was successfully extubated. Concurrent chemo-radiotherapy was performed due to the stage IV small-cell lung cancer.** *Key words: tracheal tumor; small-cell lung cancer; acute respiratory failure; bronchoscopic electro-surgery.* [Respir Care 2010;55(7):929–932. © 2010 Daedalus Enterprises]

## Introduction

Small-cell lung cancer composes 15–20% of all lung cancers.[1] It often has an aggressive clinical course with rapid growth and early widespread metastases. Thus, the majority of these patients present with extensive cancer on initial diagnosis.[1] Small-cell lung cancer rarely presents as a solitary tracheal tumor without any visible lung mass.[2,3]

This is a report of a case of solitary primary tracheal small-cell lung cancer with acute respiratory failure that was successfully treated via bronchoscopic electro-surgery and chemo-radiotherapy.

Chou-Chin Lan MD, Mei-Chen Yang MD, Chih-Hsin Lee MD, and Yao-Kuang Wu MD are affiliated with the Division of Pulmonary and Critical Care Medicine, Buddhist Tzu Chi General Hospital, Taipei Branch, and with the School of Medicine, Tzu-Chi University, Hualien, Taiwan. Shiu-Feng Huang MD is affiliated with the Department of Pathology, Buddhist Tzu Chi General Hospital, Taipei Branch, and with the Department of Pathology, School of Medicine, Tzu-Chi University, Hualien, Taiwan.

The authors have disclosed no conflicts of interest.

Correspondence: Yao-Kuang Wu MD, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Buddhist Tzu Chi General Hospital, Taipei Branch, 289 Jianguo Road, Xindian City, Taipei County 23142, Taiwan, Republic of China. E-mail: drbfci@yahoo.com.tw.

## Case Report

A 41-year-old male chef who was a smoker (one pack of cigarettes per day for 20 years) consulted at the outpatient clinic for a 2-week history of dyspnea and wheezing. He denied any noteworthy medical history. On initial examination there was expiratory wheezing but unremarkable chest radiography (Fig. 1A). He was diagnosed as having asthma and treated with bronchodilators. One day later he was brought to the emergency department due to progressive dyspnea. At the emergency department he was afebrile but tachycardic (146 beats/min), tachypneic (36 breaths/min), and using accessory breathing muscles. He was alert but irritable.

Laboratory results revealed hemoglobin 12.6 g/dL, white-blood-cell count 20.4 $\times$ $10^9$/L, neutrophils 58%, and lymphocyte 39%. Liver and renal function and electrolytes were all within normal range. Arterial blood gas analysis showed pH 7.16, $P_{aO_2}$ 163.1 mm Hg, $P_{aCO_2}$ 81.7 mm Hg, and $HCO3^-$ 29.2 mmol/L, under $F_{IO_2}$ 0.40 via mask. He was intubated and mechanically ventilated for respiratory failure, and was transferred to the intensive care unit.

Computed tomography showed a mass in the lower trachea (Fig. 1B). The lung fields had no visible mass. Fiberoptic bronchoscopy showed an irregular, nodular tumor in the lower trachea (3 cm above carina) with near-total occlusion (Fig. 2A). Biopsy was performed, and pathology examination revealed multiple nests of hyperchromatic tumor cells infiltrating the submucosal stroma, with marked

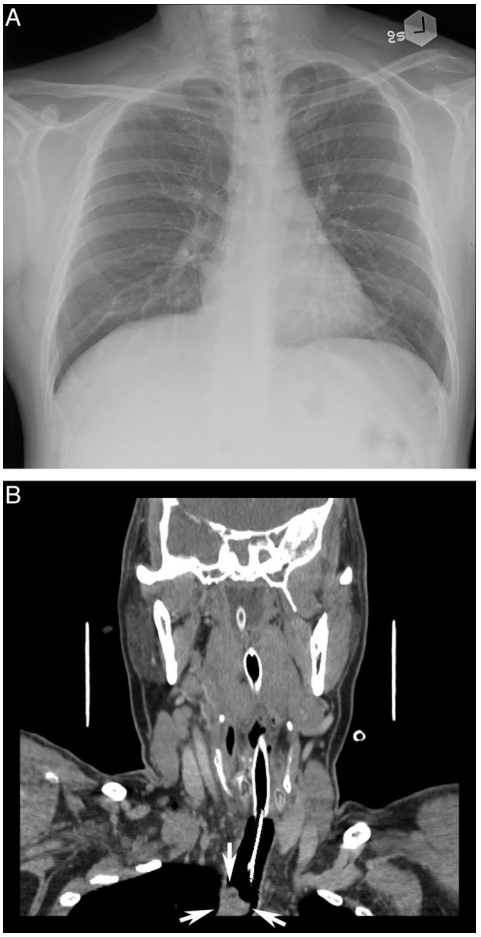


Fig. 1. A: Chest radiograph shows normal lung fields. B: Computed tomogram of the neck and upper thorax shows a tracheal mass in the lower trachea.

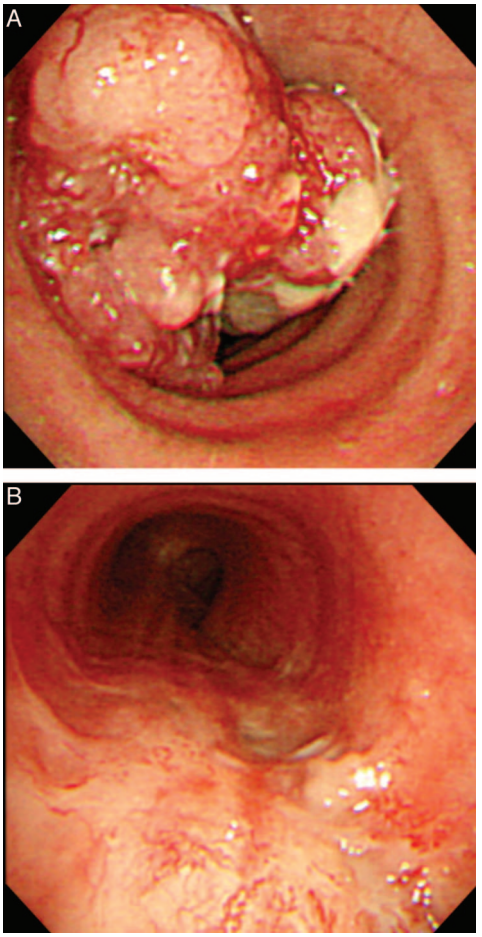


Fig. 2. A: Fiberoptic bronchoscopy shows an irregular, nodulated tumor in the lower trachea (3 cm above the carina) with near-total occlusion. B: After bronchoscopic electro-surgery and chemoradiotherapy, bronchoscopy shows only mucosal thickening, without visible tumor.

squamous metaplasia of the overlying bronchial mucosa. The tumor cells had small hyperchromatic nuclei, scanty cytoplasm, and marked crushing artifact, which was highly suggestive of small-cell carcinoma. Multiple immunohistochemical stains were performed to confirm the diagnosis. The stain for CD45 was negative, which excluded lymphoma (Fig. 3A). The stain for CK5/6 was also negative, which excluded poorly differentiated squamous-cell carcinoma (see Fig. 3B). The stain for TTF-1 was weakly positive (see Fig. 3C), which is compatible with but not specific for small-cell carcinoma. The stain for neuron-specific enolase (a marker for neuroendocrine tumor) was negative (see Fig. 3D), which could rule out carcinoid tumor but not small-cell carcinoma. Since small-cell carcinoma is a poorly differentiated neuroendocrine carcinoma, negative staining for neuroendocrine markers is not uncommon. In summary, the histology and immunohistochemical stains all supported the diagnosis of small-cell carcinoma.

The patient then underwent fiberoptic bronchoscopic electrocautery of the tracheal tumor. Electrocautery was initially done at 20W/20W, and then 35W/35W. Heat probe, knife, snare-loop, and heat forceps were used for tumor extraction. After electrocautery the patient was successfully extubated and there was complete resolution of the wheezing and dyspnea. He was then transferred to the general ward in stable condition.

Further tumor staging via bone scan revealed bony metastasis of the right 6th rib. Moreover, there was 27-mm right supraclavicular lymphadenopathy that also showed small-cell lung cancer on biopsy, for a tumor clinical stage of 4 (T4N3M1). However, surgery for the tracheal small-cell lung cancer was not performed. The patient received monthly systemic chemotherapy with 25 mg/m2 of cisplatin (Pharmachemie, Israel) and 100 mg/m2 of etoposide (Nippon Kayaku, Japan). Concurrent chest irradiation (6,000 cGy in 30 fractions) to the trachea and mediastinum was also performed.

After radiotherapy and 3 cycles of chemotherapy, computed tomogram and bronchoscopy revealed only tracheal

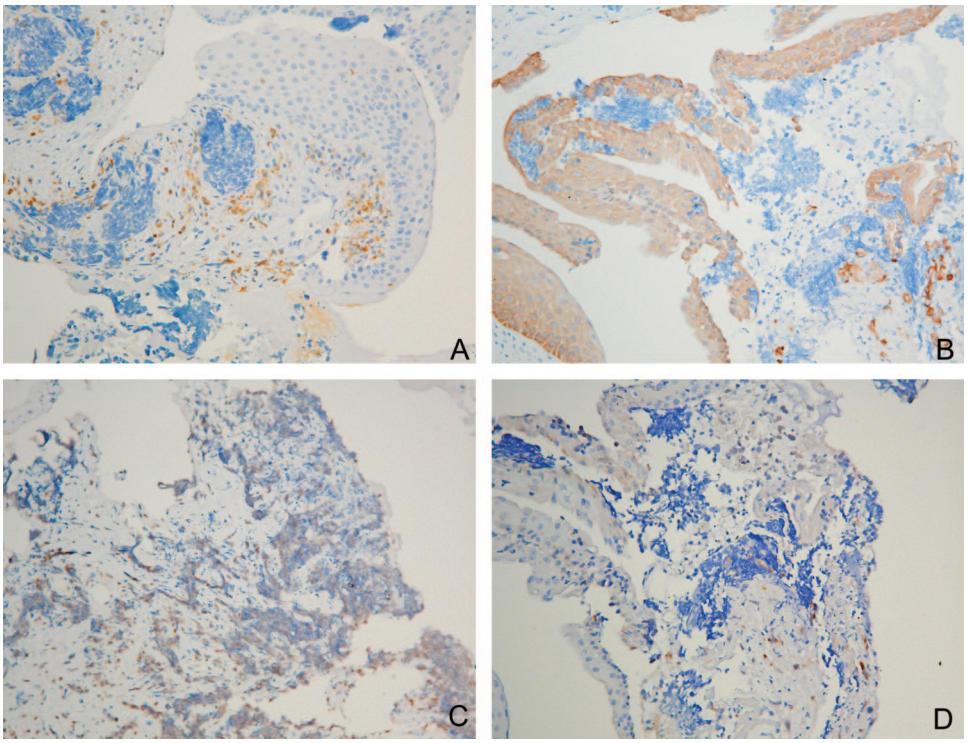


Fig. 3. Micrographs at magnification 200. A: Immunohistochemical stain for CD45 was negative. B: Stain for CK5/6 was negative. C: Stain for TTF-1 was weakly positive. D: Stain for neuron-specific enolase was negative.

mucosal thickening, without visible tracheal tumor (see Fig. 2B). One year after treatment, the patient was well and had no evidence of recurrence.

## Discussion

Patients with tumors in the upper respiratory tract presenting with dyspnea, wheezing, and cough are frequently misdiagnosed as having asthma or COPD. However, tracheal tumor with central airway obstruction should be included in the differential diagnosis, particular in those who are refractory to treatment for presumed COPD or asthma.[2] Tracheobronchial obstruction from malignant or benign lesions can cause important complications, such as acute respiratory distress, post-obstruction pneumonia, atelectasis, hemoptysis, asphyxia, or even death.[4]

Primary malignant neoplasms of the trachea are rare and account for fewer than 0.1% of malignant diseases.[2] Primary tracheal tumors can arise from the respiratory epithelium, salivary glands, and mesenchymal structures of the trachea. In adults, 90% of primary tumors are malignant,[5] compared to 10–30% in children.[6] In adults, squamous-cell carcinoma and adenoid cystic carcinoma account for two thirds of adult primary tracheal tumors.[2,5] Tracheal tumors are often a diagnostic and therapeutic challenge. Although patients present with signs and symptoms of central-airway obstruction, the definitive diagnosis of these tumors is commonly delayed, so most patients present with advanced disease.[2]

Among lung malignant neoplasms, small-cell lung cancer has the worst prognosis and usually grows and disseminates very rapidly,[1] so early detection and correct diagnosis are very important. Small-cell lung cancer often presents as an extensive disease and rarely as a primary tracheal mass.[1,3] The diagnosis of tracheal small-cell lung cancer is quite challenging, and in a patient with acute respiratory failure, solitary tracheal small-cell lung cancer should be considered, even with normal chest radiography.

Chemotherapy is the cornerstone of treatment.[7] Cisplatin plus etoposide and concomitant radiotherapy is the standard treatment for patients with extensive small-cell lung cancer.[7] This achieves high response rate (60–70%), but small-cell lung cancer has a high recurrence rate and a median survival time of 8–10 months.[7] Our patient suffered respiratory failure from tracheal occlusion by the tumor, so immediate surgery was required. Fiberoptic bronchoscopic electro-surgery is an effective option for immediate intra-luminal tumor debulking.[8]

There are many modalities to treat tracheal and bronchial lesions. Laser photo resection, electro-surgery, cryotherapy, argon plasma coagulation, and brachytherapy can be used to remove endobronchial tissue.[8-10] Laser photoresection is the application of laser energy via rigid or flexible bronchoscope.[10] It is effective for rapid tissue de-

bulking,[10,11] although it has risks, including airway perforation and hemorrhage.[11] Electrocautery (or diathermy) is the use of electrical current for heating tissue.[10] Endobronchial electrocautery has risks similar to laser photo resection, but has lower equipment costs.[9,10] Endobronchial electrocautery is a simple technique for immediate tumor debulking and rapid palliation in patients with central tracheobronchial tumors.[8] It is an effective and safe treatment that generally provides total or near-total removal of tracheal tumors, and has been the palliative treatment for inoperable cancer.[8] Cryotherapy is based on the cytotoxic effects of cold on tissues.[12] It is safe and effective but slow for debulking tissue in an emergency situation.[12] It induces cell necrosis in a 3-mm radius around the probe and is suitable for treatment of superficial tumors.[12] Argon plasma coagulation is a relatively new form of electro-surgery. Argon gas is ionized by electric current to create a non-contact, homogeneous region on the target tissue.[13] Coagulated tissue has higher resistance and drives the ionized argon gas flow away to nearby tissue. Argon plasma coagulation is suitable for treating bronchial segments that have an acute angle from the major airways, such as apical and posterior segments of the upper lobes, and apical lower-lobe segments.[10] Endobronchial brachytherapy places a radioactive source within or near an endobronchial malignancy to deliver local irradiation.[12] The disadvantage of brachytherapy is its delayed effects. The first effects can be seen one week after treatment, and the maximum effect is achieved after 3 weeks.[12] However, brachytherapy has a longer-lasting effect and greater tissue penetration than other techniques. It may be curative for very early superficial cancers.[12]

There are many interventional modalities to treat tracheal and bronchial lesions, and each method has its advantages and disadvantages. The choice of modalities depends on the patient's clinical condition, the operator's training, the availability of equipment, and the weighed benefits and risks. Laser photo resection and electro-surgery allow rapid removal of endobronchial tissue,[8-10] while cryotherapy and brachytherapy have delayed response and are not indicated for obstructive tumors in an emergency setting.[12] In patients with acute respiratory failure in need of immediate relief, laser photo resection and electro-surgery are indicated.

However, these treatments are often palliative procedures that are usually combined with other treatments, such as radiotherapy and chemotherapy. In our patient electro-surgery removed the major part of a tracheal small-cell cancer tumor and restored air passage. The patient was successfully extubated and had complete resolution of dyspnea and wheezing. As the small-cell cancer was extensive, he was further treated with chemo-radiotherapy, and he remains loco-regionally controlled on follow-up.

## REFERENCES


1. Govindan R, Page N, Morgensztern D, Read W, Tierney R, Vlahiotis V. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol 2006;24(28):4539-4544.
2. Macchiarini P. Primary tracheal tumours. Lancet Oncol 2006;7(1): 83-91.
3. Kazawa N, Kitaichi M, Hiraoka TM, Togashi K, Mio N, Mishima M, et al. Small cell lung carcinoma: eight types of extension and spread on computed tomography. J Comput Assist Tomogr 2006;30(4):653-661.
4. Wood DE. Management of malignant tracheobronchial obstruction. Surg Clin North Am 2002;82(3):621-642.
5. Webb BD, Walsh GL, Roberts DB, Sturgis EM. Primary tracheal malignant neoplasms: The University of Texas MD Anderson Cancer Center experience. J Am Coll Surg 2006;202(2):237-246.
6. Desai DP, Holinger LD, Gonzales-Crussi F. Tracheal neoplasm in children. Ann Otol Rhinol Laryngol 1998;107(9 Pt 1):790-796.
7. Rosti G, Carminati O, Monti M, Tamberi S, Marangolo M. Chemotherapy advances in small cell lung cancer. Ann Oncol 2006;17(Supp l5):99-102.
8. Sutedja G, Kralingen K, Schramel FM, Postmus PE. Fibreoptic bronchoscopic electrosurgery under local anaesthesia for rapid palliation in patients with central airway malignancies: a preliminary report. Thorax 1994;49(12):1243-1246.
9. Sheski FD, Mathur PN. Endobronchial electrosurgery: argon plasma coagulation and electrocautery. Semin Respir Crit Care Med 2004; 25(4):367-374.
10. Bolliger CT, Sutedja TG, Strausz J, Freitag L. Therapeutic bronchoscopy with immediate effect: laser, electrocautery, argon plasma coagulation and stents. Eur Respir J 2006;27(6):1258-1271.
11. Tellides G, Ugurlu BS, Kim RW, Hammond GL. Pathogenesis of systemic air embolism during bronchoscopic Nd:YAG laser operations. Ann Thorac Surg 1998;65(4):930-934.
12. Vergnon JM, Huber RM, Moghissi K. Place of cryotherapy, brachytherapy and photodynamic therapy in therapeutic bronchoscopy of lung cancers. Eur Respir J 2006;28(1):200-218.
13. Crosta C, Spaggiari L, De Stefano A. Endoscopic argon plasma coagulation for palliative treatment of malignant airway obstructions: early results in 47 cases. Lung Cancer 2001;33(1):75-80.