Case Report

A nonresponding small cell lung cancer combined with adenocarcinoma

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Abstract: This study aimed to present a case with limited-stage small cell lung cancer (SCLC) not responding to two cycles of chemotherapy. Radical resection of left lower pulmonary carcinoma was performed. The postoperative pathological diagnosis was SCLC combined adenocarcinoma, and the pTNM stage was pT1cN1M0 (IIB). The patient received three cycles of adjuvant chemotherapy and prophylactic radiotherapy in the mediastinal lymphatic drainage region. If patients with SCLC have a high level of carcinoembryonic antigen (CEA), are nonresponding to chemotherapy, or the lesion is located at the peripheral portion of the lung, then non-small cell lung cancer (NSCLC) complements may be present. Further workup (e.g., repeat or multipoint biopsy) should be offered to reach an accurate pathological diagnosis and plan suitable treatment. Surgery should be considered for patients with suspicious early-stage combined small cell lung cancer (C-SCLC). It can play an important role in diagnosis and treatment.

Keywords: Chemotherapy; combined small cell lung cancer (C-SCLC); surgery

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Introduction

Combined small cell lung cancer (C-SCLC), defined as small cell lung cancer (SCLC) combined with an additional component that consists of any of the histological types of non-small cell lung cancer (NSCLC) (usually adenocarcinoma, squamous cell carcinoma, or large cell carcinoma and, less commonly, giant cell carcinoma or spindle cell) is considered to be a subset of SCLC (1,2). C-SCLC accounts for 28% of all SCLC cases in surgical specimens (1). However, most of the studies have shown that C-SCLC accounts for 1–3.2% because less than 5% of the patients with SCLC are detected with stage T1–2N0M0. Only the patients with stage T1–2N0M0 are eligible for surgery, and it is extremely difficult to diagnose C-SCLC through biopsy (3-5). This study aimed to report a case of limited-stage SCLC not responding to chemotherapy. The patient was diagnosed with SCLC combined adenocarcinoma and treated through surgical resection.

Case presentation

A 61-year-old heavy smoker in good physical condition was diagnosed with a mass in the left lung during a health examination through computed tomography (CT) scan. Fludeoxyglucose-positron emission tomography scan showed a mass in the left lower lung with hilar lymph nodes and no distant or cerebral metastasis. Bronchoscopy examination revealed SCLC. Two cycles of chemotherapy were given (etoposide combined with carboplatin/cisplatin), and stable disease was achieved (*Figure 1*). A radical R0 resection of left lower pulmonary carcinoma was performed, and the pathological diagnosis was SCLC combined adenocarcinoma (tumor 2.5 cm × 2 cm × 1.8 cm). The positive lymph nodes were left lower paratracheal nodes 0/6, aortopulmonary nodes 0/5, subcarinal nodes 0/4,

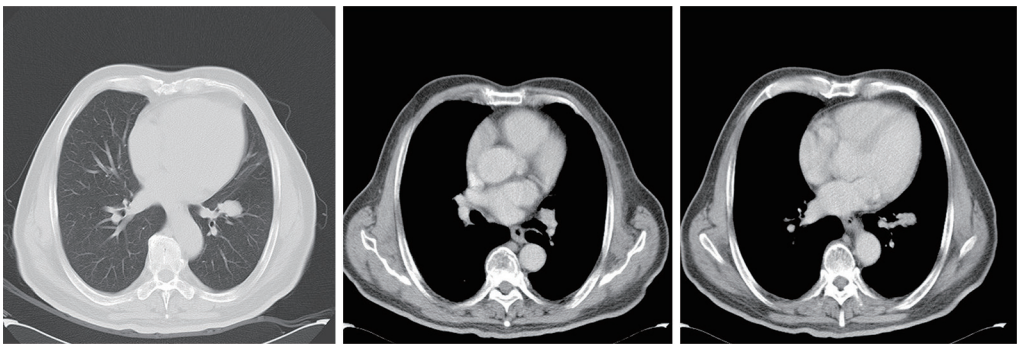

Figure 1 Chest CT scan after two cycles of chemotherapy (October 30, 2015). CT, computed tomography.

paraesophageal nodes 0/1, hilar nodes 1/9, interlobar nodes 4/5, lobar nodes 0/3 and pTNM stage was pT1cN1M0 (IIB) according to the eighth edition of the TNM classification for lung cancer. The results of immunohistochemistry (IHC) analysis were as follows: CK/LMW (+), Ck8/18 (+), Syn (+), chromogranin A (+), CD56 (+), Ki-67 (+, 90%), P40 (–), P63(–), ALK (D5F3) (–), ALK-NC (–), Ck5/6 (–), CK7 (+), TTF1 (+), and napsin A (–) (*Figure 2*). The epidermal growth factor receptor (EGFR) mutation was found to be negative using the amplification refractory mutation system. The patient received two cycles of adjuvant chemotherapy with etoposide/carboplatin. Prophylactic radiotherapy was given in the mediastinal lymphatic drainage region, and the dose was as follows: hilum 5,000 cGy/25F, upper mediastinum 4,000 cGy/25 F, and spinal cord 3,000 cGy. One cycle of pemetrexed combined with carboplatin was given before radiotherapy. About 4 months after completing the treatment, bone metastasis occurred accompanied with back pain (*Figure 3*). *Figure 4* shows the change in neuron-specific enolase (NSE), carcinoembryonic antigen (CEA), and squamous cell carcinoma (SCC) antigen. The sequence of anticancer treatments is shown in *Table 1*.

Discussion

SCLC is sensitive to first-line chemotherapy and radiotherapy, and lack of response to chemotherapy may be due to NSCLC complements (6,7). The tumors in patients with C-SCLC are easily located in the peripheral portion of the lung (3,8). The serum CEA level is invariably elevated in lung adenocarcinoma (9,10). The serum CEA level can be used as a reference marker in the diagnosis of SCLC combined adenocarcinoma (11). This patient did not respond to the initial two cycles of chemotherapy and received surgery, which confirmed SCLC combined adenocarcinoma. If the primary lesion is in the peripheral portion of the lung, high levels of CEA are observed, and the patient doses not respond to chemotherapy, the possibility of a tumor with combined histology should be considered in patients with SCLC on the basis of limited biopsy material.

Surgery in selected patients with limited-stage SCLC was associated with improved survival outcomes (12). Babakoohi *et al*. identified 22 patients with C-SCLC and compared the findings with the results obtained from 406 patients with pure SCLC. Surgery was significantly more common in patients with C-SCLC (2). Patients with C-SCLC carry a better prognosis than those with pure SCLC (2). The EGFR mutation is rare in patients with SCLC. It might occur more often in patients with C-SCLC, especially combined with adenocarcinoma, compared with patients with pure SCLCs (13-15). A few case reports showed that some patients with pure SCLC or C-SCLC having EGFR mutation respond to tyrosine kinase inhibitor (TKI) (15-17). It is thought that TKIs can also be used in C-SCLC with EGFR mutation, especially in second-line or third-line treatment. In this patient, no EGFR mutation was found.

Due to the difference of treatment and prognosis between C-SCLC and pure SCLC, further workup (e.g., repeat or multipoint biopsy) should be offered to reach an accurate pathological diagnosis and plan suitable treatment for those suspicious C-SCLC. Surgery should be considered for patients with suspicious early-stage C-SCLC. It can play an important role in diagnosis and treatment.

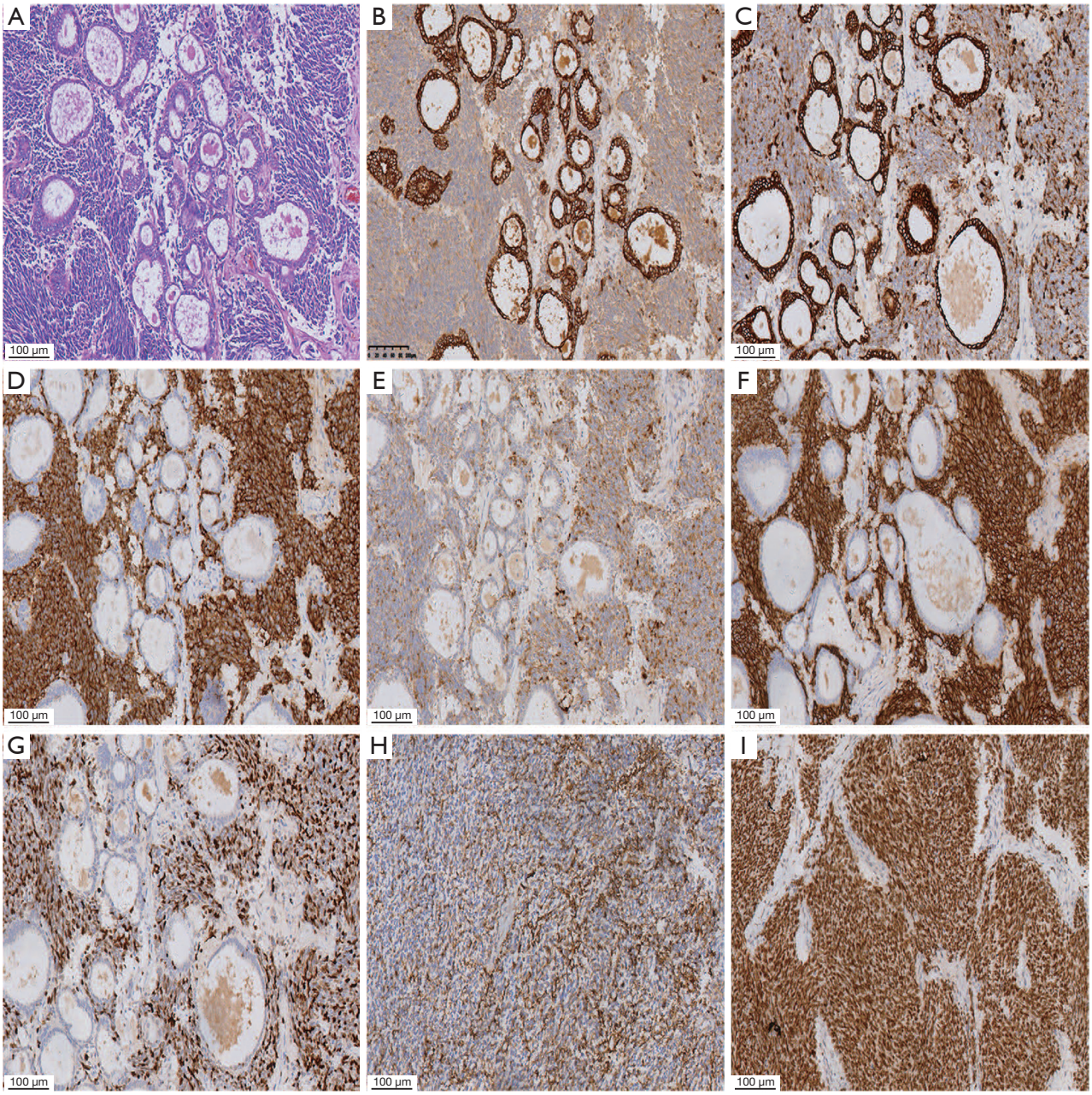

Figure 2 The pathology of the patient with SCLC combined with adenocarcinoma. (A) Hematoxylin and eosin staining; (B) CK/LMW (+); (C) Ck8/18 (+); (D) Syn (+); (E) chromogranin A (+); (F) CD56 (+); (G) Ki-67 (+, 90%); (H) CK7 (+); (I) TTF1 (+). (×200). SCLC, small cell lung cancer.

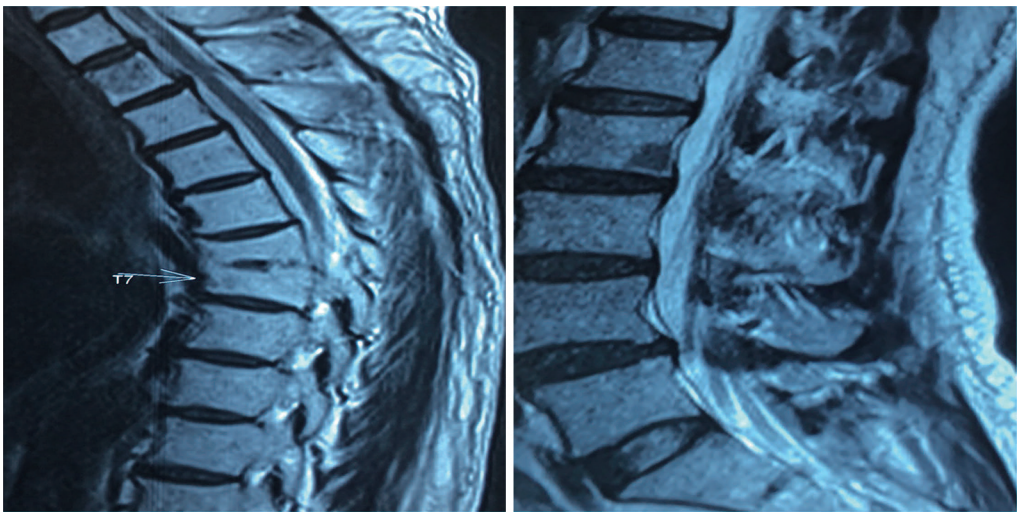

Figure 3 CT scan of the thoracic and lumbar vertebrae (July 20, 2016). CT, computed tomography.

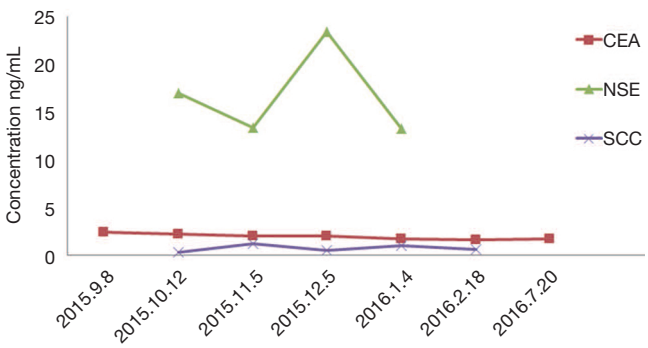

Figure 4 Variation curve of NSE, CEA, and SCC. NSE, neuron-specific enolase; CEA, carcinoembryonic antigen; SCC, squamous cell carcinoma antigen.

Table 1 Sequence of anticancer treatments

Date	Treatment
September 2015	Complete fludeoxyglucose-positron emission tomography scan and bronchoscopy examination
October 2015	Complete two cycles of chemotherapy
November 2015	Underwent radical surgery
January 2016	Complete two cycles of adjuvant chemotherapy
March 2016	Complete prophylactic radiotherapy for mediastinal lymphatic drainage area and one cycle of chemotherapy
July 2016	Detected with bone metastasis

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Footnote

Conflicts of Interest: Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2017.06.16). The authors have no conflicts of interest to declare.

Ethical statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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