

Spontaneous Regression of Small Cell Lung Cancer: A Case Report

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Abstract

Spontaneous regression (SR) is extremely rare in small cell lung cancer (SCLC). The present study reports a rare case of SCLC accompanied by partial SR in a 68-year-old man. The patient was scheduled to receive chemoradiotherapy for SCLC. Computed tomography (CT) simulation images for radiotherapy revealed partial regression of the primary tumor, while lymph node metastasis progression was observed. On ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography/CT, an abnormally high uptake of FDG was not observed in the primary exhibiting SR, while an extremely high uptake was identified in the lymph node metastases. The patient also presented with bilateral double vision, which suggested neurological paraneoplastic syndrome. He received chemoradiotherapy and a complete response was obtained. Until the last follow-up (58 months since the initiation of chemoradiotherapy), the patient was free from tumor progression.

Keywords: Small cell lung cancer; Spontaneous regression; Paraneoplastic sensory neuropathy

Introduction

Spontaneous regression (SR) of cancer is defined as the partial or complete, transient or permanent disappearance of a malignant tumor without the administration of any medical treatment [1]. Renal cell carcinoma and melanomas, immunotherapy-responsive malignancies were more frequently associated with SR. SR is extremely rare in small cell lung cancer (SCLC), with ~ten reported cases [2-8].

The mechanism of SR are still largely unknown, although host immune response against neoantigens expressed by tumors has been most often implicated [9]. Mechanism other than immune response may be operative. Many reports of SRs have implicated surgery or operative trauma as an element that can increase immunological resistance to tumor growth and the removal of portion of the tumor (e.g. nephrectomy in patients with metastatic clear cell renal cell carcinoma) may facilitate the destruction of the remaining tumor by the host immune system [10].

The present study reports a rare case of SCLC accompanied by partial SR.

Case Report

A 68-year-old male patient with a 120 pack/year history of smoking was admitted to St. Luke's International Hospital in November 2008 for suspected lung cancer. The patient had undergone a right lower lobectomy for a pT1N0M0, stage IA lung adenocarcinoma, classified by TNM Classification of Malignant Tumors, in June 1996 [11], with no evidence of recurrence since. A thoracic computed tomography (CT) (Aquilion, Toshiba, Otawara) scan performed on November 18, 2008 revealed the presence of a left upper lobe nodule (17 mm × 12 mm), a left lower lobe nodule (26 mm × 21 mm), a left hilar lymph node mass (30 mm × 20 mm), and an ipsilateral mediastinal lymph node mass (20 mm × 10 mm) (Figure 1). Laboratory examinations revealed that gastrin-releasing peptide precursor (normal range: <81 pg/ml), neuron-specific enolase (normal range: <10 ng/ml), and cytokeratin 19 fragment (normal range: <3.5 ng/ml) were within the normal ranges (14.4 pg/ml, 10.1 ng/ml, and 1.2 ng/ml, respectively). Cytological examination following transbronchial

lung biopsy performed on December 12, 2008 diagnosed the left upper lobe nodule as squamous cell carcinoma, and the left lower lobe nodule as SCLC (Figure 2). From early-January 2009, the patient suffered from bilateral double vision, although a neurologist of St. Luke's International Hospital diagnosed no deterioration of the extraocular muscles. Muscle tonus and strength were normal, no cerebellar ataxia was observed, deep tendon reflexes were normal and sensory function was intact. ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) (Celesteion, Toshiba, Otawara) performed on January 10, 2009 revealed a moderately high uptake in the left upper lobe nodule (maximum standardized uptake value (SUVmax), 3.9), and an extremely high uptake in the left hilar (SUVmax, 18) and mediastinal masses (SUVmax, 17). However, there was not an abnormally high uptake in the left lower lobe nodule (SUVmax, 2.5) (Figure 3). Brain magnetic resonance imaging (MRI) performed on January 23, 2009 did not detect any metastases or any other abnormalities. The patient was clinically diagnosed with double SCLC with ipsilateral hilar and mediastinal lymph node metastases (cT1N2M0, stage IIIA) and squamous cell carcinoma (cT1N0M0, stage IA) [11].

The patient was scheduled to receive chemoradiotherapy (45 Gy in 30 fractions (twice daily), concurrently with 4 courses of cisplatin (80 mg/square) and etoposide (100 mg/square × 3)) for SCLC and stereotactic body radiotherapy (SBRT) (48 Gy in 4 fractions) for squamous cell carcinoma. CT simulation images for radiotherapy performed on January 26, 2009 revealed partial regression of the SCLC (15 mm × 10 mm), and progression of the lymph node metastases (Figure 1). From late-January to mid-April, the patient received chemoradiotherapy

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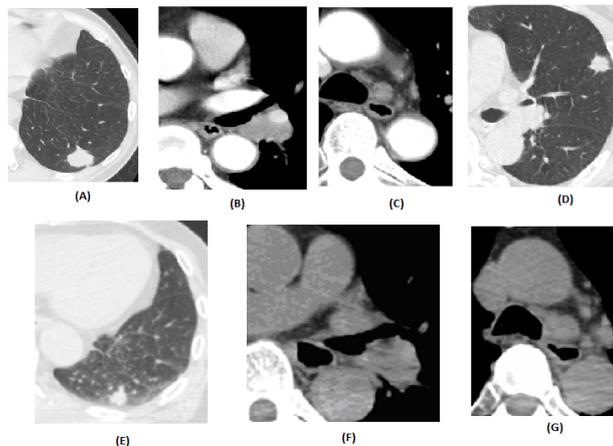


Figure 1: A left lower lobe nodule (A), a left hilar lymph node mass (B), a mediastinal lymph node mass (C), and a left upper lobe nodule (D) were detected in CT images at diagnosis. CT simulation images for radiotherapy (January 26, 2009) showed regression of the left lower lobe nodule (E), while lymph node metastases were progressive (F, G).

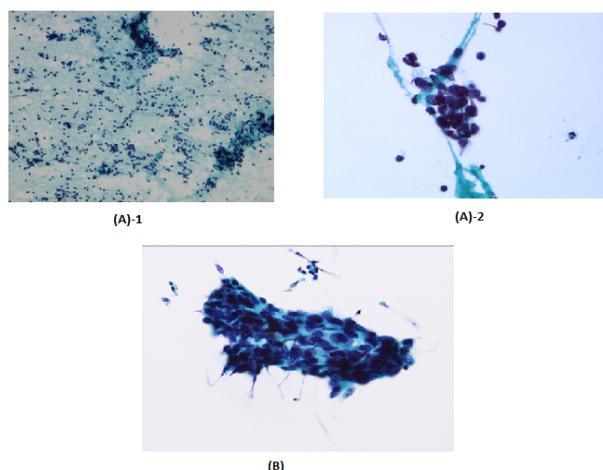


Figure 2: Cytological examination in the present case. Diagnosis of small cell carcinoma for the left lower lobe nodule (A)-1 (4x) and A)-2) (40x) and squamous cell carcinoma for the left upper lobe (B) were established.

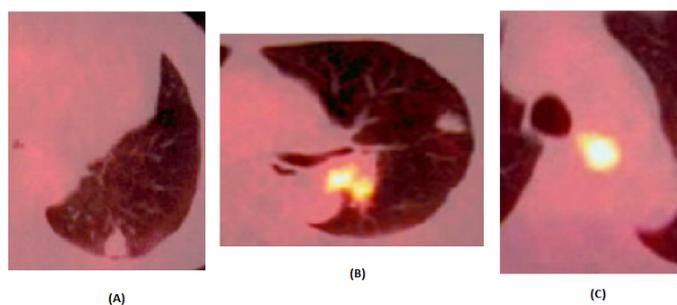


Figure 3: No abnormally high uptake was found in the left lower lobe nodule (A), while a slightly high uptake in the left upper lobe nodule (B) and an extremely high uptake in the left hilar mass (B) and mediastinal mass (C) were found in FDG-PET-CT images.

for SCLC, and SBRT for squamous cell carcinoma. The double vision gradually subsided following the initiation of chemoradiotherapy, and completely disappeared in June 2009. A complete response was obtained for SCLC and therefore the patient received prophylactic cranial irradiation (25 Gy in 10 fractions) in June.

A fourth lung cancer was identified in the apical region of the left lung in February 2012. The patient was diagnosed with squamous cell carcinoma (cT1aN0M0, stage IIIA) [12] by transbronchial lung biopsy and received proton radiotherapy (66 cobalt Gy equivalent in 10 fractions) between March and April of the same year. At the last follow-up in November 2013, the patient was free from tumor progression.

Discussion

The present study reports a rare case of SCLC accompanied by partial SR. To the best of our knowledge, the present study is the first case report of SR in SCLC that includes FDG-PET/CT findings. SCLC is considered a highly aggressive tumor, which, in the majority of cases, is accompanied by an extremely high uptake of FDG [13]. However, in the present case, no high uptake of FDG was detected in the primary tumor, which is to be expected, since the tumor exhibited SR. By contrast, progression of lymph node metastases was observed by a high uptake of FDG, revealing a discrepancy between the metastases and the primary lesion: however, a pathological confirmation of SCLC was not obtained for the lymph node metastases due to technical difficulties.

The reason for SR of the primary tumor remains unclear. Several studies have reported that SR was accompanied by a neurological paraneoplastic syndrome (encephalomyelitis or sensory neuropathy) in SCLC [2-5]. The anti-tumor immune response may be important in the presentation of SR [2]. The present case also presented with a neurological paraneoplastic syndrome, although the presence of specific autoantibodies, including anti-Hu antibodies and anti-Yo antibodies [14] was not examined. The present patient presented with bilateral double vision without any abnormalities by brain MRI, and the symptom disappeared after the treatment. It is reasonable that we regard the symptom as an anti-tumor immunological symptom.

Surgical trauma has been reported as a possible cause of SR. Cole reported that 71 of the 176 cases with SR of cancer had received surgical trauma [1], although underlying mechanism remains unclear. In the present case, the transbronchial lung biopsy may have induced SR.

Conclusion

We report a rare case of SCLC which did not accompany with an abnormally high uptake on FDG-PET/CT and accompanied by partial SR. This information may help clinicians correctly diagnose SR in SCLC.

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