



Case report

Spontaneous regression of small cell lung cancer combined with cancer associated retinopathy



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ABSTRACT

Spontaneous regression (SR) is defined as the complete or partial disappearance of disease without anti-cancer treatments. We report a case of SR of small cell lung cancer (SCLC) combined with cancer associated retinopathy (CAR). A 65-year-old woman was admitted to our hospital to examine abnormal shadows of the lung with visual loss. She was diagnosed with SCLC associated with CAR. Subsequent chest X-ray and CT scan showed partial regression of both primary tumor and lymph node metastasis without anti-cancer treatment. Recoverin antigen was present on the tumor cells and anti-recoverin antibody was observed in the patient's serum. Activation of recoverin-specific antitumor cytotoxic T lymphocyte (CTL) was observed in this patient. SCLC was considered to reduce spontaneously by the activation of recoverin-specific antitumor CTL. To the best of our knowledge, this is the first report of SR in SCLC combined with CAR.

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1. Introduction

Small cell lung cancer (SCLC) accounts for 20% of lung cancers [1] and often leads to paraneoplastic syndrome, which is a remote effect on various organs without direct invasion or metastasis of tumor cells. Cancer associated retinopathy (CAR) is a rare paraneoplastic syndrome that is usually associated with SCLC [2]. Patients with CAR typically present with photosensitivity, ring scotoma, and attenuated retinal arterioles along with undetectable signals on an electroretinogram (ERG) [3]. The autoantibodies that react with photoreceptor proteins, including recoverin, might induce degeneration of photoreceptors and result in poor visual prognosis in patients with CAR [4]. It was reported that recoverin was expressed in tumor tissues in 68% of patients with SCLC and anti-recoverin antibodies were found in sera in 15% of those patients, respectively. However, none of these patients developed CAR [5].

Abbreviations: CAR, cancer associated retinopathy; CTL, cytotoxic T lymphocyte; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; ERG, electroretinogram; SR, spontaneous regression; SCLC, small cell lung cancer.

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Spontaneous regression (SR) is defined as the complete or partial disappearance of disease without effective anticancer treatments, continuing for 1 month. Although SR occurs in many types of cancers, it is rare, especially in SCLC [6,7]. Here, we report a case of SR of SCLC combined with CAR in a 65-year-old woman.

2. Case report

A 65-year-old woman with an existing smoking history of 35 pack-years was admitted to our hospital for evaluation of a right upper nodule revealed on a chest X-ray film (Fig. 1A). Chest computed tomography (CT) scan revealed a primary tumor in the right upper lobe with right supraclavicular and mediastinal lymph node swelling (Fig. 1B–D). Laboratory examination showed elevated levels of gastrin-releasing peptide precursor (pro-GRP) and neuron-specific enolase (NSE), at 115.0 pg/ml (normal range less than 80.9 pg/ml) and 15.5 ng/ml (less than 12.0 ng/ml), respectively. Tumor specimens of the right lower paratracheal lymph node obtained by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) were positive for neuroendocrine makers including CD56, chromogranin A and synaptophysin and confirmed the histological diagnosis of SCLC (Fig. 2A).

The patient complained of blurred vision in both eyes 11 days after admission. Her best-corrected visual acuity was finger

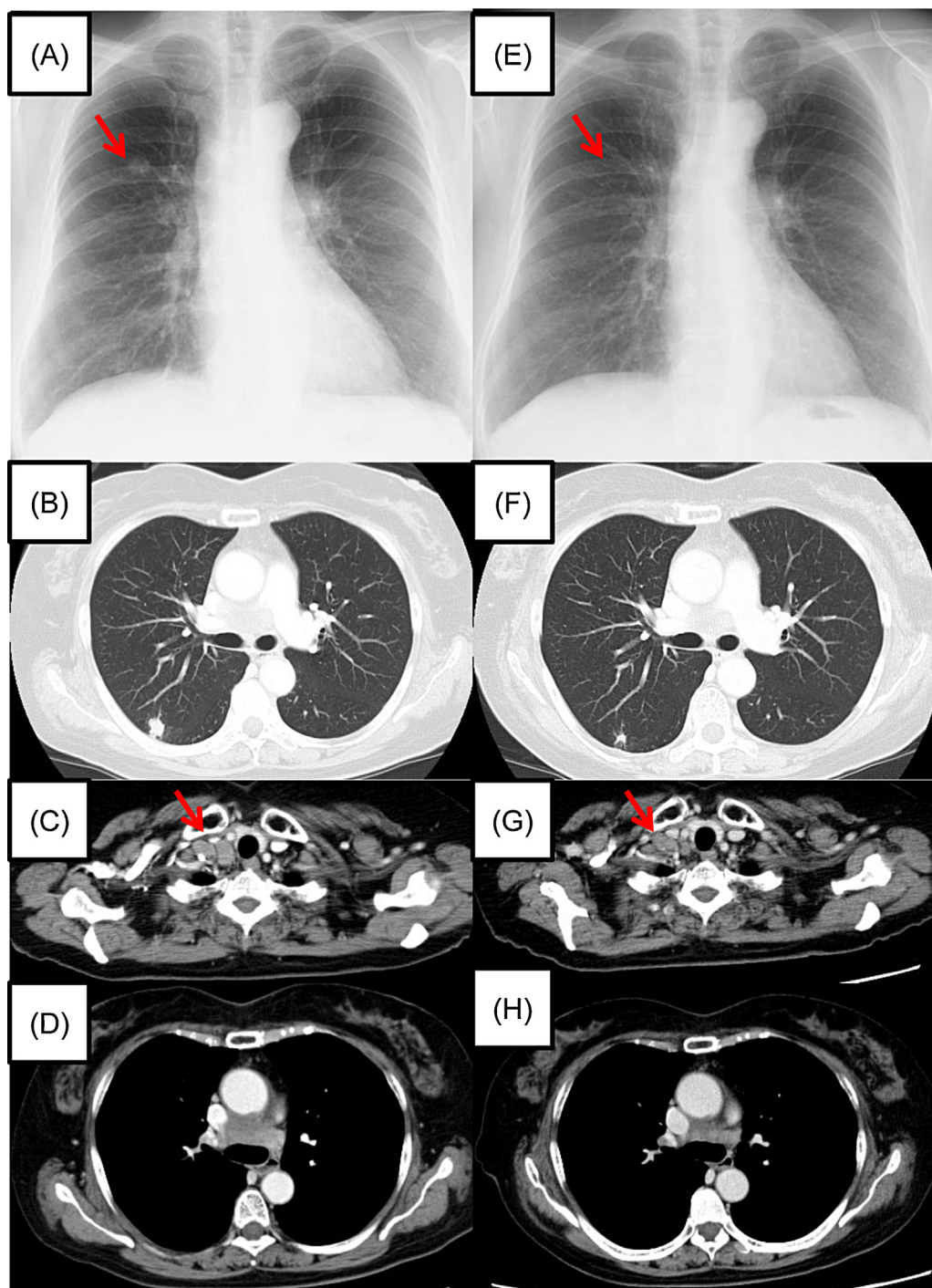


Fig. 1. Chest X-ray and CT show spontaneous regression of primary tumor and lymph node metastasis in the present case. (A) Right upper mass (arrow) in first examination. (B) Primary tumor in the right S2 in first examination. (C) Right supraclavicular lymph-node metastasis (arrow) in first examination. (D) Mediastinal lymph node metastasis in first examination. (E) Partial spontaneous regression of the right upper mass, subsequent chest X-ray. (F) The primary tumor, (G) right supraclavicular lymph node and (H) mediastinal lymph node decreased, subsequent CT.

counting in the right eye and 0.1 in the left eye. Although fundoscopic examination showed the appearance of both eyes to be normal, Goldmann perimetry showed a large central scotoma in the right eye and a ring scotoma in the left eye. ERG showed poor responses in both eyes. Recoverin antigen was present in the lung cancer cells and anti-recoverin antibody was observed with high titer (1:2000) in the patient's serum (Fig. 2B and 3). Finally, she was diagnosed with limited disease of SCLC (cT1bN3M0 stage IIIB) associated with CAR. After diagnosis of SCLC, chest X-ray and CT scan

prior to anticancer treatment revealed the SCLC to have partially regressed (Fig. 1E–H). Furthermore, levels of both pro-GRP and NSE had already decreased before EBUS-TBNA examination, and decreased further to normal range. *In vitro*, IFN- γ ELISPOT assay was performed, using recoverin peptide to stimulate peripheral blood mononuclear cells taken from the patient. The number of CD8+ T cells secreting IFN- γ that reacted to R64 peptide (recoverin-derived HLA-A24 restricted peptide R64) was significantly larger than that of T cells without peptide in the patient (Fig. 4A and B).

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