

## CASE REPORT

# Spontaneous regression of metastatic squamous cell lung cancer

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### Key Clinical Message

Spontaneous regression (SR) of cancer is a rare but confirmed spectacular phenomenon, and it is even rarer in the context of advanced NSCLC. It is essential to understand this phenomenon in order to elucidate the nature of neoplastic disease and develop new treatment methods.

### Keywords

Lung cancer, metastatic, neoplastic disease, pulmonary, spontaneous regression.

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## Introduction

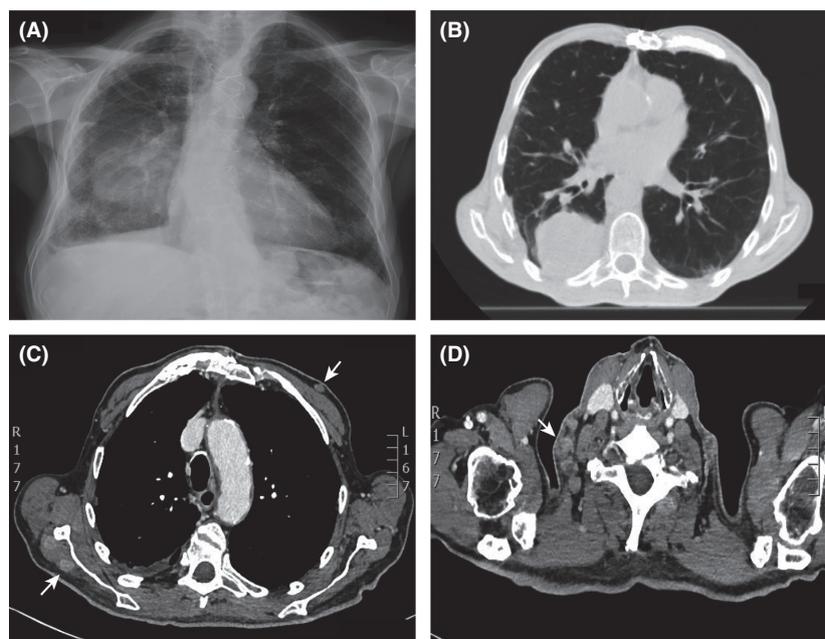
Partial or complete spontaneous cancer regression is a rare phenomenon, particularly in patients with lung cancer. We describe a case of an 82-year-old man referred to our Hospital with an abnormal shadow on chest X-ray, cervical lymph nodes, and cutaneous nodules. He was diagnosed of stage IV squamous cell lung cancer. The patient denied to receive anticancer treatment. In follow-up, the primary tumor decreased in size and the metastatic cutaneous lesions and cervical lymph nodes spontaneously regressed on the following computed tomography scan. This was thought to be a partial spontaneous regression of the cancer, and he was treated with palliative thoracic radiotherapy. One year after ending radiotherapy treatment, the patient died of a myocardial infarction.

Spontaneous regression (SR) of cancer is an extremely rare phenomenon that has been defined as a complete or partial disappearance of all or at least some relevant disease that is either temporary or permanent in nature without any medical treatment or with treatment that is considered inadequate at producing the resulting regression [1, 2]. Everson divides SR into four categories: primary tumor regression, metastatic tumor regression

(primary focus is defined pathologically), metastatic tumor regression (no pathological diagnosis of primary tumor), and radiologically considered metastasis tumor regression [3]. SR is a very rare phenomenon [4], especially in the case of squamous cell lung cancer, with very few reports in the literature to date [5].

## Case Report

In January 2016, an 82-year-old man that was referred to the Central University Hospital of Asturias, for an evaluation of an abnormal shadow on his chest X-ray. He was a pack-a-day smoker for 45 years and had a history of type II diabetes treated with medication. Physical examination showed palpable bilateral cervical lymph nodes and cutaneous nodules on his abdomen, arms, neck, and lip. Chest radiography showed an alveolar infiltrate in the right lower lobe (Fig. 1A), and the CT scan revealed a round mass in the right lower lobe (Fig. 1B), multiple nodules in the chest wall (12 × 18 mm nodule in the right pectoral muscle and 6 mm nodule in the intercostal muscles between the sixth and seventh left ribs; Fig. 1C), and cervical necrotic lymph nodes (Fig. 1D). Percutaneous aspiration cytology of the tumor on the left side of



**Figure 1.** (A) The chest X-ray showed an alveolar infiltrate in the right lower lobe. (B) CT scan revealed a round mass in the right lower lobe. (C) Multiple nodules in the chest wall (12 × 18 mm nodule in the right pectoral muscle and 6 mm nodule in the intercostal muscles between the sixth and seventh left ribs). (D) Cervical necrotic lymph nodes.

the neck (cervical lymph node) and CT-guided needle biopsy of the right lower lobe mass were performed, and pathological examination established the diagnosis of squamous lung cell carcinoma with metastases to the cervical lymph nodes. Finally, a biopsy of one of the cutaneous nodules was performed, confirming the diagnosis of squamous lung cell carcinoma metastases. He was diagnosed to have advanced lung cancer with cervical lymph node and cutaneous metastasis (cT3N3M1C-stage IVB).

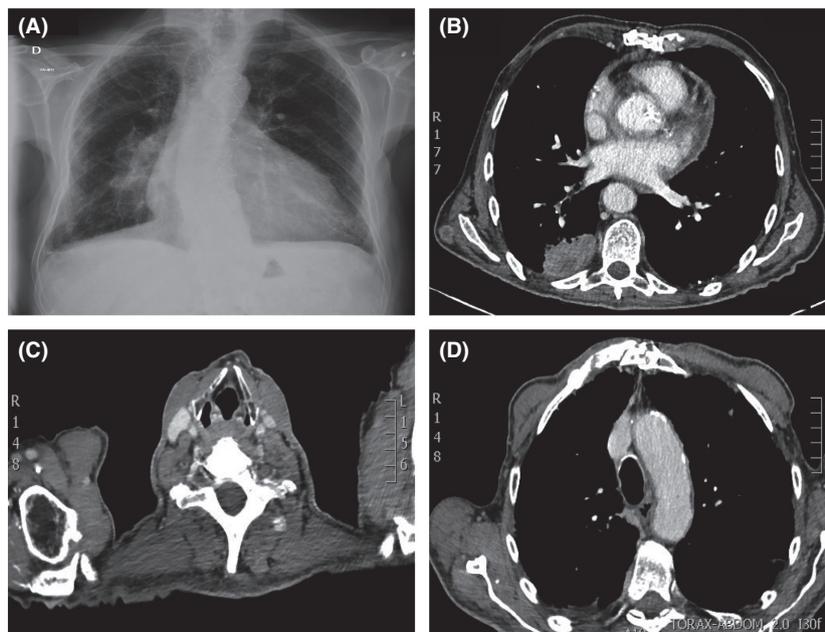
The patient denied receiving anticancer treatment. At follow-up, 3 months after the diagnosis, chest radiography and CT scan showed that the primary tumor decreased in size (Fig. 2A and B) and that metastatic cutaneous lesions (arms, neck, and lip), cervical lymph nodes, and multiple nodules in the chest wall had spontaneously regressed (Fig. 2C and D). This result was thought to be partial SR of cancer, and he was treated with palliative thoracic radiotherapy. The cutaneous metastatic lesions and cervical lymph nodes had complete SR, and the lung mass stayed stable for a year. One year after ending radiotherapy treatment, the patient died of a myocardial infarction.

## Discussion

Spontaneous regression of cancer is an exceedingly uncommon phenomenon that is even rarer in lung cancer [6]. Regression should last at least 1 month and should

exceed the waxing and waning of stable disease. This definition of SR is unequivocal for tumor regression without any medical treatment or after treatment failure. However, in some cases, it may be quite difficult to distinguish between treatment-induced remission and SR coincidental to inadequate therapy [7]. The incidence of SR of advanced non-small-cell lung cancer (NSCLC) is relatively low; approximately 20 cases were reported from 1950 to 2004 [6], and no more than 15 new cases have been reported in the last 12 years [6, 7].

The mechanisms underlying SR of cancer are controversial. Possible mechanisms include apoptosis, immunological and cytokine-mediated mechanisms, differentiation, hormonal mechanisms, inhibition of angiogenesis or telomerase, and psychoimmunological mechanisms induced by causative factors, such as infection, fever, drugs, radiation, and trauma, which includes surgery, hormones, pregnancy, and carcinogens [8, 9]. Tumors derived from embryonic stem cells and tumors related to hormonal secretions, the most commonly described of which are adenocarcinoma of the kidney, neuroblastoma, melanoma, and some sarcomas, have a greater capacity for SR. Certain previous studies have reported SR of metastatic lesions following removal of the primary lesion, whereas other studies have reported SR associated with infection [7, 10]. There have been some reports on spontaneous regression of FDG/PET-positive tumors [11, 12]. All of them concerned patients with hematological malignancies, except



**Figure 2.** (A and B) Chest radiography and the CT scan showed a decrease in the size of the primary tumor. (C and D) Metastatic cutaneous lesions (arms, neck, and lip), cervical lymph nodes, and multiple nodules in the chest wall spontaneously regressed.

for one patient with lung cancer [11]. In this patient with lung cancer, squamous cell carcinoma was confirmed pathologically by surgical resection performed several months after PET/CT scan [11].

In the present case, histological lung cancer diagnosis was established by specimens obtained during CT-guided needle biopsy of the lung mass; the left cervical lymph node and one of the cutaneous nodules were confirmed to be metastatic from lung cancer. Although histological confirmation of metastatic lung squamous cell carcinoma was obtained, the metastatic cutaneous nodules disappeared shortly following skin biopsy. In our case, however, SR of the metastatic lesion was observed without any treatment of the primary or metastatic lesions; in addition, there was no infection of the primary or metastatic sites. In the present case, not only did SR occur in the cervical lymph node and cutaneous metastatic lesions but also the primary lung mass was reduced in size 3 months after obtaining the pathological specimens. The cases of SR of lung cancer published in recent years do not permit the identification of common characteristics. All types of histological varieties have been published indiscriminately in initial or very advanced stages in patients with a history of smoking or not and with or without distant metastases [13]. The only common factor is that at some point in its evolution and with no therapeutic intervention, a partial regression of the primary tumor or complete regressions of the metastatic sites occurred.

In summary, SR of cancer is a rare but confirmed spectacular phenomenon, and it is even rarer in the context of advanced NSCLC. The mechanism of this event remains a mystery, and no single factor seems to be responsible for it. It is essential to understand this phenomenon in order to elucidate the nature of neoplastic disease and develop new treatment methods.

## Conflict of Interest

None declared.

## Authorship

CM and PC: involved in patient management. CM and MA: provided CT images. PC: provided editing and reviewed the manuscript. MA: wrote the manuscript.

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