

Case Report

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# Complete Spontaneous Regression of Squamous-Cell Lung Cancer: A Case Report

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## Keywords

Non-small-cell lung cancer · Follicular lymphoma · Core needle biopsy · Computed tomography · Spontaneous regression

## Abstract

Spontaneous regression of cancer is an extremely rare phenomenon, and it has been described in only a few cases of pulmonary cancer. We report a case of complete spontaneous regression of squamous-cell lung cancer (SCLC) following a core needle biopsy in a 67-year-old female patient with two previous lung cancers and concomitant follicular lymphoma. The patient was diagnosed with SCLC after 4 core needle biopsies from a nodule in the left upper lobe and at the same time suspected of having follicular lymphoma. Treatment for the lung cancer was delayed by approximately 8 weeks because the diagnosis of lymphoma was both challenging and time-consuming. A computed tomography scan was performed in relation to the scheduled treatment for SCLC, showing that the pulmonary nodule had disappeared completely. Most other cases of spontaneous regression of lung cancer hint at the involvement of immunological factors, and this case possibly involves a combination of mechanical and local immunological factors. Genetic and immunological analysis of patients showing spontaneous regression of cancers could provide valuable information.

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## Introduction

Spontaneous regression of cancer is a recognized, yet rare, phenomenon [1]. It has been defined as the complete or partial disappearance of a malignant tumor in the absence of treatment or in the presence of therapy that is considered inadequate at producing a significant influence on the disease [2]. The phenomenon has been reported for different types of cancer, but it has only been described in few cases of lung cancer [3, 4], and it is more seldom in non-small-cell lung carcinomas than in any other cancer [5].

The mechanism of spontaneous regression of cancer is poorly understood and is believed to be multifactorial [2, 6, 7]. Growing evidence points toward an immunological imbalance for cancer development and progression, and the regression of cancer often occurs simultaneously with infections or trauma [4, 8]. We report this case of complete spontaneous regression of squamous-cell lung cancer (SCLC) following a core needle biopsy.

## Case Report

The patient is a 67-year-old Caucasian female, former smoker, with a history of two previous primary lung cancers, both adenocarcinomas. The first cancer was diagnosed 8 years earlier, located in the left upper lobe, and was staged T2aN0M0. The patient had a lobectomy without complications. There were no signs of relapse or new cancer on regular control computed tomography (CT) until 6 years later, when a CT revealed a growing nodule in the right upper lobe. An adenocarcinoma was diagnosed and staged T1aN0M0. Both tumors were TTF-1 positive and could not histologically be distinguished from one another. Because of the 6-year delay, the second tumor was interpreted as a new and separate tumor. Due to reduced lung function following the lobectomy, she was successfully treated with stereotactic body radiation therapy.

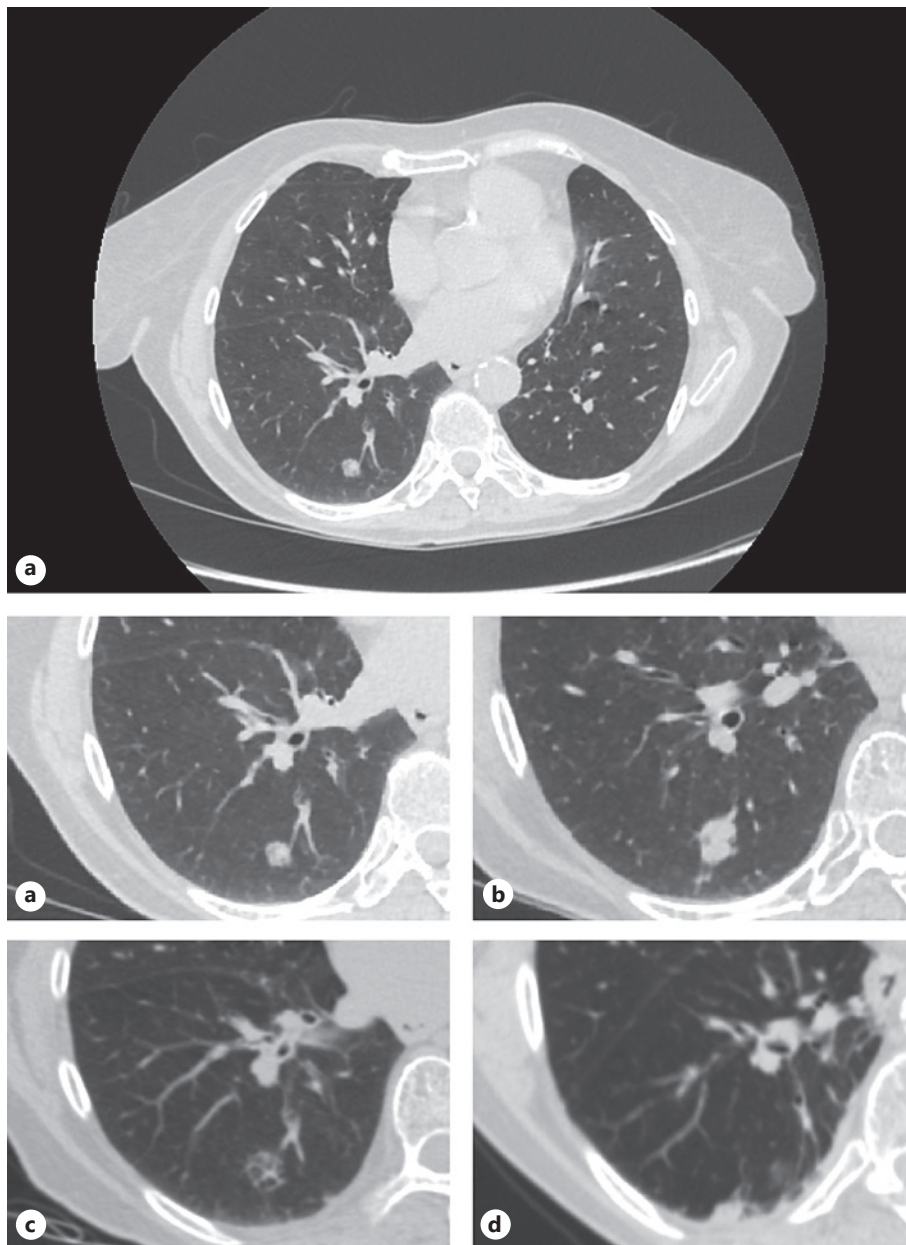
One year later, she developed a 9.5 mm nodule in the right lower lobe (shown in Fig. 1a). Positron emission tomography/CT showed almost no uptake of fluorodeoxyglucose. Three core needle biopsies were performed over a 2-month period, and all were without definite pathological findings.

Four months after the discovery of the nodule, a new CT revealed growth of the nodule to 15.4 mm (shown in Fig. 1b) and positron emission tomography/CT now indicated fluorodeoxyglucose uptake in the nodule. A successful core needle biopsy showed SCLC (shown in Fig. 2). The CT simultaneously showed a pathological lymph node conglomerate in the abdomen that was diagnosed to represent a follicular lymphoma. Obtaining a sufficient diagnostic biopsy from the lymphoma turned out to be both challenging and time-consuming, and treatment of the lung cancer was delayed for approximately 8 weeks.

It was decided to offer microwave ablation (MWA) of the lung cancer. Given the time delay caused by the lymphoma, a new CT was performed prior to treatment, revealing that the nodule had decreased considerably in size (shown in Fig. 1c). The MWA was scheduled only a few days later, and yet another CT scan was performed as part of the procedure. This showed that the nodule had disappeared completely (shown in Fig. 1d). Finally, the MWA was not performed on this patient.

The case was discussed on a multidisciplinary team conference after the complete regression, and a second opinion on the pathological findings was decided. Several pathologists from different hospitals reexamined (blinded to the prior history) pictures of the preparations from the biopsies. The conclusion of SCLC was unambiguous. The patient did not clinically, by blood test or physical examination, show signs of any other disease.

After spontaneous regression of the SCLC, the follicular lymphoma in the abdomen was treated to complete remission with bendamustine and rituximab. As of October 2021, 63 months

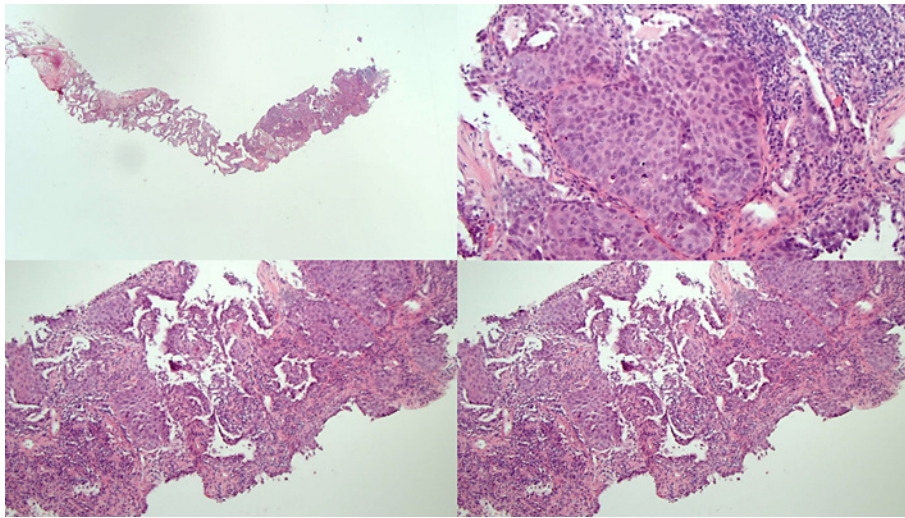


**Fig. 1.** **a** First CT scan with the SCLC measuring 9.5 mm. **b** Second CT scan showing growth to 15.4 mm, 4 months after scan **a**. **c** CT scan after the investigation for lymphoma showing a decrease in size and density, approximately 8 weeks after scan **b**. **d** CT scan before scheduled MWA showing complete regression, a few days after scan **c**.

after the CT in Figure 1d, the patient has showed no sign of relapse from the SCLC on follow-up CT performed every 3 months for the first 2 years after the diagnosis.

### Discussion

In this report, we have presented a case of complete spontaneous regression of SCLC following a core needle biopsy. This case report has several strengths: there was a clear potential trigger for regression (biopsy), which provides a hint for future research. The tumor



**Fig. 2.** Histology from the successful core needle biopsy.

disappeared completely, and the follow-up period is more than 5 years. The histopathological diagnosis was confirmed by several pathologists in a second opinion. Additionally, growth from 9.5 mm to 15.4 mm in a period of 4 months is compatible with SCLC, which typically has a doubling time of 126 days ( $\pm 58$  days) [9].

Spontaneous regression of cancer has mainly been attributed to different immunologic mechanisms, and it has been suggested that infection or trauma could induce an immunological response leading to the disappearance of the cancer. A study of 176 cases of spontaneous regression by Everson and Cole [10] found that up to 40% of the cases included an operative trauma. An increased immunological response was found in most cases of spontaneous regression in lung carcinomas in a recent review of cases from 1988 to 2018 [4].

Spontaneous regression of SCLC has previously been reported. In 2018, Matsui et al. [11] described a case of partial regression of SCLC with mediastinal lymph node metastasis. In this case, the primary tumor regressed following biopsy, while metastasis of mediastinal lymph nodes progressed. Another case described the regression of SCLC following biopsy [12]. These cases highlight the role of local trauma in spontaneous regression of SCLC. The likely role of the immune system in regression of SCLC has also been reported. Spontaneous regression of liver metastases from SCLC has been reported in a patient with rheumatoid arthritis following discontinuation of methotrexate treatment [13], and complete spontaneous regression was observed in a patient with concomitant *M. tuberculosis* infection in a case from 2013 [14].

Partial regression of a primary pulmonary tumor and multiple metastases in stage IV SCLC has also been described, but no evidence of systemic immunological abnormalities or infections is mentioned in this case [15]. In the current case, the patient did not show any signs of infection or systemic immunological abnormalities. It is not unlikely that the trauma and local inflammation from repeated needle biopsies are the causes of the regression, thus making it a combination of mechanical and immunological factors.

Spontaneous regression of malignant tumors should make us reconsider our understanding of the tumorigenesis. However, because of the rarity of these events, it is difficult to perform in-depth prospective analysis of this phenomenon. Genetic and immunological analysis of patients showing spontaneous regression of cancers could provide valuable information in the future.



## Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with national guidelines.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

## Funding Sources

No funding was received for this study.

## Author Contributions

Allan Klitgaard and Jakob Lager were involved in the design and drafting of the case report. Anders Løkke, Jakob Lager, Torben Riis Rasmussen, and Ole Hilberg were involved in patient care. Ole Hilberg gathered images of scans and histology. Allan Klitgaard, Anders Løkke, Jakob Lager, Torben Riis Rasmussen, and Ole Hilberg critically revised the manuscript and approved the final manuscript.

## Data Availability Statement

All data generated or analyzed in this study are included in this article. Further inquiries can be directed to the corresponding author.

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