



## Case report

## Spontaneous regressions in non-small cell lung cancer with different clinical outcomes

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## ABSTRACT

**Introduction and importance:** Spontaneous regression (SR) of cancer is extremely rare in non-small cell lung cancer and the exact pathogenesis is unclear.**Case presentations:** A 69-year-old man underwent a right upper lobectomy for a squamous cell carcinoma histologically confirmed 8 weeks prior. A histopathological examination of the surgical specimen revealed no viable cancer. He remains disease free at 5 years after surgery. A 77-year-old man presented with a metastatic bone tumor compatible with a non-small cell lung cancer origin. He had undergone a surgical biopsy for a right lung nodule of which the histopathological examination revealed only scar tissue a year prior. He died of cancer 4 months after the diagnosis of a bone metastasis.**Clinical discussion:** The unknown etiology of an SR of cancer is still to be resolved.**Conclusion:** Patients with an SR of cancer may yield a variety of clinical outcomes and a meticulous observation is essential.

## 1. Introduction

Spontaneous regression (SR) of cancer is the partial or complete disappearance of a malignancy without any effective medical treatment, and the exact pathogenesis remains unclear [1,2]. There are a limited number of non-small cell lung cancer (NSCLC) cases in the literature [3,4]. We here in report two SR cases of NSCLC with different clinical outcomes. This work has been reported in line with the SCARE criteria [5].

## 2. Case presentations

## 2.1. Case 1

A 69-year-old man with a 16-year history of rheumatoid arthritis presented with a right lung mass (Fig. 1). A transbronchial lung biopsy revealed a poorly differentiated carcinoma (Fig. 2a), consistent with a squamous cell carcinoma (Fig. 2b). A staging work up revealed no metastatic lesions, and a right upper lobectomy was performed 8 weeks after the biopsy. He had no other invasive procedures, infectious

diseases, or novel medications during this period. A histopathological examination of the surgical specimen revealed only a few atypical squamous cells in the necrotic tissue without any viable tumor cells (Fig. 3). He remains disease free at 5 years after the surgery.

## 2.2. Case 2

A 77-year-old man with a history of hypertension, benign prostatic hyperplasia, and type C hepatitis presented with a sixth thoracic vertebral fracture. A year earlier, he had undergone a wedge resection of a right lung nodule suspicious of an NSCLC (Fig. 4a). A postoperative histopathological examination showed scar tissue without any malignancy (Fig. 5). Although the preoperative imaging before the lung resection had revealed a hilar and mediastinal lymphadenopathy (Fig. 4b), a further histological assessment was not undertaken. He was diagnosed with an inflammatory lung nodule with involvement of the surrounding lymph nodes at that time.

A tissue biopsy from the broken vertebra detected a poorly differentiated adenocarcinoma (Fig. 6). Besides the affected vertebra, a whole-body imaging with fluorodeoxyglucose-positron emission

**Abbreviations:** SR, spontaneous regression; NSCLC, non-small cell lung cancer.

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**Fig. 1.** A chest CT showed an irregular mass in the right upper lobe in case 1.

tomography showed a significant uptake in the mediastinal and hilar lymph nodes. No lung lesions were evident. Although lacking the rigorous pathological evidence, the pulmonary nodule resected a year prior was assumed to have been a primary lung cancer that had regressed spontaneously. He was finally diagnosed with a metastatic NSCLC, which had progressed after an SR of the primary site. He died of cancer 4 months after the diagnosis of the bone metastasis (16 months after the initial lung resection). A pathological autopsy revealed a poorly differentiated metastatic adenocarcinoma in the intrathoracic lymph

nodes and vertebral body with bone marrow invasion.

### 3. Discussion

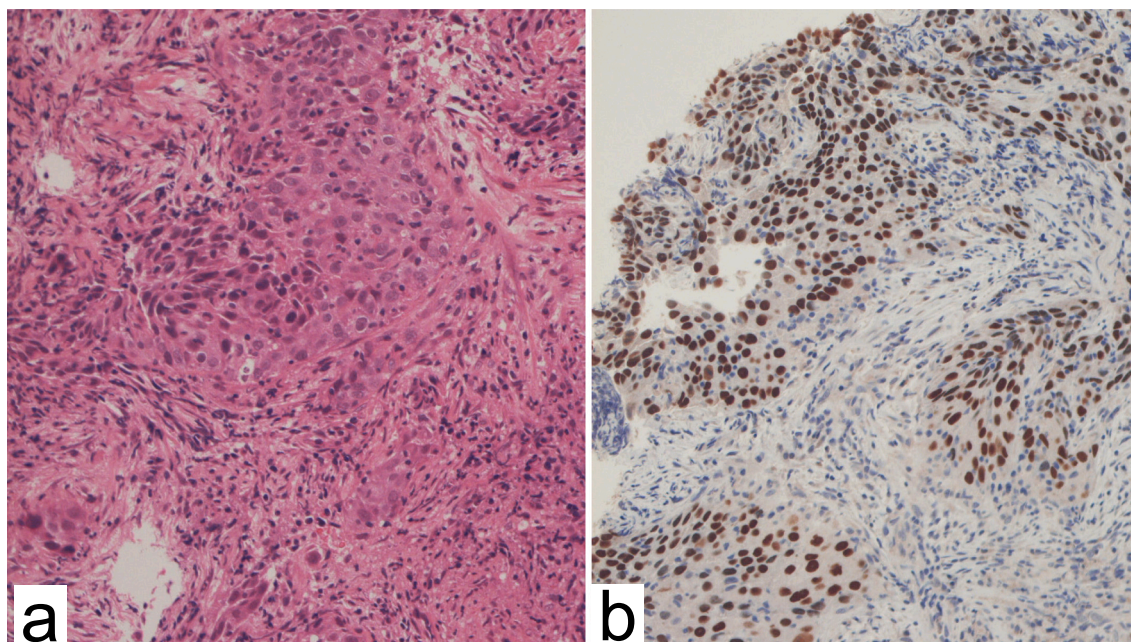
An SR of cancer is the partial or complete disappearance of a malignancy without any effective medical treatment. Case 1 had a history of rheumatoid arthritis, but no new drugs or therapy was given between the lung biopsy and surgery. The precise event history before the lung resection in case 2 is unknown. Although current hypotheses about an SR include activated autoimmunity after inflammation, infections, surgeries, or biopsies, the exact pathogenesis remains unclear [2,4,6–10].

Case 1 achieved a 5-year survival without any recurrence, whereas case 2 subsequently died of metastatic disease. Even advanced NSCLC after an SR could achieve a long term survival [11,12], whereas an originally stage I patient might develop a distant metastasis [13]. It is highly likely that the mediastinal lymph nodes were already involved at the time of the lung surgery because of the autopsy findings in case 2. Further, a vertebral metastasis consequently emerged despite the SR at the primary site. Although the preoperative imaging had shown a speculated nodule with a mediastinal lymphadenopathy suspicious of stage III NSCLC in case 2, no further histological assessment or post-operative observation was undertaken because of the benign pathology of the lung. In patients with lymphoma, a careful follow up is recommended because of the disease progression after an SR of the original tumor [7,14]. Additional histological investigation of the mediastinal lymph node or a short-term follow up might have detected the disease progression earlier in case 2.

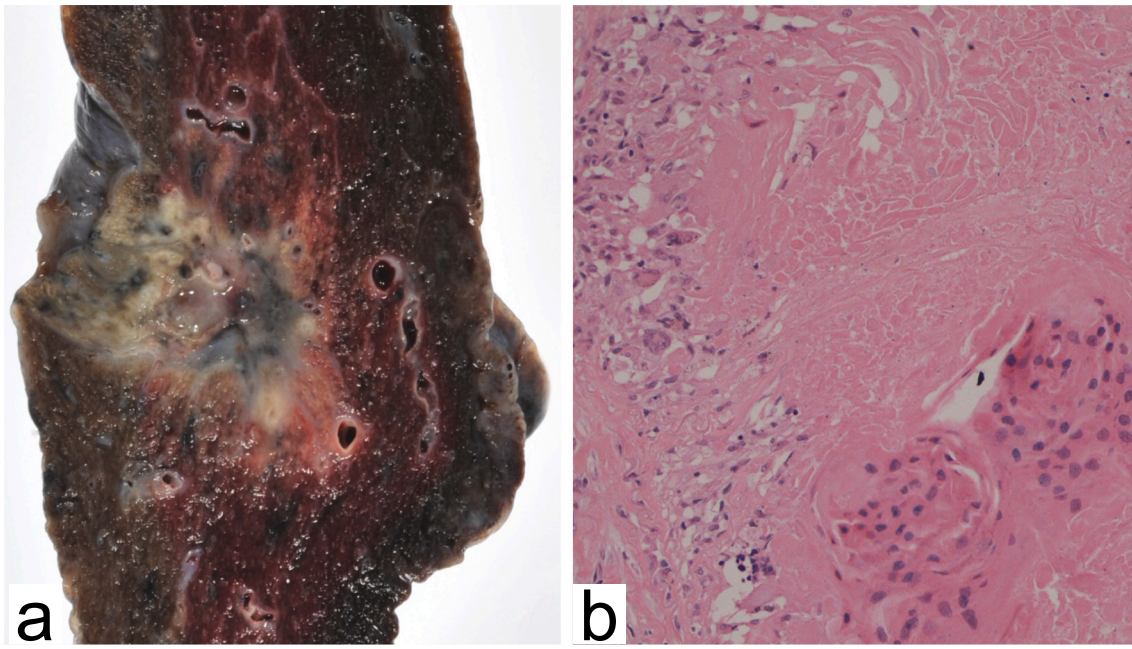
These results suggest that meticulous observation is essential not only in patients with pathologically proven SR, but also in patients with clinically suspicious SR. Radiological suspicion of a metastasis should be followed up due to the potential for SRs.

### 4. Conclusion

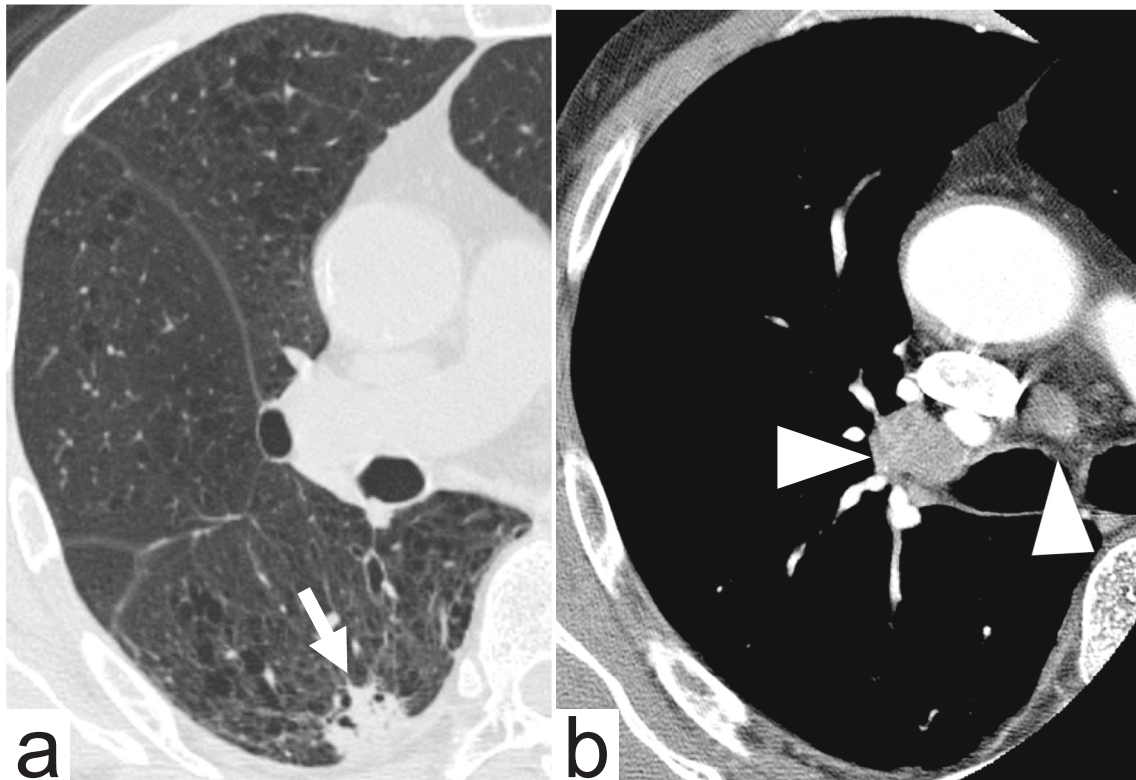
The pathogenesis of an SR remains unclear, and the clinical outcomes vary widely. We should be aware of this rare but fatal etiology and a meticulous observation is essential both in cases with a pathologically proven and clinically suspicious SR.



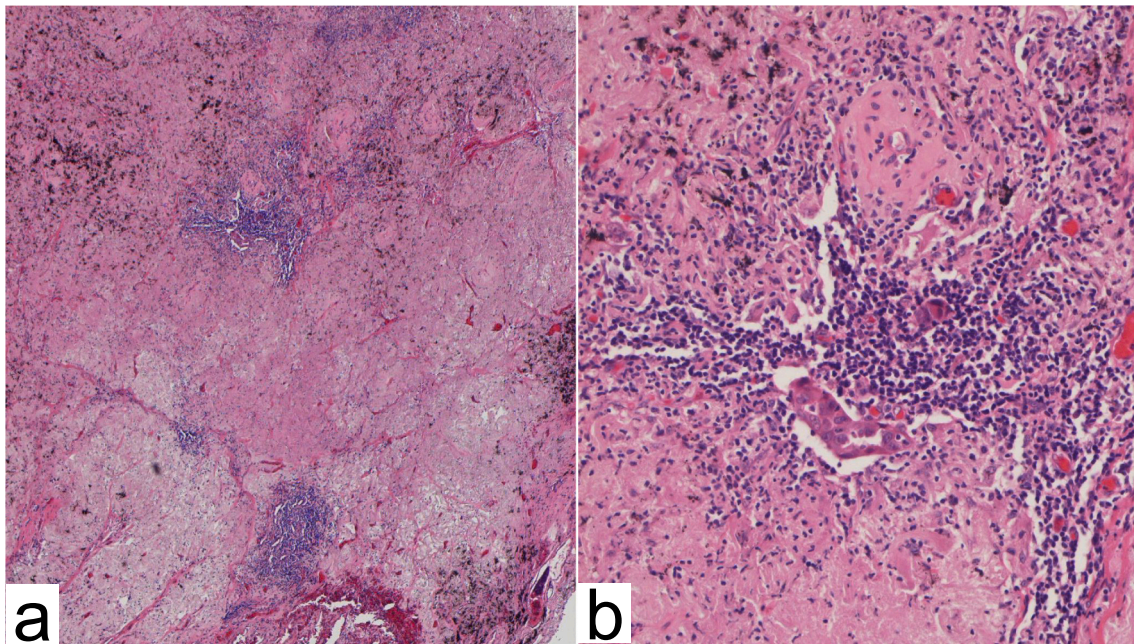
**Fig. 2.** (a) A transbronchial biopsy in case 1 revealed a poorly differentiated carcinoma. (b) Tumor cells were positive for p40, consistent with a squamous cell carcinoma.



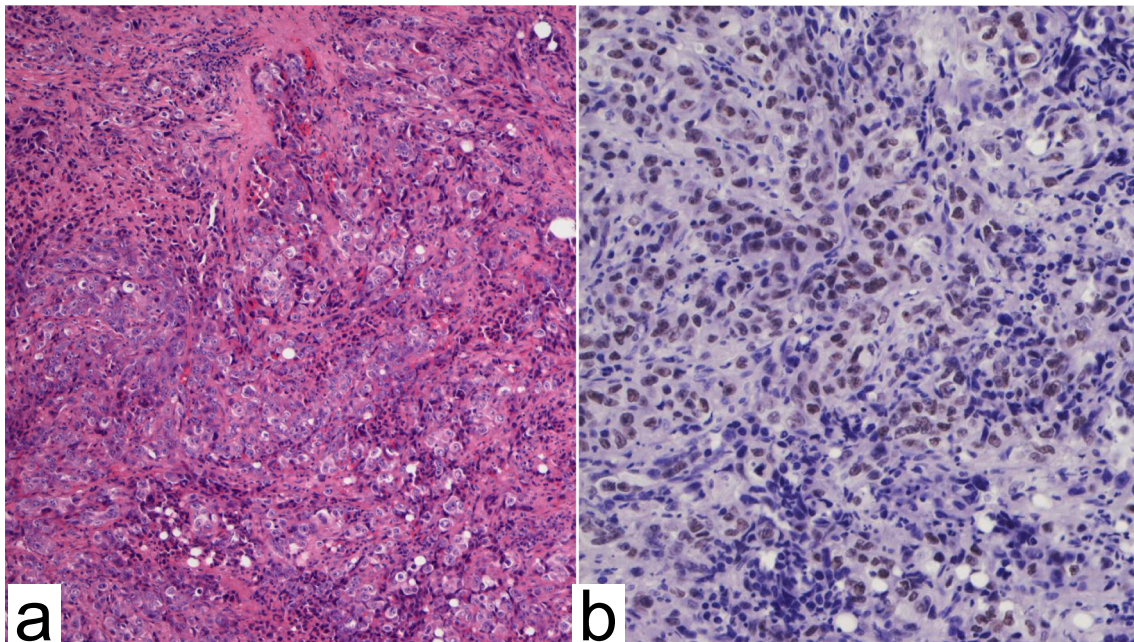
**Fig. 3.** (a) A cut surface of the surgical specimen revealed an irregular, gray-white mass. (b) A microscopic examination revealed some necrotic tissue and a small amount of squamous cell atypia without any malignant tissue.



**Fig. 4.** (a) A chest CT a year prior showed a spiculated nodule in the right lower lobe in case 2 (arrow). (b) Hilar and mediastinal lymphadenopathies were also found (arrowheads).



**Fig. 5.** (a) A surgical specimen of the resected lung in case 2 revealed fibrotic scar tissue formation. (b) The scar tissue was composed of clusters of lymphocytes without any malignant tissue.



**Fig. 6.** (a) A tissue biopsy from the broken vertebra in case 2 revealed a poorly differentiated carcinoma. (b) Tumor cells were positive for thyroid transcription factor-1, consistent with metastatic adenocarcinoma.

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Not applicable.

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#### Ethics approval

Not applicable.

#### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images before surgery. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contributions

MY wrote this paper. YO reviewed the pathological findings. All authors read and approved the final manuscript.

**Registration of research studies**

Not applicable.

**Guarantor**

Toru Nakamura.

**Declaration of competing interest**

The authors declare that they have no competing interests.

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**Provenance and peer review**

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