

REGRESSION OF PRIMARY TUMOR IN LUNG ADENOCARCINOMA: A RARE CASE WITH PERSISTENT NODAL METASTASIS

Tatiana Moreira Marques^{*1}, Pedro Veiga², Ana Margarida Silva³, Gonalo Paup rio³, Filipe Leite³

¹ General Surgery Department, Unidade Local de Sa de de Matosinhos

² Pathology Department, Instituto Portugu s de Oncologia do Porto

³ Thoracic Surgery Department, Instituto Portugu s de Oncologia do Porto

* Corresponding author: tatianafmmarques@gmail.com

Abstract

Spontaneous regression (SR) of pulmonary adenocarcinoma is an exceedingly rare event, characterized by the unexplained disappearance or reduction of a tumor without adequate medical intervention.

We report a case of a 60-year-old male with a history of heavy smoking and previous gastric adenocarcinoma. A surveillance CT scan identified a suspicious nodule in the right upper lung. PET/CT and biopsy confirmed adenocarcinoma. The patient underwent right upper lobectomy, and histology showed no residual cancer, consistent with SR. Lymph node metastasis was detected, leading to a staging of pTxN2R1M0. The patient is currently with no signs of recurrence.

SR in pulmonary adenocarcinoma is extremely rare, and its mechanisms are not well understood. Ongoing research and careful follow-up are essential for better understanding and management.

Keywords: Spontaneous Regression; Pulmonary Adenocarcinoma; Lymph node metastasis

INTRODUCTION

Spontaneous regression (SR) of a malignant tumor is described as its partial or complete dissipation in the absence of any treatment. It can be temporary or permanent, but it is very rare either way, occurring in nearly one in 100 000 patients.¹

Although this singularity has been described in some cancers, namely renal cell carcinoma, leukemia or lymphoma, malignant melanoma, and neuroblastoma, there are few cases describing SR in pulmonary adenocarcinoma.^{2,3}

The mechanism of SR remains unclear. The strongest hypothesis relies on an immunological response, triggered by external factors, such as biopsy and/or surgical trauma. Other theories rely on hormonal changes or infections.^{1,2,3}

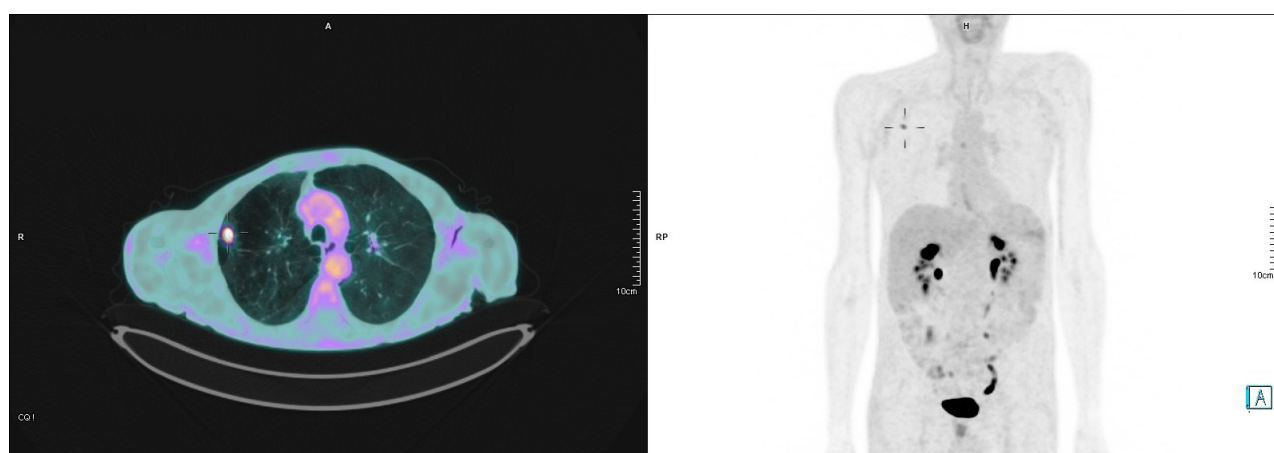
METHODS

This report describes a case of spontaneous regression of primary lung adenocarcinoma, with persistent nodal metastatic involvement.

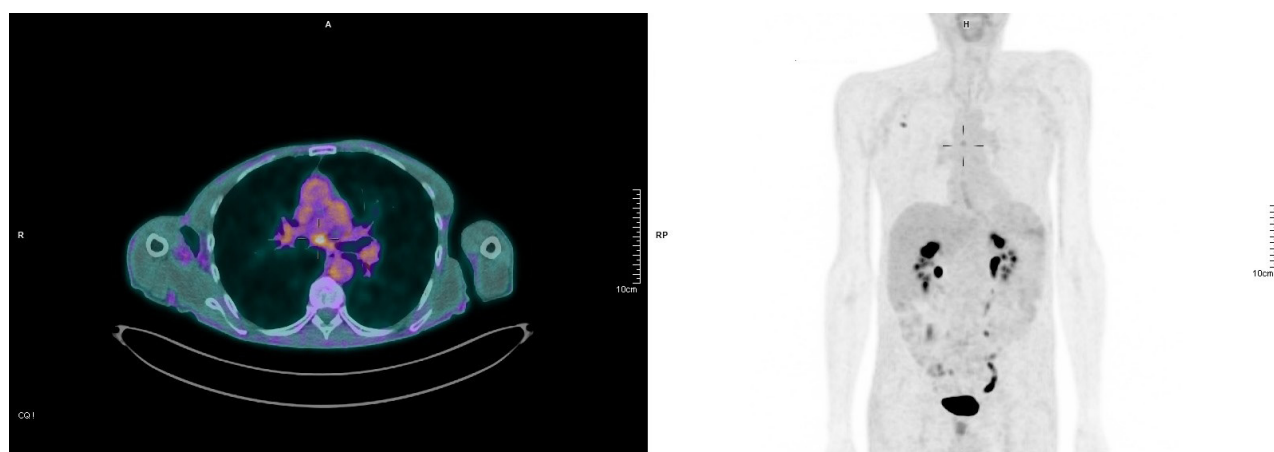
CLINICAL CASE

Herein we present the case of a 60-year-old Caucasian male with a history of heavy smoking (40 pack-year) and gastric adenocarcinoma, who underwent subtotal gastrectomy approximately two years ago. A follow-up chest computed tomography (CT) scan revealed an 11 mm solid nodule in the right upper lobe of the lung. Positron emission tomography (PET)/CT showed two hypermetabolic lesions in the right upper lobe of the lung with a standardized uptake value (SUV) max of 5.54 (image 1). It also unveiled an increase in fluorodeoxyglucose (18-FDG) metabolic activity near the esophagus, at the level of the carina (SUV max 3.2), suggesting a mediastinal metastasis (image 2). A transthoracic core biopsy was made, revealing an adenocarcinoma PD-L1 (image 3) and thyroid transcription factor 1 [TTF1] positive. A staging endobronchial ultrasound (EBUS) was performed, and lymph node stations 4R, 4L, 7, 11R and 11L were sampled. All specimens were adequate for pathological assessment and negative for metastasis.

After a multidisciplinary meeting, as PET scan


Figure 1

Hypermetabolic lesion in the right upper lobe of the lung on PET/CT.


Figure 2

Hypermetabolic activity at the level of the carina on PET/CT.

showed a peripheral nodule with a SUV of 5, with no positive lymph nodes and after EBUS, it was assumed that there was a low probability of a positive mediastinoscopy, so surgery was proposed. Due to the time elapsed between the initial PET/CT and the surgery, the exam was repeated. It showed a decrease in 18-FDG activity in the two hypermetabolic lesions in the right upper lobe of the lung (SUV max 1.2), with persistent activity in the subcarinal lymph node (SUV max 3.28).

The patient underwent an uniportal video-assisted thoracoscopic (UVATS) right upper lobectomy with lymphadenectomy (stations 2R, 3a, 4R, 7, 8 and 10R). The postoperative period was uneventful, and the patient was discharged on the 7th postoperative day. The surgical specimen from the lobectomy revealed a nodular lesion with cystic areas, measuring 2x1 cm, with negative margins. The histologic examination revealed extensive

fibrosis, an inflammatory infiltrate mainly consisting of mononuclear cells, and areas of calcification, suggesting a site of previous tumour involvement, but with no evidence of residual tumour (image 4). These findings are consistent with SR of the lung tumour. However, fragments of the station 2R lymph nodes were positive for pulmonary adenocarcinoma metastasis (positive for TTF1, image 5, no PD-L1 was assessed), leading to a staging of pTxN2R1M0 according to the 8th edition of the TNM classification. There was no evidence of metastatic disease in any of the remaining lymph nodes. It was considered an R1 due to the 2R node being only partially removed, or since only a fragment of it being available, thus a complete removal could not be assured. Consequently, the patient was recommended for chemotherapy and radiotherapy.

Follow up CT scan at three months post-surgery reveals no evidence of tumour recurrence.

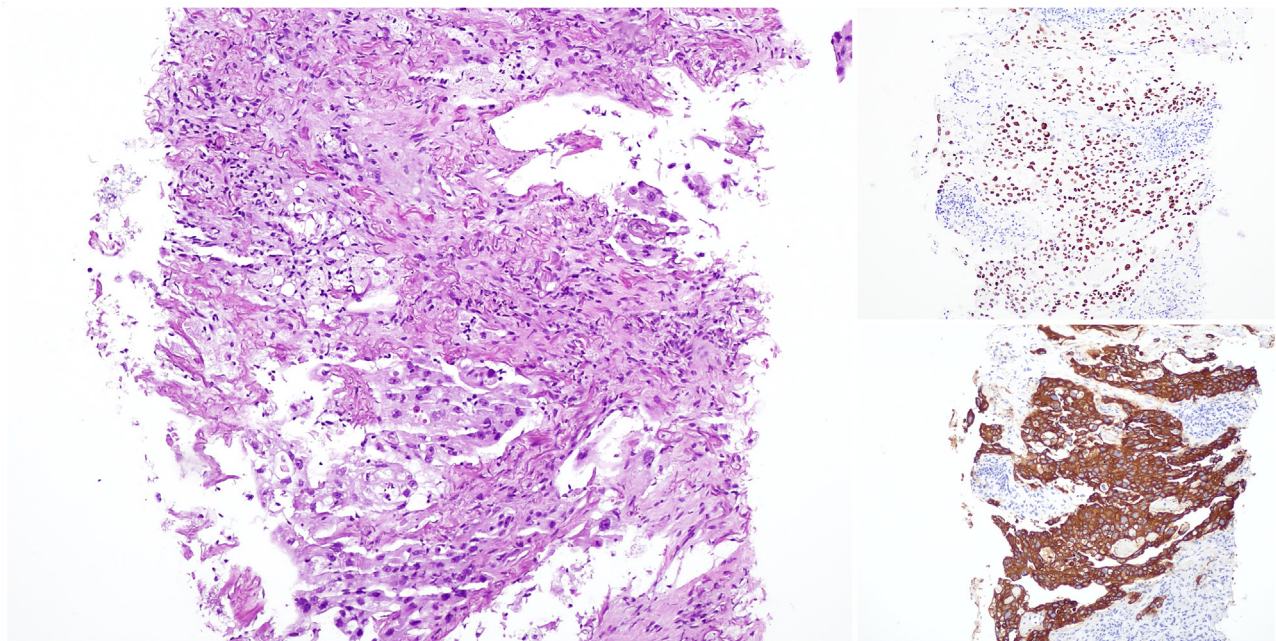


Figure 3

Pulmonary parenchyma involved by adenocarcinoma, with positive immunohistochemical staining for TTF-1 (upper right image) and CK7 (lower right image).

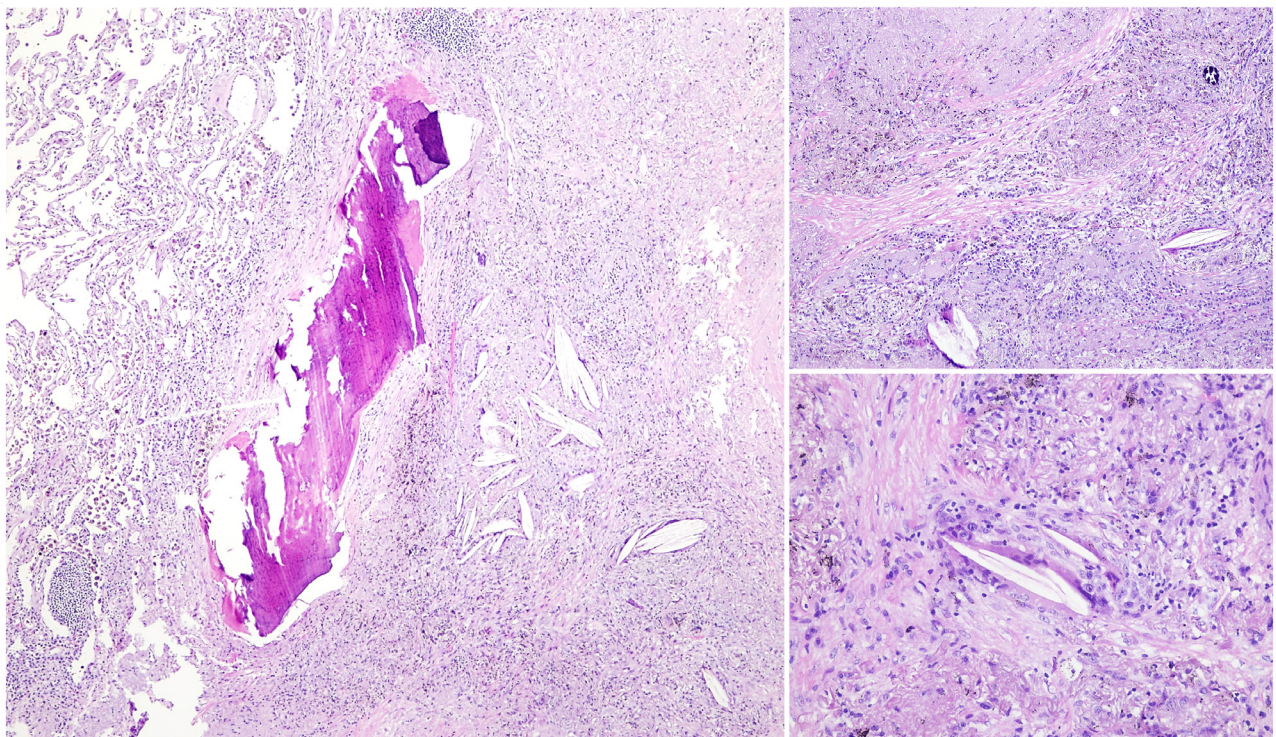


Figure 4

Pulmonary parenchyma exhibiting extensive fibrosis and predominantly mononuclear inflammatory infiltrate, with foci of calcification. A foreign body-type giant cell reaction is also observed surrounding cholesterol clefts.

DISCUSSION

Over the last century, lung carcinoma has evolved from a rare disease to the most common cancer worldwide and the leading cause of cancer-related deaths.⁴ Smoking is the single most significant risk factor in the development of lung cancer, accounting for up to 90% of cases.⁴

SR of malignant disease, as commonly defined, refers to the complete or partial, temporary or permanent disappearance of all or at least certain key parameters of a well-diagnosed malignant disease, either without medical treatment or with treatment deemed insufficient to cause the observed regression.² It has been documented since 1956, when Everson and Cole defined it by publishing a report that included 176 cases from 1900 to 1964.⁵ The mechanisms underlying spontaneous tumor regression remain unclear. Some reported cases suggest that autoimmune processes may be activated following events such as surgery, biopsy, or site infection, which likely

explains the SR in our patient. Other contributing factors include hormonal mechanisms, destruction of the tumor-feeding artery during the biopsy or increased apoptosis. When SR occurs at metastatic sites after the removal of the primary tumor, it is believed to trigger an immune response that eradicates the remaining tumor.^{1, 6, 7}

Within lung cancer most of the reported spontaneous regression occurred in Small Cell Lung Carcinomas, with only four cases of SR occurring in adenocarcinomas, as seen in this case.⁶

To the best of our knowledge, we believe that the SR in this case was due to an immunologic response triggered by the biopsy, as lung cancer is recognized as an immunogenic tumor that responds to immunotherapy (anti-PD1/PD-L1), particularly in heavy smokers.⁸ Nevertheless, our patient had lymph node metastasis, which did not respond in the same way as the primary lesion, leading to the hypothesis that the immunologic response occurred only at the biopsy site, or possibly due to a local inflammatory or mechanical factor.

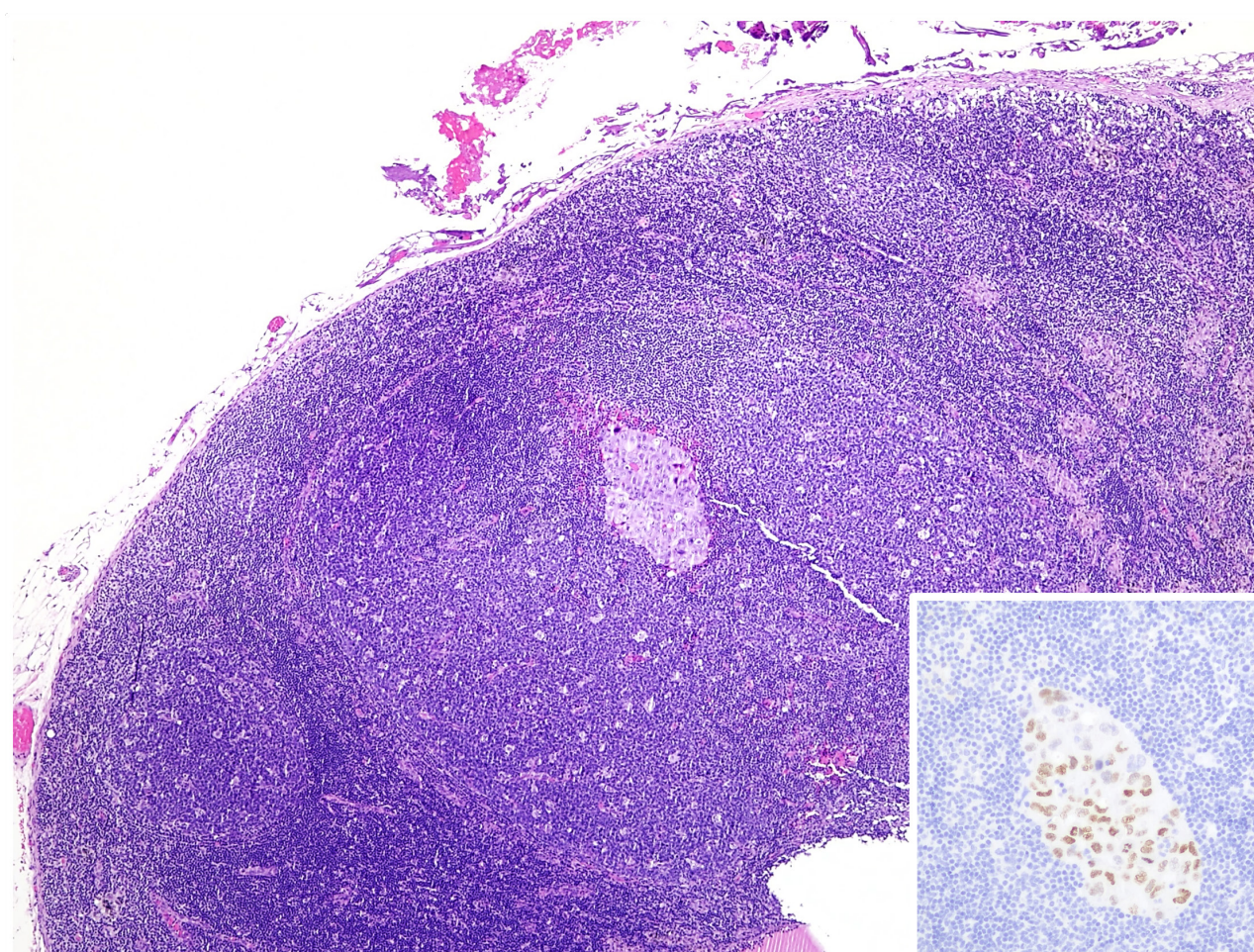


Figure 5

Lymph node fragment with metastatic pulmonary adenocarcinoma (TTF-1 positive).

CONCLUSION

Spontaneous regression of pulmonary adenocarcinoma is an uncommon phenomenon, with its underlying mechanism still not well understood. Further research is necessary to better understand this circumstance. Continued follow-up of patients who have experienced SR may provide important insights into its potential and progression.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

REFERENCES

1. Chung C, Park DI, Kim SY et al. Spontaneous regression of non-small cell lung cancer that progressed after multiple chemotherapies: A case report. *Thoracic Cancer* 6 (2015): 805–807.
2. Ogawa R, Watanabe H, Yazaki K et al. Lung cancer with spontaneous regression of primary and metastatic sites: A case report. *Oncology Letters* 10 (2015): 550-552.
3. Shatola A, Nguyen KN, Kamangar E et al. Spontaneous Regression of Non-small Cell Lung Cancer: A Case Report and Literature Review. *Cureus* 12 (2020): e6639.
4. Groot PM, Wu CC, Carter BW et al. The epidemiology of lung cancer. *Transl Lung Cancer Res* 7 (2018): 220-233.
5. Everson T, Cole W: Spontaneous regression of cancer: preliminary report. *Ann Surg* 144 (1956):366-383.
6. Kaira K, Imai H, Mouri A et al. Progression to Lymph Node Metastasis After Spontaneous Regression of Pulmonary Adenocarcinoma Following Biopsy. *In vivo* 38 (2024): 1498-1502.
7. Kumar T, Patel N, Talwar A. Spontaneous regression of thoracic malignancies. *Respiratory Medicine* 104 (2010), 1543-1550.
8. Inui M, Sano A, Asai I et al. Spontaneous regression of small cell lung cancer. *Cancer Treat Commun* 3 (2015):21-3.