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Spontaneous regression of a pulmonary adenocarcinoma after core needle biopsy

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ABSTRACT

Spontaneous regression (SR) of cancer, especially lung cancer, is a rare biological event with a mechanism that is not currently understood. Immunological mechanisms seem to be the stronger explanation in SR of a lung cancer. We report the rare case of SR of a lung adenocarcinoma stage IA, in a 75-year-old man, which was incidentally diagnosed and histologically confirmed. Due to the patient's comorbidities and his poor pulmonary function, stereotactic radiotherapy was scheduled. However, by the time the treatment was due to start, the tumor was no longer detectable.

Keywords

Carcinoma; Non-Small-Cell Lung; Lung Neoplasms; Neoplasm Regression, Spontaneous

CASE REPORT

Our patient was a 75-year-old Caucasian man with a medical history of heavy smoking, obstructive pulmonary disease, sleep apnea, arterial hypertension, infra-renal aortic aneurism, cardiac failure, endarterectomy of the ascending aorta, and aortic valve substitution.

He underwent a surveillance thoracoabdominal computed tomography (CT) scan 3 years ago that showed a suspicious 19 mm nodule in the right superior lobe (Figure 1), which was investigated by a transthoracic core biopsy. The pathology report revealed an adenocarcinoma with tubular pattern and same mucosecretory cells. The immunohistochemistry study with TTF1 was positive in neoplastic cells, to confirm the pulmonary origin of the adenocarcinoma

(Figures 2A and 2B). A positron emission tomography (PET)-CT was performed and showed no other sites of radiotracer uptake, besides the pulmonary nodule (Figure 3) rendering the cT1N0M0 as stage IA.

The patient then underwent pulmonary function tests that disclosed he was not a candidate for surgery (forced vital capacity [FVC]: 93.7%; forced expiratory volume in the first second [FEV1]: 40.9%; FEV 1/FVC ratio: 32.93%; and diffusion capacity of the lungs for carbon monoxide [DLCO]: 39.3%).

The case was analyzed in a multidisciplinary meeting, and was decided that stereotactic radiotherapy, would be the most appropriate treatment, because of his comorbidities and poor pulmonary function.

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Three months after the core biopsy and 1 month after PET-CT, a planning CT scan before starting radiotherapy was conducted and the nodule was no longer seen. During this period, the patient didn't have any infection, or started any new medication, namely systemic corticosteroid, or other immunosuppression. We performed sequential CT and PET-CT, which confirmed that the tumor had indeed disappeared (Figures 4 and 5). The histology was reviewed and the pathologist confirmed the diagnosis of lung adenocarcinoma.



Figure 1. Chest computed tomography scan revealing an irregular 19 mm nodule in the right superior lobe.

The patient is currently undergoing regular follow-up examinations at this hospital, and has not shown any evidence of disease for the past 3 years.

This manuscript is in accordance with the institutional ethics committee, and the patient signed an informed consent.

DISCUSSION

Spontaneous regression (SR) of a cancer is defined as total or partial disappearance without treatment or in the presence of a known inappropriate/ineffective treatment in oncological diseases.¹

This phenomenon is rare, but possible, and it has been found in several cases described in the literature. Everson and Cole,² and Cole,³ reported 176 cases of SR from 1900 to 1964, with an estimated incidence of 1 out of 60,000-100,000 people with cancer.

The tumors in which this phenomenon is most frequently described are kidney cancer, neuroblastomas, and lymphomas.³ Currently, there are 17 well-documented case reports of lung cancer with SR (10 non-small cell lung cancer and 7 small cell lung cancer) (Table 1).⁴⁻²⁰

The exact mechanisms of the SR are unknown, but there are several hypotheses described in the literature; namely (i) immunological mechanisms; (ii) the existence of SR after a serious local infection; (iii) the suspension of immunosuppression therapy;

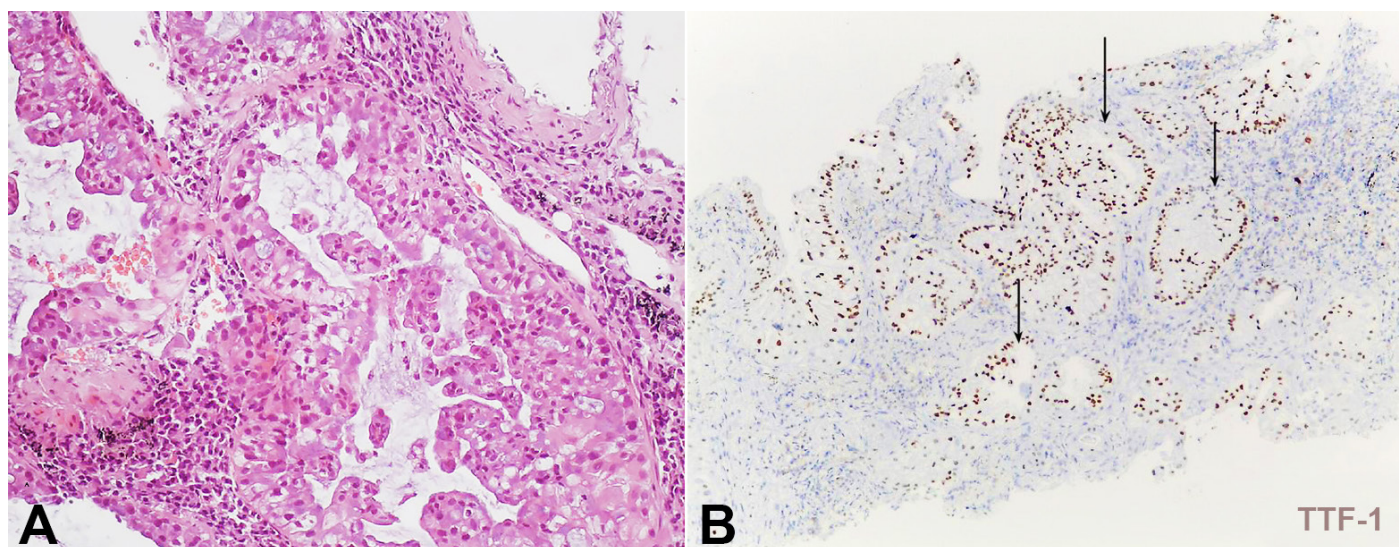


Figure 2. Microphotography of the lung biopsy. **A** – Acinar adenocarcinoma, with moderate pleomorphism (H&E, 200X); **B** – Positivity for TTF-1 (100X).

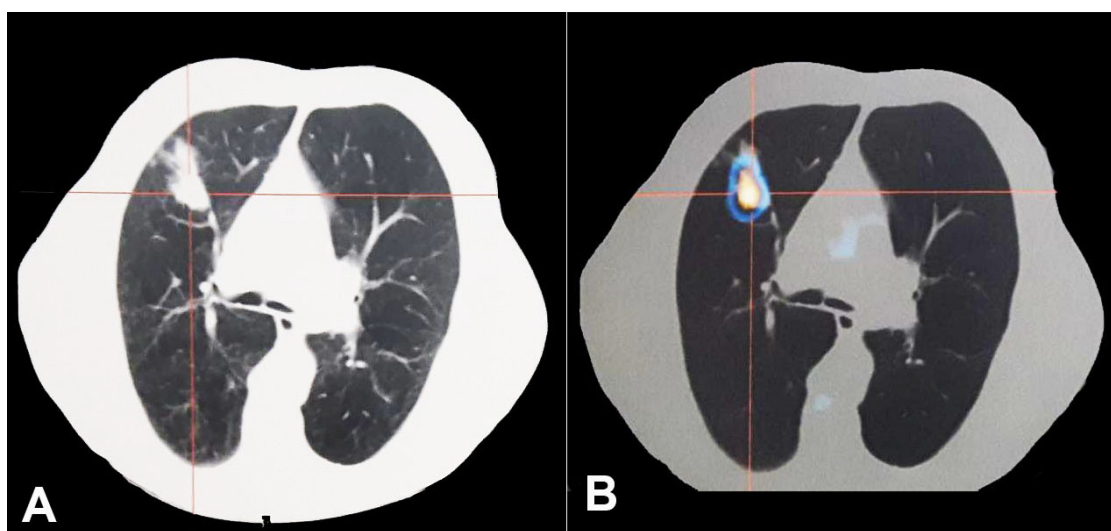


Figure 3. Chest positron emission tomography-computed tomography (PET-CT) (5 months after first CT, 3 months after biopsy). **A** – Axial CT acquisition; **B** – Increased 18F-deoxyglucose (FDG) uptake in the right superior lobe (standardized uptake value max = 6.8) without other FDG captation.

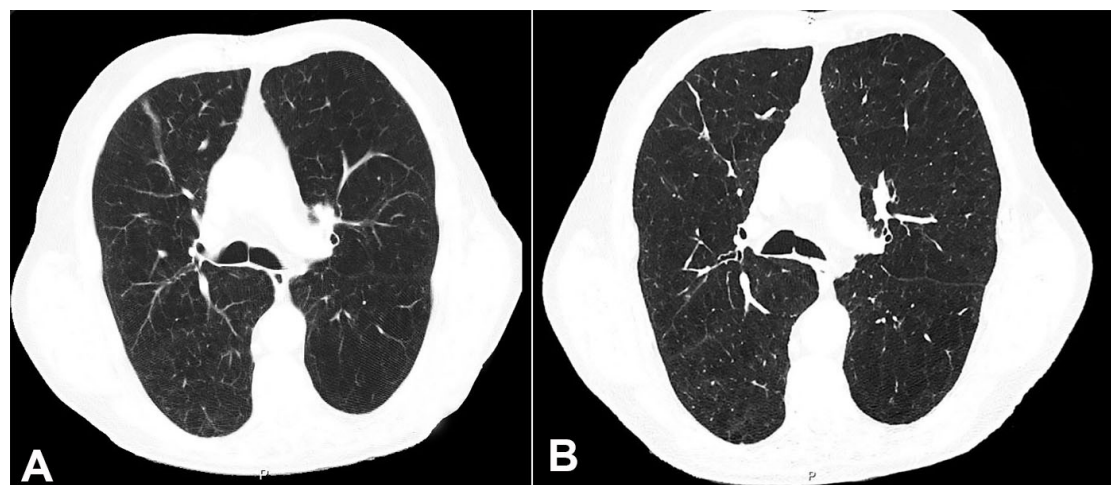


Figure 4. Chest computed tomography (CT). **A** – Six months after first CT and 4 months after the biopsy; note the vanishing of the right superior lobe 19 mm nodule; **B** – Absence of the nodule relapse 3 years after the diagnosis.

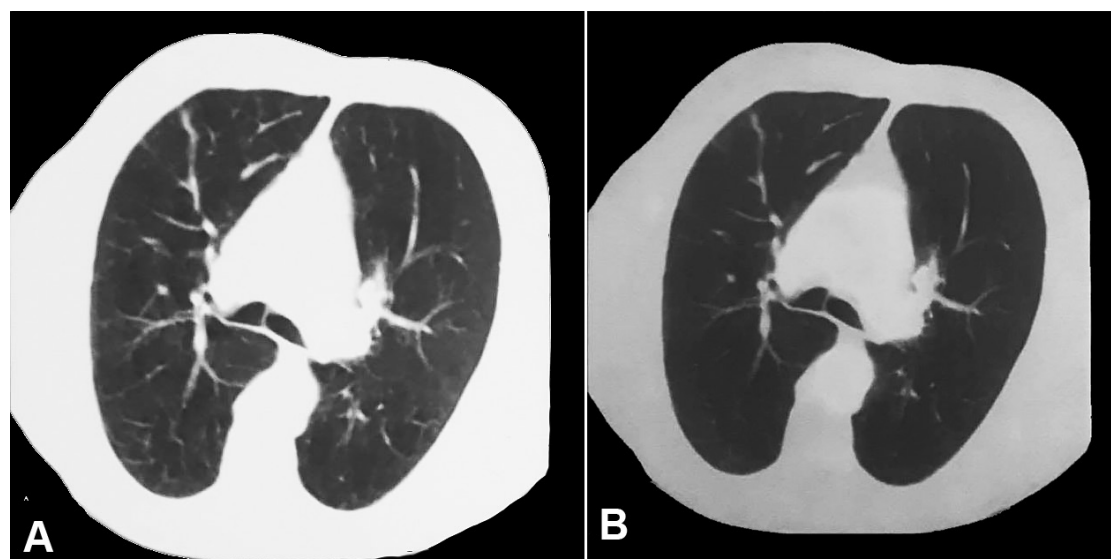


Figure 5. Chest positron emission tomography-computed tomography (PET-CT) performed 1 year after diagnosis. **A** – CT axial image acquisition; **B** – Absence of 18F-deoxyglucose captation.

Table 1. Spontaneous remission of lung cancer proven in histological examinations: review of the literature

Reference	Sex/Age and Histology	Possible Factors Related to SR
Menon & Eaton ⁴ United States	Male/44 Non-small cell lung cancer	SR after immune reconstitution in a patient with HIV
Inui et al. ⁵ Japan	Female/69 Small cell lung cancer	No mechanisms of SR proposed
Lopez-Pastorini et al. ⁶ Germany	Male/76 Large cell lung cancer	Immune response after biopsy
Kitai et al. ⁷ Japan	Female/65 Small cell lung cancer	Anti-tumor immunity against recovering might have resulted in SR in this case
Choi et al. ⁸ Korea	Male/71 Squamous cell carcinoma	Tuberculosis might have stimulated the immune system
Furukawa et al. ⁹ Japan	Male/56 Squamous cell carcinoma	Bullous wall deformation and the generation of phlegm might have led to the reduction in tumor size
Mizuno et al. ¹⁰ Japan	Male/62 Large cell carcinoma	A transformed clone resistant to previous immunity might have developed. Surgical intervention might have suppressed the patient's immunity against a microscopic adrenal viable tumor, and accelerated tumor progression
Gladwish et al. ¹¹ Canada	Female/81 Squamous cell carcinoma	Psychoneuroimmunological mechanisms Alternative herbal remedy, Essiac
Mawhinney et al. ¹² United Kingdom	Female/83 Small-cell lung cancer	The association between the paraneoplastic syndrome and spontaneous tumor regression is strongly suggestive that an anti-tumor immune-mediated response is the underlying mechanism
Nakamura et al. ¹³ Japan	Male/71 Adenocarcinoma	Systemic immunity against NY-ESO-1 contributed to the tumor regression in this case
Agarwal et al. ¹⁴ India	Male/70 Small-cell lung cancer	No mechanisms of SR proposed
Lee et al. ¹⁵ Korea	Female/70 Small-cell lung cancer	SR was likely to be attributable to infection immune activation
Hirano et al. ¹⁶ Japan	Female/55 Small-cell lung cancer	Anti-neuronal antibody may react with both tumor and nervous tissue
Pujol et al. ¹⁷ France	Female/75 Squamous cell carcinoma	The immunology of anti-Hu paraneoplastic syndrome by itself could induce tumor response
Horino et al. ¹⁸ Japan	Male/ 86 Small-cell lung cancer	Paraneoplastic sensory neuronopathy
Cafferata et al. ¹⁹ Italy	Male/68 Adenocarcinoma	No mechanisms of SR proposed
Kappauf et al. ²⁰ Germany	Male/61 Adenocarcinoma	No mechanisms of SR proposed

SR = spontaneous regression.

(iv) immune reconstitution in HIV patients; and
(v) paraneoplastic syndrome.²¹

Other possibly related factors described in the literature are: hormonal mechanisms; tumor necrosis; destruction of the tumor feeding artery during the biopsy; angiogenesis and telomerase inhibition; increased apoptosis; psycho-neurological factors; suspension of exogenous carcinogens; and the differentiation of malignant cells into benign ones.^{3,22}

In this case, we did not find any certain mechanism of SR among those already described.

One possible explanation could be the destruction or emboli of the feeding artery of the tumor by the core needle biopsy. Another theory might be that the

injury caused by this procedure could somehow elicit an inflammatory response or even release antigens that were hidden, with a consequent activation of the immune system.

Despite the absence of evidence of an immunological mechanism, such as paraneoplastic syndrome or an infection, we believe that the main mechanism in this patient's case was probably his immune system activated by the needle core biopsy. Corroborating with this hypothesis is the recognition of lung cancer as an immunogenic tumor, especially in heavy smoking patients, which has been associated with response to immunotherapy (anti-PD1/PD-L1) and a higher neoantigen burden.⁵

CONCLUSION

The SR of a cancer is possible, and is a well-documented phenomenon in the literature. The mechanism of this event remains a mystery, and further research is essential to fully comprehend this unusual phenomenon.

In this case, the immune system of the patient activated by the needle core biopsy seems to be an important mechanism of SR.

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