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## Pulmonary tuberculosis mimicking lung cancer progression after 10 years of cancer remission

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### Abstract

Differentiation between pulmonary tuberculosis and lung cancer is often challenging for clinicians, especially that both conditions can coexist. This is due to the fact that the clinical and radiological symptoms of both diseases can be similar.

Our case report presents a patient who was treated for advanced lung cancer 10 years earlier and currently has been hospitalized again because of a strong clinical and radiological suspicion of the cancer progression, but whose final diagnosis was tuberculosis.

**Key words:** lung cancer, suspicion of progression, tuberculosis

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### Introduction

Lung cancer (LC) is the leading cause of cancer deaths worldwide [1]. Despite advances in early detection and standard treatment, it is often diagnosed at an advanced stage and has a poor prognosis. Tuberculosis (TB) is well known as a diagnostic chameleon and can resemble malignancy. In the thorax, it manifests as lung cancer — with pulmonary infiltrates and/or mediastinal lymphadenopathy [2]. Clinical symptoms of both diseases may be similar too. Therefore, differentiation between pulmonary tuberculosis and lung cancer can be challenging for clinicians, especially that both conditions can coexist.

We present a case of a young woman who was treated for advanced lung cancer 10 years earlier and currently has been hospitalized again because of a strong clinical and radiological suspicion of

the cancer progression, but whose final diagnosis was tuberculosis.

### Case report

A 33-year-old woman was referred to our Department first in 2006 with a 2-week history of chest pain and abnormalities on radiography. She had no prior medical history and did not smoke cigarettes. Computed tomography scans of the chest presented a middle lobe bronchus tumor measuring 2.8 × 3.2 cm in a conglomerate of enlarged mediastinal lymph nodes, causing the middle lobe artery occlusion and infarct in the segment 4 of the right lung (Fig. 1). On bronchoscopy, richly vascularized tumor in the middle lobe bronchus was found. Basing on the pathologic examination of the small biopsy specimen completed by using immunohistochemical staining

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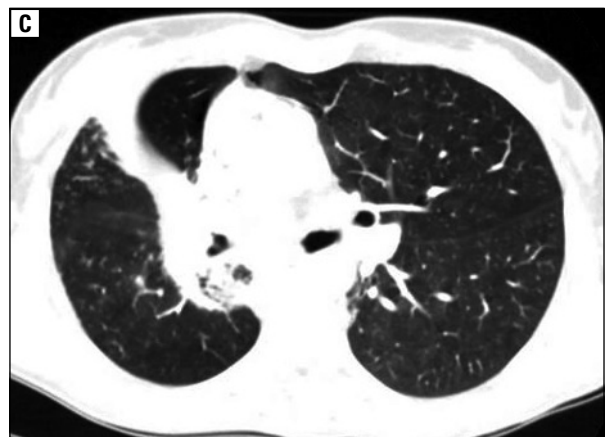
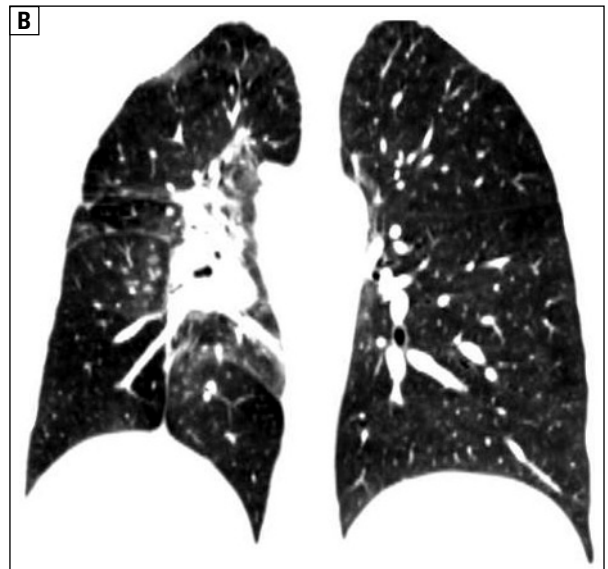
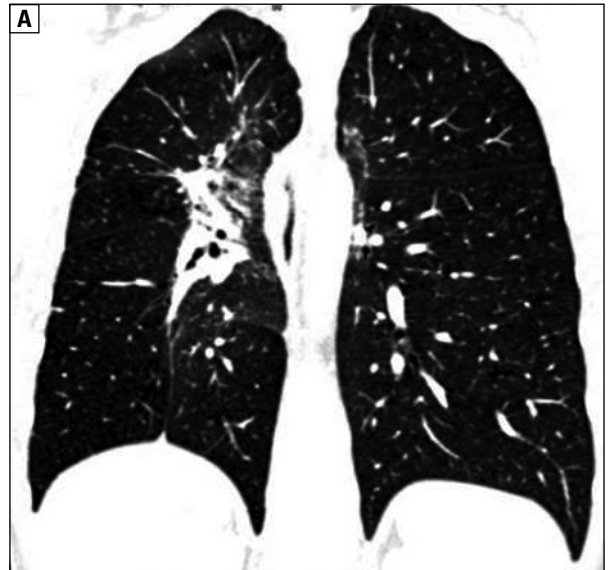
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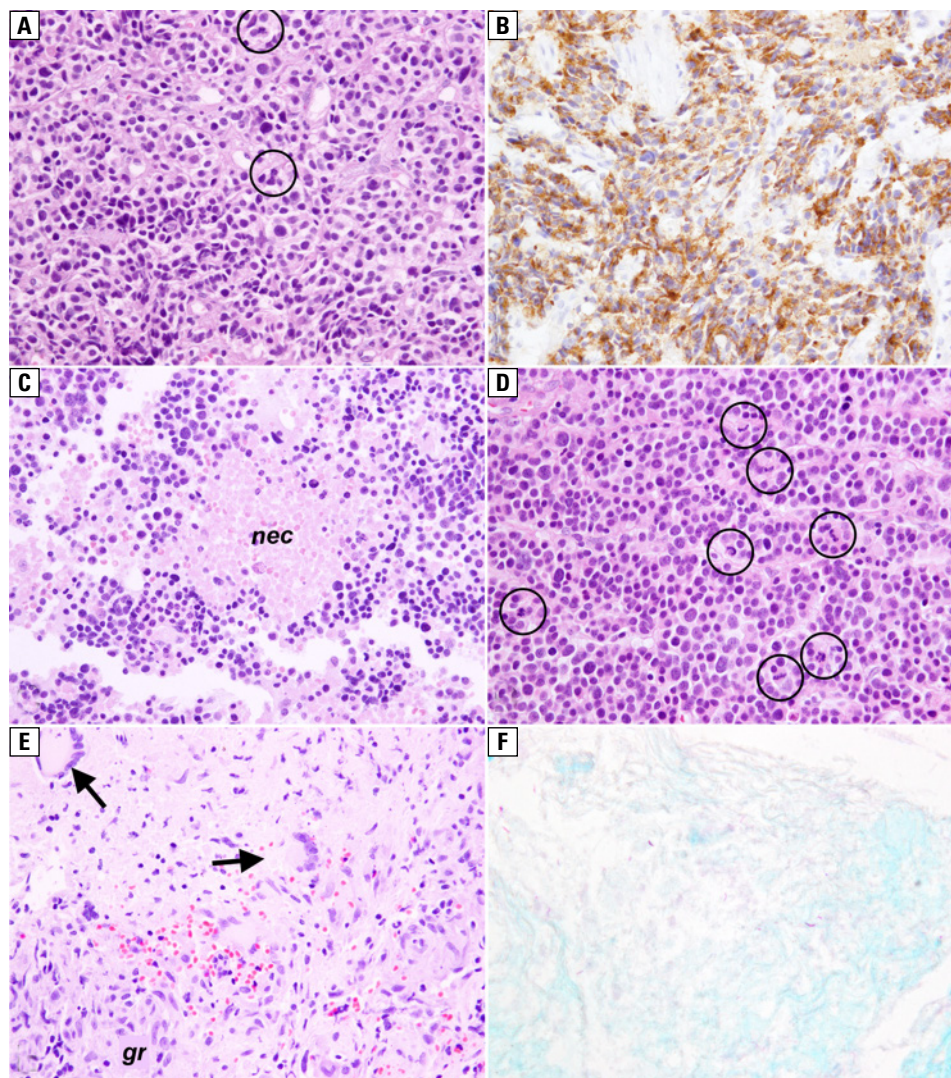


**Figure 1.** Chest CT, 2006, contrast enhanced, mediastinal window. Solid mass with central necrosis in the right hilum with narrowing the middle lobe bronchus. Peripheral lung infarct (white arrow) in the 4<sup>th</sup> segment of the middle lobe due to lobar artery invasion. Enlarged subcarinal lymph nodes with central necrosis

(CK AE1/AE3+, chromogranin A+, synaptophysin+), the diagnosis of “carcinoid tumor” was suggested. Due to massive lymphadenopathy, surgical treatment was not possible. The patient received chemotherapy (cisplatin and etoposide) and radiotherapy 4500 cGy/t, which caused partial regression of the tumor and complete decline of the peripheral infiltrate. Two years later, in 2008, the patient developed headaches and dizziness. MRI study showed cystic tumor in the left occipital lobe. The woman underwent craniotomy, but the pathologic examination of the tumor was different from the previous one and revealed malignancy including the foci of necrosis and mitotic figures, with positive immunohistochemical staining (CK AE1/AE3+, synaptophysin+, chromogranin+). The tumor was reclassified as a large cell metastatic neuroendocrine carcinoma. The surgical treatment was provided by using central nervous system radiotherapy (3000 cGy/t). For the next 8 years the patient had no symptoms, but in 2016, she was admitted again to our Department because of hemoptysis, cough and dyspnea. She had no reported fever nor weight loss. Computed tomography scans, in comparison with the last test (Fig. 2A), showed progression in the right lung: atelectasis of the middle lobe and new infiltrates in the lower lobe. Slightly larger were right hilar and mediastinal lymph nodes (Fig. 2 B, C). On bronchoscopy, a decaying tumor with necrosis in the middle lobe bronchus was found, with infiltrates in the main and in the lower lobe bronchus on the right side. There was a strong suspicion that the patient had progression of lung cancer, but the pathologic examination of



**Figure 2.** **A** — chest CT, 2013, contrast enhanced, lung window, coronal plane. Perihilar radiation — induced fibrosis; **B, C** — chest CT, 2016, contrast enhanced, lung window, coronal plane. The study, compared with the prior CT (Fig. 3) shows an increase in size of the right hilum due to mass suspected of tumor recurrent (**A**), middle lobe atelectasis is present due to lobar bronchus narrowing (**B**)



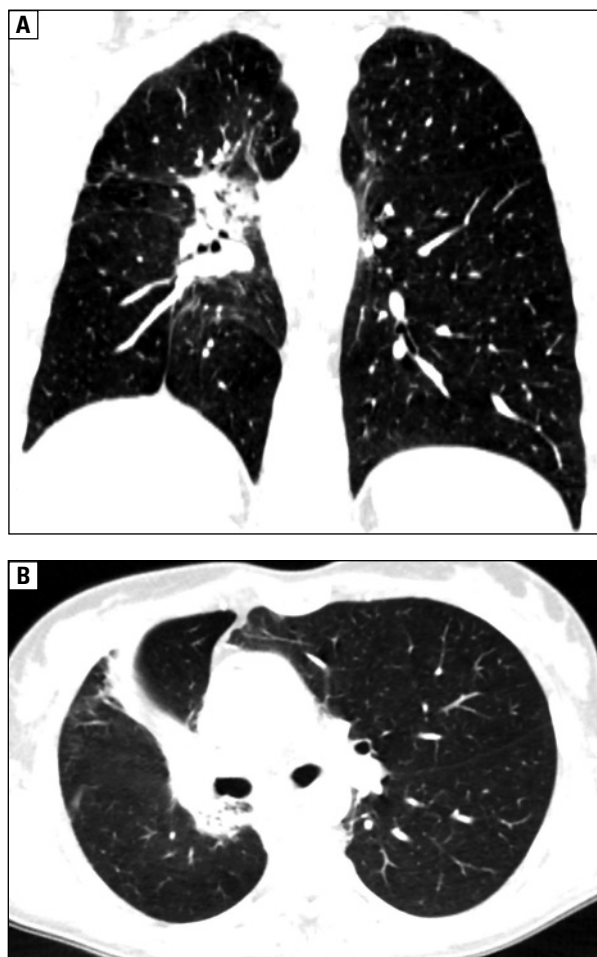
**Figure 3. A–F: A–B. Lung tumor (2006), bronchoscopic section.** Organoid pattern and a certain degree of cellular atypia are seen. There were no foci of necrosis. Three mitotic figures were found in the whole sample, two of them are seen on the picture (circles) (A). Positive immunohistochemical expression of chromogranin (B). The diagnosis of “carcinoid tumor” was suggested. **C–D — metastatic brain tumor (2008).** Small foci of necrosis (*nec*) and 21 mitotic figures/10 high power fields (7 of them in the circles) were observed in the sample. The tumor was reclassified as a large cell neuroendocrine carcinoma. **E–F — lung lesion (2016), bronchoscopic section.** The sample contained necrotic tissue (at the top) surrounded by epithelioid granulomas (*gr*) and multinucleated giant cells (arrows) (E). Ziehl-Neelsen staining revealed multiple Mycobacteria (purple structures) (F). No evidence of recurrent carcinoma was observed. (A, C, D, E — H&E staining, magn. × 400; B — chromogranin A, magn. × 400; F — Ziehl-Neelsen staining, magn. × 1000)

the all samples from the tumor, infiltrated bronchial wall and enlarged lymph nodes revealed no malignancy but instead, caseous granulomatous inflammation with positive Ziehl-Neelsen staining (Fig. 3 A–F). In direct microscopy of sputum and bronchial wash, acid-fast bacilli (AFB) were found; DNA test for Mycobacterium TB complex was positive. The documented growth of Mycobacterium tuberculosis in culture of sputum and bronchial wash confirmed the diagnosis of tuberculosis. The patient received standard anti-TB therapy composed of pyrazinamide, isoniazid, ethambutol and rifampicin. During the first two

weeks of the treatment the clinical symptoms already receded, the results of sputum cultures 2 months later have become negative, and control CT one year after the end of treatment (Fig. 4 A, B) showed improvement with the continuous well-being of the patient.

### Discussion

Tuberculosis and lung cancer have been confused and misdiagnosed for years. Radiological features seen on CT scans like consolidations, cavities, lymphadenopathy are suggestive of



**Figure 4.** Chest CT lung window (A) coronal plane; lung window axial plane (B): Images compared with the prior CT scans (B, C) reveal a decrease in size of the right hilum. Middle lobe atelectasis became smaller. The radiation — induced fibrosis is present as previously

lung cancer and also typical of pulmonary tuberculosis. Clinical symptoms of both diseases can be similar too [3]. Therefore, tuberculosis can imitate or mask lung cancer. Hammen [4] described two patients with a strong suspicion of lung cancer, in whom finally tuberculosis was diagnosed. Similarly, Dalar and colleagues [5] demonstrated a case series of patients with tuberculosis mimicking lung cancer. In their report, the authors discussed the observation concerning the fact that very rarely postprimary pulmonary tuberculosis presenting with large nodular and mass-like forms on a chest X-ray or CT scan, can be considered as having a neoplastic pattern. In turn, Dhandapani *et al.* [6] described a patient with pulmonary tuberculosis masking lung cancer. Finally, Paci *et al.* [7] presented a case of pulmonary tuberculosis mimicking lung metastasis. They described a 72-year-old male with a history of colorectal carcinoma and right hepatectomy for

a single liver metastasis. The patient underwent adjuvant chemotherapy. The CT scan of the chest performed 6 months after hepatectomy revealed multiple bilateral pulmonary nodular lesions. He underwent multiple wedge resections of the right lung; and the biopsy demonstrated numerous well-formed granulomas with large areas of necrosis with positive Ziehl-Neelsen stain. No carcinoma was identified. Similarly, our patient also had a history of cancer, and therefore, the suspicion of cancer progression was very strong, especially that initially, the stage of the disease was advanced and the woman had a history of late metastasis. Additionally, the CT scan and bronchoscopy were very suggestive, which together with the clinical symptoms (hemoptysis, cough and dyspnea) pointed out the progression of cancer. Finally, tuberculosis was diagnosed, and in all taken samples no cancer was found. In contrast to our case, the patient described by Paci *et al.* [7] had no history of fever, weight loss or productive cough — his result of fiberoptic bronchoscopy was negative, and pulmonary lung lesions were detected relatively quickly after chemotherapy (6 months), while in our case symptoms of tuberculosis occurred 10 years after chemotherapy.

Accurate diagnosis of tuberculosis is very important to establish further treatment of the patient. Van den Brande *et al.* [8] reported four elderly persons with cough who were referred with the presumptive diagnosis of bronchial carcinoma based on chest X-ray and the macroscopic view on fiberoptic bronchoscopy but whose final diagnosis was endobronchial tuberculosis. Chest X-ray showed atypical pulmonary infiltrates in three patients but was normal in one individual, and bronchoscopic examination revealed ulcerative and/or stenotic lesions. The authors strongly suggested that in such cases endobronchial tuberculosis should be considered in differential diagnosis, especially in the elderly. This case series, as well as our case, indicates that the key in the diagnosis of the two diseases is a histological — supplemented by bacteriological — examination.

Usually, CT and whole-body <sup>18</sup>F-fludeoxyglucose-positron emission tomography-computer tomography (PET-CT) are not differentiating, although interesting results have been demonstrated by Lang *et al.* [9]. In their retrospective study, they analyzed asymptomatic pulmonary tuberculosis mimicking lung cancer on imaging. They characterized asymptomatic patients with pulmonary tuberculosis who were initially diagnosed with lung cancer according to their CT or

PET-CT presentations. In the subjects with tuberculosis, all lesions exhibited suspected malignant signs on the chest CT, and the maximum standard uptake value (SUVmax) of PET-CT imaging was between 2.65 and 10.9. Compared with lung cancer, the factors associated with pulmonary tuberculosis included an age < 60 years (82% vs 46%,  $p = 0.03$ ), being male (77% vs 51%,  $p = 0.025$ ), the presence of diabetes (55% vs 16%,  $p < 0.01$ ), spiculated margins (82% vs 44%,  $p = 0.002$ ) and a lower SUVmax ( $p = 0.036$ ). The optimal cut-off level was SUVmax 8.45 for discriminating between pulmonary tuberculosis and lung cancer (sensitivity 63%, specificity 88.9%, respectively). The results of the study revealed the methods of distinguishing between the two similar diseases and may increase awareness of the fact that although imaging of lesions may resemble lung cancer, diagnosis of tuberculosis should be considered concurrently.

As it is known, tuberculosis and lung cancer can occur simultaneously or sequentially. Silva *et al.* [10] analyzed 24 patients diagnosed with both diseases. The diagnoses of tuberculosis and lung cancer occurred simultaneously in 10 patients, whereas tuberculosis was identified prior to lung cancer in 14 cases. The median time between the two diagnoses was 5 years (interquartile range: 1–30 years). The prevalence of active tuberculosis among lung cancer patients varies depending on spatial and regional factors. Lung cancer patients who are more prone to develop tuberculosis are Asian and Caucasian males, at the average age of 60. The prevalence of tuberculosis is higher in patients with chest X-ray evidence of old tuberculosis and/or history of tuberculosis, chronic obstructive pulmonary disease, heavy cigarette smoking, increased alcohol consumption, and/or diabetes mellitus [11]. None of these affected our patient. The only risk factors that could have been taken into account was lung cancer and immunosuppressive treatment, but both circumstances took place 10 years earlier.

In conclusion, differentiation between lung tuberculosis and lung cancer, according to the

clinical and radiological findings, can be challenging. Both diseases present parenchymal infiltrates and can have similar symptoms. Our case shows that tuberculosis can imitate lung cancer development and proves that history of lung cancer and the growth of lung lesions on CT do not always indicate cancer progression. Therefore, despite the previously established diagnosis of advanced cancer in patients with new symptoms and new radiological lesions, full diagnostic procedures should be performed. The final diagnosis can be surprising and what is important — it can afford to apply an appropriate treatment and avoid undergoing unnecessary surgery and toxic chemotherapy.

### References:

1. Siegel R, Ma J, Zou Z, et al. Cancer statistics, 2014. *CA Cancer J Clin.* 2014; 64(1): 9–29, doi: [10.3322/caac.21208](https://doi.org/10.3322/caac.21208), indexed in Pubmed: [24399786](https://pubmed.ncbi.nlm.nih.gov/24399786/).
2. Global Tuberculosis Report. WHO 2013.
3. Bhatt M, Kant S, Bhaskar R. Pulmonary tuberculosis as differential diagnosis of lung cancer. *South Asian J Cancer.* 2012; 1(1): 36–42, doi: [10.4103/2278-330X.96507](https://doi.org/10.4103/2278-330X.96507), indexed in Pubmed: [24455507](https://pubmed.ncbi.nlm.nih.gov/24455507/).
4. Hammen I. Tuberculosis mimicking lung cancer. *Respir Med Case Rep.* 2015; 16: 45–47, doi: [10.1016/j.rmcr.2015.06.007](https://doi.org/10.1016/j.rmcr.2015.06.007), indexed in Pubmed: [26744652](https://pubmed.ncbi.nlm.nih.gov/26744652/).
5. Dalar L, Sokucu S, Karasulu A, et al. Tuberculosis Can Mimic Lung Cancer: A Case Series. *Turkish Thoracic Journal/Türk Toraks Dergisi.* 2013; 14(1): 30–35, doi: [10.5152/ttd.2013.06](https://doi.org/10.5152/ttd.2013.06).
6. Dhandapani S, Dheenadayalu NA, Shanmugam S, et al. Pulmonary tuberculosis masking lung cancer - A case report. *Respir Med Case Rep.* 2015; 16: 35–37, doi: [10.1016/j.rmcr.2015.06.005](https://doi.org/10.1016/j.rmcr.2015.06.005), indexed in Pubmed: [26744649](https://pubmed.ncbi.nlm.nih.gov/26744649/).
7. Paci M, Cavazza A, Guglielmo F, et al. Pulmonary tuberculosis mimicking lung metastasis. *J Thorac Oncol.* 2008; 3(6): 660–661.
8. Van den Brande P, Lambrechts M, Tack J, et al. Endobronchial tuberculosis mimicking lung cancer in elderly patients. *Respir Med.* 1991; 85(2): 107–109, indexed in Pubmed: [1887126](https://pubmed.ncbi.nlm.nih.gov/1887126/).
9. Lang S, Sun J, Wang X, et al. Asymptomatic pulmonary tuberculosis mimicking lung cancer on imaging: A retrospective study. *Exp Ther Med.* 2017; 14(3): 2180–2188, doi: [10.3892/etm.2017.4737](https://doi.org/10.3892/etm.2017.4737), indexed in Pubmed: [28962139](https://pubmed.ncbi.nlm.nih.gov/28962139/).
10. Silva DR, Valentini DF, Müller AM, et al. Pulmonary tuberculosis and lung cancer: simultaneous and sequential occurrence. *J Bras Pneumol.* 2013; 39(4): 484–489, doi: [10.1590/S1806-37132013000400013](https://doi.org/10.1590/S1806-37132013000400013), indexed in Pubmed: [24068271](https://pubmed.ncbi.nlm.nih.gov/24068271/).
11. Christopoulos A, Saif M, Sarris E, et al. Epidemiology of active tuberculosis in lung cancer patients: a systematic review. *The Clinical Respiratory Journal.* 2014; 8(4): 375–381, doi: [10.1111/crj.12094](https://doi.org/10.1111/crj.12094).