

# Primary lung carcinoma combined with pulmonary amyloidosis secondary to syphilis infection

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**Abstract:** A 55-year-old female patient was found to have a pulmonary nodule combined with multiple lung cysts detected on CT scan. Video-assisted thoracoscopic surgery (VATS) lobectomy was performed and the nodule showed adenocarcinoma while the whole left upper lobe showed a heavy deposition of amyloid. Syphilis infection was detected and was suspected contributing to secondary pulmonary amyloidosis. Although very rare, pulmonary amyloidosis should be added to the differential diagnosis for solid pulmonary nodules. Furthermore, widespread lung cysts located apart from pulmonary nodules is especially rare in pulmonary amyloidosis secondary to syphilis infection.

**Keywords:** Lung carcinoma; pulmonary amyloidosis; syphilis

Submitted Nov 08, 2017. Accepted for publication Dec 30, 2017.

doi: 10.21037/jtd.2018.01.38

View this article at: <http://dx.doi.org/10.21037/jtd.2018.01.38>

## Introduction

Amyloidosis is an uncommon disease associated with the deposition of abnormal insoluble proteinaceous amyloid fibrils in the extracellular tissue. It may exist as a primary disease or secondary to a wide variety of chronic conditions such as tuberculosis, chronic renal disease, rheumatoid arthritis and ankylosing spondylitis. Localized pulmonary amyloidosis is rare, while solitary pulmonary nodules mimicking lung cancer are common imaging findings. We describe an unusual case of primary lung carcinoma combined with pulmonary amyloidosis secondary to syphilis infection, where widespread lung cysts are a dominant feature as well as lung nodules.

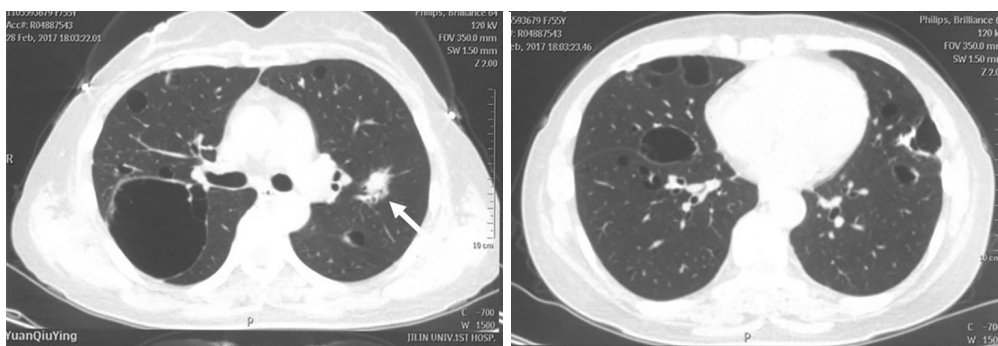
## Case presentation

A 55-year-old non-smoking female presented with a pulmonary nodule combined with multiple lung cysts detected on chest CT scan. Chest CT revealed a pulmonary nodule measuring 2.2 cm × 1.5 cm in the lingual segment of the left upper lobe, suggesting a high possibility of

malignancy. Multiple bilateral lung cysts of various sizes were also present in the central and subpleural regions. The wall of the cysts showed focal, punctate calcifications, especially apparent in the mediastinal windows (*Figure 1*). The patient did not have any other significant medical condition.

Laboratory tests showed elevated tumor markers (*Table 1*). The TP-PA test showed positive and the Venereal Disease Research Laboratory (VDRL) test showed a 1:4 VDRL titer. The brain magnetic resonance and the cerebrospinal fluid tests showed normal. Additional history revealed that the patient was diagnosed with syphilis infection since 1997. Thus, the history and laboratory findings were compatible with tertiary syphilis.

Video-assisted thoracoscopic left upper lobectomy was performed on March 27, 2017. Postoperative pathology confirmed the pulmonary adenocarcinoma (*Figure 2A*) with bronchopulmonary and mediastinal lymph node metastasis (T1N2M0, IIIa). Interestingly, the subpleural cyst wall showed dense aggregates of acellular, homogeneous, eosinophilic material and multinucleated giant cells. Congo red staining showed salmon pink staining on



**Figure 1** Axial chest CT images showed multiple cystic nodules of varying size in both lungs and a dominant nodule (white arrow) in the lingual segment of the left upper lobe.

**Table 1** Tumor markers detected before and after VATS lobectomy (H indicates higher than normal range)

| Tumor markers    | Before   | After    | Normal range |
|------------------|----------|----------|--------------|
| CEA (U/mL)       | 135.00 H | 109.30 H | 0.00–5.00    |
| CA19-9 (U/mL)    | 41.7 H   | 37.6     | 0.0–34.0     |
| CA125 (U/mL)     | 17.2     | 14.9     | 0.0–35.0     |
| CA242 (U/mL)     | 29.5 H   | 39.3 H   | 0.0–20.0     |
| CA72-4 (U/mL)    | 1.8      | 0.9      | 0.0–9.8      |
| CA15-3 (U/mL)    | 10.6     | 9.9      | 0.0–25.0     |
| AFP (ng/mL)      | 2.9      | 2.6      | 0.0–20.0     |
| SCCAg (ng/mL)    | 1.3      | 1.9 H    | 0.0–1.5      |
| NSE (ng/mL)      | 16.5 H   | 11.5     | 0.0–16.3     |
| TPS (U/mL)       | 73.22    | 24.04    | 0.00–80.00   |
| Cyfra211 (ng/mL) | 2.75     | 1.40     | 0.00–3.50    |
| ProGRP (μg/mL)   | 62.9 H   | 22.0     | 0.0–50.0     |

VATS, video-assisted thoracoscopic surgery.

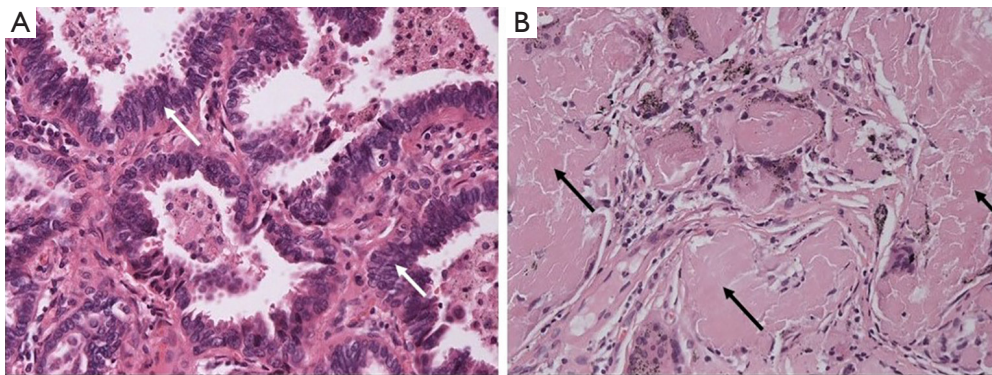
light microscopy (*Figure 2B*). Histological findings were consistent with localized nodular pulmonary amyloidosis. All subsequent investigations including serum and urine protein electrophoresis and immunofixation were normal, indicating the diagnosis with secondary pulmonary amyloidosis.

The patient was discharged 4 days after surgery and received routine benzathine penicillin regimen (benzathine penicillin G 240 MU, IM, QW ×3). She received chemotherapy (MP protocol, pemetrexed disodium 500 mg/m<sup>2</sup> + cisplatin 75 mg/m<sup>2</sup>, d1, Q3W ×4) and radiotherapy (3DCRT, 50 Gy/2 Gy/fx) after surgery.

No severe adverse effects appeared and no signs of local recurrence or distal disease were found at 3-month and 6-month follow-up visit. However, the multiple bilateral lung cysts remained unchanged on chest CT.

## Discussion

Amyloidosis is a heterogenous group of disorders in which insoluble fibrillar proteins are deposited in extracellular tissues. Amyloidosis may present in systemic or localized forms, primary or secondary. Systemic amyloidosis is usually associated with myeloma, tuberculosis, chronic renal disease



**Figure 2** Pathological findings. (A) The lung adenocarcinoma (white arrows, hematoxylin-eosin staining, 200×); (B) amyloid deposits (black arrows) within the subpleural cyst wall with occasional foreign body giant cells and mild infiltration of chronic inflammatory cells (hematoxylin-eosin staining, 200×).

or rheumatoid arthritis and may affect multiple organs, such as the gastrointestinal system, heart and kidneys. Pulmonary involvement in systemic amyloidosis is not uncommon. However, the respiratory tract (that is, lungs and blood vessels) is commonly affected in localized disease (1). Nodular pulmonary amyloidosis are typically asymptomatic and incidental findings of pulmonary nodules on routine chest radiographs are a common mode of presentation. Because of its nodular appearance, nodular pulmonary amyloidosis is usually misconstrued as neoplasm. On CT, pulmonary nodules have sharp and lobulated margins, and are usually found in a subpleural or peripheral location, more frequently in the lower lobes. Over time, nodules may grow slowly and cavitate, calcify, or resolve spontaneously. Calcification can be seen in 20–50% of nodules on CT images (2). PET/CT with  $^{18}\text{F}$ -FDG is used to identify focal areas of increased cellular metabolism. Several case reports mention patients with nodular pulmonary amyloidosis who underwent  $^{18}\text{F}$ -FDG PET/CT, most of them showing an increased FDG uptake, but no FDG uptake has also been mentioned (3). For multiple pulmonary nodules, the differential diagnosis should include malignant neoplasm, and histological confirmation is mandatory. In any case a patient with single or multiple nodules highly suggesting malignancy, pathological examination should be performed through biopsy or surgery.

In our patient, we found a pulmonary adenocarcinoma combined with widespread cyst formation in her lungs, which was associated with nodular pulmonary amyloidosis (Figure 2B). The cysts were thin-walled, and there was no cavitation of the visualized pulmonary nodules to suggest

that the cysts were secondary to extensive cavitation of nodules. While cavitation of existing pulmonary amyloid nodules is a well-recognized feature of nodular pulmonary amyloidosis, widespread lung cysts located apart from pulmonary nodules is rare, mostly in association immune diseases (4). We report that our patient is the sixth reported case of a lung nodule consisting of adenocarcinoma and amyloid deposition (5,6).

Pulmonary syphilis is rare and there are only 14 cases were reported in the English language literature (7). Radiological presentation included infiltrates and solitary or multiple nodules, sometimes associated with pleural effusion and mimicking malignant lesions (8). Diagnosis of osseous or pulmonary syphilis in reported cases was most often made based on radiological images resolving on penicillin in the context of positive serology. Considering VDRL positive and past history, we proposed the diagnosis of nodular pulmonary amyloidosis secondary to syphilis infection. However, after anti-syphilis treatment, the multiple lung cysts showed no remission at the 3-month follow-up, indicating the amyloidosis a chronic course which needs a long-time follow up. We believe this is the first case report of localized pulmonary amyloidosis secondary to syphilis infection.

Our case highlights a rare manifestation showing that localized pulmonary amyloidosis may be caused by syphilis infection. Widespread lung cysts located apart from pulmonary nodules may be a rare manifestation of pulmonary amyloidosis. It is difficult to differ malignant nodules from nodular pulmonary amyloidosis. CT, PET/CT, tumor marker may help but pathological examination

should be proposed when necessary.

### Acknowledgements

None.

### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Informed Consent:* Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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**Cite this article as:** Zhao L, Xu X, Zhang Y, Li S, Shi X, Cui Y. Primary lung carcinoma combined with pulmonary amyloidosis secondary to syphilis infection. J Thorac Dis 2018;10(2):E145-E148. doi: 10.21037/jtd.2018.01.38