

## CASE REPORT

# Multiple Postoperative Lung Infections after Thymoma Surgery Diagnosed as Nontuberculous Mycobacterial Infection

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### SUMMARY

**Background:** Thymomas are thymic epithelial-derived, most common primary anterior mediastinal masses. Nontuberculous mycobacteria (NTM) are species that do not cause leprosy and belong to species outside the Mycobacterium tuberculosis complex.

**Methods:** With the clinical application of targeted next-generation sequencing (tNGS), we promptly confirmed a case of NTM infection combined with NTM infection after thymoma surgery, and we performed a joint literature analysis of the two diseases to improve clinicians' understanding and recognition of lung infections after thymoma surgery.

**Results:** Chest CT of both lungs showed multiple hyperdense shadows. Sputum bacterial culture and characterization detected Neisseria Dryad and Streptococcus Grass Green. The presence of Mycobacterium abscessus infection was confirmed by alveolar lavage fluid sent for second-generation macro gene sequencing.

**Conclusions:** The body's immune function decreases after thymoma surgery. When empirical anti-infection treatment for recurrent pneumonia in the lungs is ineffective, we should be alerted to the possibility of the presence of pulmonary nontuberculous mycobacterial infection, and next-generation sequencing should be performed promptly to arrive quickly at a diagnosis.

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#### KEYWORDS

nontuberculous mycobacteria, mycobacterium abscessus, thymoma, bronchoalveolar lavage, next-generation sequencing (NGS), treatment

#### CASE REPORT

Nontuberculous mycobacteria (NTM) are ubiquitous in the environment, but NTM disease is rare [1]. To date, more than 140 species of NTM have been identified. They can cause a wide range of mycobacterial infections, with pulmonary infections being the most common, at about 65 - 90% [2]. Globally, there is an increasing number of infections caused by nontuberculous mycobacteria (NTM), which greatly increases the difficulty of treating these bacteria as they are resistant

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to many common antibiotics. Among them, *Mycobacterium abscessus* grows rapidly and can cause severe respiratory, skin, and mucosal infections in humans [3]. NTM is generally considered to be less virulent than *Mycobacterium tuberculosis*, and individuals with congenital or acquired immunodeficiency are more susceptible to attack by pathogenic bacteria. Among them, the lung is the most commonly affected organ, and NTM pulmonary disease (NTM-PD) frequently occurs among patients who already have lung disease.

The patient is a young woman, 24 years old, who was hospitalized in our hospital on January 9, 2024 for intermittent cough and sputum for 9 months. Admission examination: T: 36.2°C, P: 120 times/minute, R: 21 times/minute, BP: 111/89 mmHg. Breath sounds in both lungs clear, not heard dry and wet rales, the remaining examination did not show any abnormality. The patient developed cough and white foamy sputum 9 months ago. She had fever at the beginning of the disease, and her temperature returned to normal after applying anti-inflammatory drugs, but her cough and sputum were not relieved. Five months ago, she was operated on the right side of the mediastinum at Peking University Aerospace Clinical College, and the pathology results showed thymoma type AB. Three months ago, chest CT showed multiple inflammatory lesions in both lungs, and bronchoscopy was performed. The bronchoscopy brushings showed acid-fast bacilli, *Mycobacterium tuberculosis* tested negative, and empirical anti-tuberculosis treatment was given for one week in the local hospital. The patient was given voriconazole, rifampicin, ethambutol, and azithromycin at the same time. However, neither her clinical symptoms nor her imaging appear to be significantly improved. In order to seek further diagnosis and treatment, she came to our hospital.

Relevant laboratory results after admission were monocyte  $0.65 \times 10^9/L$ , D-dimer 1,346 ng/mL, plasma fibrinogen 5.02 g/L, alanine transferase 4 U/L, creatine kinase 25 U/L, creatinine 38  $\mu\text{mol/L}$ , and antinuclear antibody spectrum: ANA (+). Our hospital chest CT suggests: 1. multiple inflammatory lesions in both lungs, 2. irregularity of the sternal bone. Sputum bacterial culture and identification detected dry *Neisseria*, grass green streptococcus, fungal series did not see obvious abnormalities.

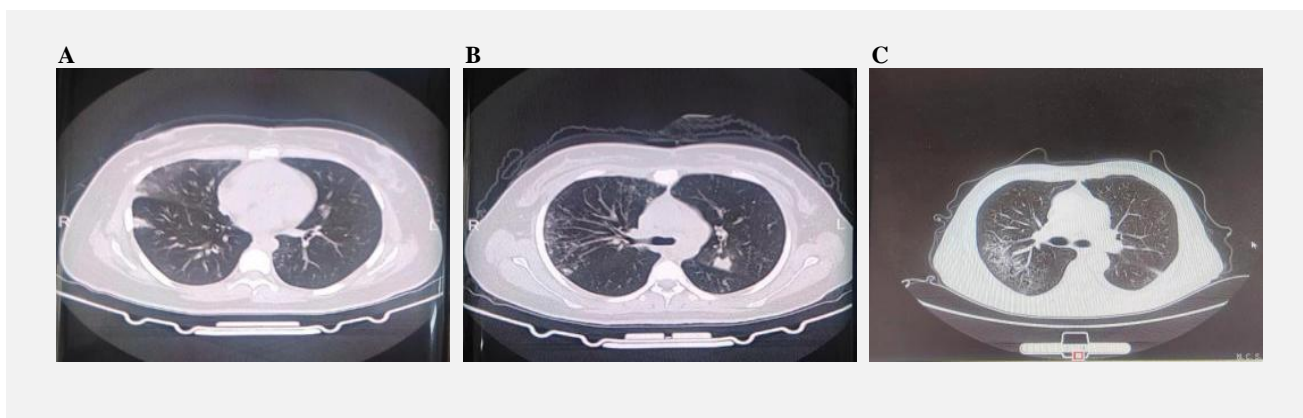
On January 11, 2024, fiberoptic bronchoscopy was performed, and the microscopic findings were as follows: the main bronchus of the right lung and the bronchial openings of each lobe segment were patent, scattered yellowish-white purulent secretions were seen, and a large amount of yellowish-white purulent secretions was seen. Bronchoalveolar lavage was performed in the posterior basal segment of the lower lobe of the left lung, and the lavage fluid was sent for pathogenetic testing; the results of the lavage fluid sent for testing were negative for Xpert, mNGS: *Mycobacterium abscessus*. After admission, moxifloxacin and bromhexine were given as symptomatic treatment; the patient's coughing symptoms were reduced compared with the previous

period, but she still had intermittent coughing symptoms, which were difficult to relieve. The *Mycobacterium abscessus* infection detected in the current hospitalization was at a different site than the previous one, which made it difficult to alleviate the symptoms. Since the patient had a history of allergy to piperacillin tazobactam and minocycline, the number of antimicrobials that could be used was very limited. Finally, according to the consensus of the experts on *Mycobacterium tuberculosis*, the patient was given a combination of clarithromycin, moxifloxacin, and rifabutin as the antimicrobial therapy against NTM.

## DISCUSSION

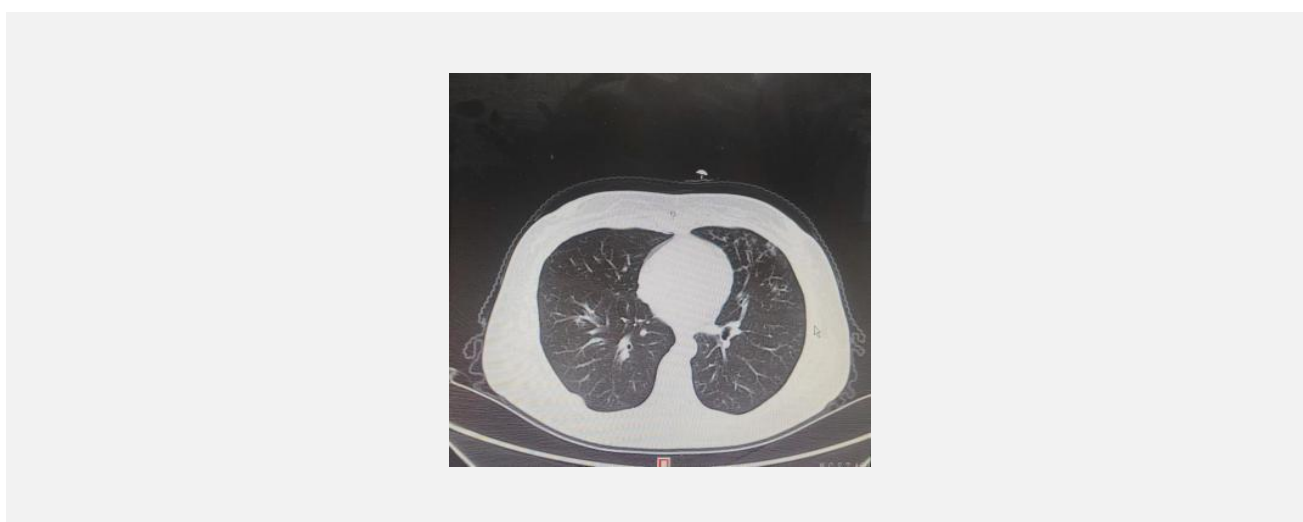
Thymoma is the most common primary tumor of the anterior mediastinum, but accounts for less than 1% of all adult malignancies [3]. Due to its rarity, thymoma has not been intensively studied. The 2004 WHO classification of thymoma classifies thymoma into five distinct histological subtypes based on the morphology of the tumor epithelium and the ratio of lymphocytes to epithelial cells: types A, AB, B1, B2, and B3 [4]. However, due to the typical morphological heterogeneity of thymomas, several subtypes usually coexist in the same tumor. The pathologic type of the patient in this case report was type AB, which is characterized by a mixture of spindle/oval shaped epithelial cells with lymphocyte-rich areas characteristic of both type A and B thymoma. Therefore, classifying them into a single tumor classification is difficult, there may be sampling limitations based on needle biopsy to sample all subtypes of thymoma present. In addition, the WHO classification system does not predict a good clinical prognosis [5-8]. With the increased use of CT for the evaluation and follow-up surveillance of a wide range of tumors, thymoma is being diagnosed in an increasing number of asymptomatic patients [9]. In general, it is difficult to distinguish between thymoma and the less common thymic epithelial malignancies, thymic carcinoma and thymic carcinoid tumors. However, thymic carcinoma and carcinoid tumors are much more aggressive and commonly show local or metastatic spread [10]. Typically, thymomas appear on CT scans as regularly shaped spherical, well-defined, anterior mediastinal masses measuring 5 - 10 cm, although they have been described as ranging from a few millimeters to 34 cm in diameter [11]. They are usually closely associated with the upper pericardium, although they may appear anywhere from the thoracic inlet to the pericardial border.

NTM are ubiquitous in the environment, but their occurrence is uncommon. The *Mycobacterium abscessus* present in this case is readily found in aerosols and man-made water sources such as direct drinking water pipes, bathtubs, etc. NTM are categorized into fast-growing mycobacteria (RGM; < 7 days) and slow-growing mycobacteria (SGM;  $\geq 7$  days) based on the incubation time and growth characteristics in the laborato-



**Figure 1. October 30, 2023, chest CT.**

**A - December 21, 2023, chest CT, B - and January 8, 2024, chest CT - C. All three images showed multiple inflammatory lesions in both lungs.**



**Figure 2. February 3, 2024, chest CT showed significant absorption of lung inflammation after two weeks of anti-NTM treatment compared to the previous period.**

ry [12]. The Mycobacterium abscessus in our patient was RGM. Studies in many countries have shown that the rate of positive cultures for NTM has increased considerably in recent years. A number of factors have contributed to the increased incidence and prevalence of NTM, including increased virulence mutations in the NTM gene, decreased immunity, increased incidence of chronic lung diseases, and environmental and climatic changes, in addition to the popularization of ancillary tests used for the diagnosis of NTM and increased awareness of NTM among healthcare professionals.

The patient in this case had a previous AB thymoma, the surgical removal of which may have had an impact on the functioning of the immune system. Abnormal regulation of lymphocytes in the thymus can lead to

autoimmunity and/or immunodeficiency. Autoimmunity may also be caused by cross-immunization of antigens in other tissues with T-associated antigens. Since it was difficult to distinguish the causative agent of this pneumonia infection in the patient from the symptoms and lung imaging, fiberoptic bronchoscopy was performed, and NGS was performed on the alveolar lavage fluid, which revealed Mycobacterium abscessus with a detection sequence number of 57, which is of great clinical significance for the treatment as well as the prognosis of this disease. Figures 1 (A - C) show the CT images of infection remaining in the lungs on October 30, 2023, December 21, 2023, and January 8, 2024, respectively. As seen in the figures, the patient's right lower lung infection was reduced in December compared to October

after a period of medication. The patient's repeat chest CT after two weeks of anti-NTM treatment suggested that bilateral pneumonia had improved (Figure 2), and the treatment was effective. This reinforces the clinical significance of bronchial lavage fluid NGS examination in this patient.

## CONCLUSION

The lesson we learned from this patient's case is that in patients with prolonged community-acquired pneumonia and prior coexisting thymoma, fiberoptic bronchoscopy should be performed aggressively when empirical anti-infective therapy is not satisfactory, and that alveolar lavage fluid second-generation metagenomic sequencing technology plays an important role in both the diagnosis and treatment of the disease. Physicians should be aware of the complications of thymoma and be alert to specific pathogen infections of the lungs caused by immune dysfunction after thymoma surgery.

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### Ethical Approval:

This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in the studies were in accordance with the ethical standards. Informed consent was obtained.

### Declaration of Interest:

No conflicts of interest.

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