Clin. Lab. 2023;69:XXX-XXX

CASE REPORT

Mycobacterium Tuberculosis Infection in AECOPD Combined with Pulmonary Embolism: a Case Report

Jing S. Bai, Qin Zhang, Jing X. Liu, Jing M. Wang, Qian C. Chen, Xin Y. Zhou, Rong X. Liu, Shan Gao, Ai S. Fu, Yan L. Ge

Department of Respiratory Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

SUMMARY

Background: **Mycobacterium tuberculosis belongs to the group of mycobacteria, most of which can cause a delayed hypersensitivity reaction in the body and is a bacterium that causes tuberculosis. Mycobacterium tuberculosis infection often presents with symptoms of tuberculosis toxicity and rarely with respiratory distress. At the same time, chest imaging often shows an ill-defined solid shadow in the apical and posterior segments of the upper lobe and, less frequently, in the dorsal segment of the lower lobe, and less frequently a diffuse nodular shadow. We report a case of AECOPD combined with pulmonary embolism infected with Mycobacterium tuberculosis.**
Methods: **Bronchoscopy, Next-generation sequencing (NGS).**
Results: **Antacid staining of bronchoalveolar lavage fluid suggested that a small amount of Mycobacterium antacid was visible. NGS was sent for examination and it suggested the presence of Mycobacterium tuberculosis with a sequence number of 5 (reference range ≥ 0). Treatment such as bronchodilation and antituberculosis was given.**
Conclusions: **In patients with dyspnea, it is crucial to find the causative agent and to promptly improve relevant examinations such as pulmonary arteriography and bronchoscopy, and if necessary, to make a definitive diagnosis by NGS.**
(Clin. Lab. 2023;69:xx-xx. DOI: 10.7754/Clin.Lab.2022.220815)

Correspondence:
Yan L. Ge
North China University of Science and Technology Affiliated Hospital
Tangshan, Hebei
China
Phone: +86 15932081296
Email: 495732196@qq.com

Case Report accepted August 24, 2022

KEYWORDS

mycobacterium tuberculosis, pulmonary thromboembolism, acute exacerbation of the chronic obstructive pulmonary disease, bronchoscopy, next-generation sequencing

CASE REPORT

A 69-year-old male was admitted to the hospital with the primary cause of intermittent dyspnea with cough and sputum for 7 months, aggravated for 10 days. He complained of dyspnea with no obvious cause 7 months ago, intermittent, significantly aggravated after activity, accompanied by cough and sputum, coughing white mucous sputum, consulted in the local community hospital, pulmonary function suggests mixed ventilation dysfunction, mainly obstructive, given "budesonide formoterol 320 μg inhalation 2/day", the treatment effect is average. In the past 10 days, the above symptoms wors-

ened, and the patient coughed up yellow mucous sputum, which could not be easily coughed up, without fever, blood in sputum and hemoptysis, or chest pain. The patient had a history of "cerebral hemorrhage" for 3 years and had no residual limb or speech disorders. He denied a history of tuberculosis. On admission, the examination revealed bilateral weak respiratory movements, prolonged respiratory phase, expiratory effort, widened rib space, barrel-shaped chest, over-clear sound on percussion of both lungs, low breath sounds in both lungs, and scattered wet rales could be heard. The rest of the examination did not show any significant abnormalities. After admission, routine blood test showed: WBC 12.8 x 10^9/L (reference value 4 x 10^9/L - 10 x 10^9/L), NEU 11.02 x 10^9/L (reference value 1.8 x 10^9/L - 6.3 x 109/L), LYM 0.85 x 10^9/L (reference value 1.1 x 10^9/L - 3.2 x 10^9/L), MON 0.68 x 10^9/L (reference value 0.1 x 10^9/L - 0.6 x 10^9/L), while refinement of infection indicators suggested: CRP 80.2 mg/L (reference value 0 mg/L - 8 mg/L), SAA 45.79 mg/L (reference value 0 mg/L - 10 mg/L), PCT 0.08 ng/mL (reference value 0 ng/mL - 0.05 ng/mL), ESR 55 mm/hour (reference value 0 mm/hour - 15 mm/hour), fibrinogen 5.58 g/L (reference value 2 g/L - 4 g/L), and no significant abnormalities were seen in biochemical tests. A CT scan of the chest showed diffusely visible multiple nodular dense shadows in both lungs, inflammatory lesions in both lungs and bronchodilation in the lower lobes of both lungs. We initially diagnosed acute exacerbation of chronic obstructive pulmonary disease with a sputum culture suggestive of Pseudomonas aeruginosa 3+, so the patient received anti-infective therapy: intravenous (IV) Piperacillin Sodium and Tazobactam Sodium at a dose of 4.5 g twice daily. At the same time, we also applied the treatment of bronchial relaxation and expectorant. After 72 hours of anti-infective treatment, the patient's blood count returned to normal on recheck, but the patient's dyspnea symptoms did not improve significantly. As the coagulation series suggested D-dimer < 500 ng/mL, initially no attention was paid to the problem of pulmonary embolism. Later, the perfect pulmonary arteriogram suggested that filling defects were seen in the local pulmonary artery branches in the left lower lobe, and the local pulmonary artery branch thrombosis in the left lower lobe was considered (Figure 1, 2). We immediately initiated anticoagulation therapy: subcutaneous injection of low molecular heparin sodium at a dose of 0.4 mL twice daily combined with oral warfarin at a dose of 3 mg once daily. The INR is maintained between 2 and 3.

However, the patient's wheezing symptoms worsened after 24 hours, and blood gas analysis showed that PH 7.45, PO2 71 mmHg, PCO2 35.5 mmHg, PaO2/FiO2 244.83 mmHg, considering the presence of type I respiratory failure. The patient was temporarily treated with asthma treatment: intravenous methylprednisolone sodium succinate at a dose of 40 mg. A repeat chest CT showed no significant improvement in the inflammatory lesions in both lungs, and anti-infective therapy was adjusted: intravenous meropenem at a dose of 1 g twice daily. After 1 week of anticoagulation, the patient's pulmonary arteriogram showed that the thrombosis of the local pulmonary artery branches in the lower lobe of the left lung had not changed significantly, and chronic thrombosis was considered. The patient's dyspnea was slightly relieved, and the chest CT has repeated, suggesting that the inflammatory lesions in both lungs were more progressive than before. No significant changes were seen in the diffuse multi-nodular high-density shadow in the diffuse multi-nodular high-density shadow in both lungs (Figure 3, 4). Bronchoscopy was performed, and bronchoalveolar lavage was performed in the middle lobe of the right lung. The lavage fluid antacid staining suggested the presence of a small amount of Mycobacterium tuberculosis (Figure 5, 6), and the NGS test suggested the presence of Mycobacterium tuberculosis with sequence number 5 (reference range ≥ 0). The patient was discharged after 1 week of first-line anti-tuberculosis treatment and is currently on regular anti-tuberculosis therapy.

DISCUSSION

A good diagnostic process has been developed for exploring the causes of dyspnea. However, when multiple diseases combine to cause dyspnea, finding the cause becomes the focus of treatment. In this case, we initially considered dyspnea due to AECOPD alone, but the symptoms did not improve after the infection was initially controlled. Although the D-dimer was < 500 ng/mL [1] and the Wells score was < 2 [2], the possibility of pulmonary thromboembolism could not be completely excluded, and the presence of a localized pulmonary thrombus in the lower lobe of the left lung was confirmed after the completion of pulmonary angiography. After anticoagulation treatment, the symptoms of dyspnea still did not improve significantly. Meanwhile, chest CT suggested diffuse multiple nodular high-density shadows in both lungs not consistent with the typical manifestations of COPD, and we suspected the possible presence of diffuse panbronchitis [3]. After bronchoscopy, pathology of the lavage fluid suggested the presence of Mycobacterium antacid, and finally, NGS confirmed the presence of Mycobacterium tuberculosis infection. The most common clinical manifestation of diffuse panbronchitis is cough and/or dyspnea, and high-resolution CT usually shows multiple lobar central nodules, with dilated fine bronchi and bronchiectasis reported in many cases [4]. In our patient, chest imaging suggested diffuse multiple nodular shadows along with bronchial dilatation in the lower lobes of both lungs, and diffuse pan-bronchiolitis was initially suspected. In recent years, a study on diffuse panbronchiolitis conducted by Li H et al. noted that only 10% of patients could be diagnosed within 1 year [5].

In response to chest imaging suggestive of diffuse multinodular shadowing, the presence of Mycobacterium

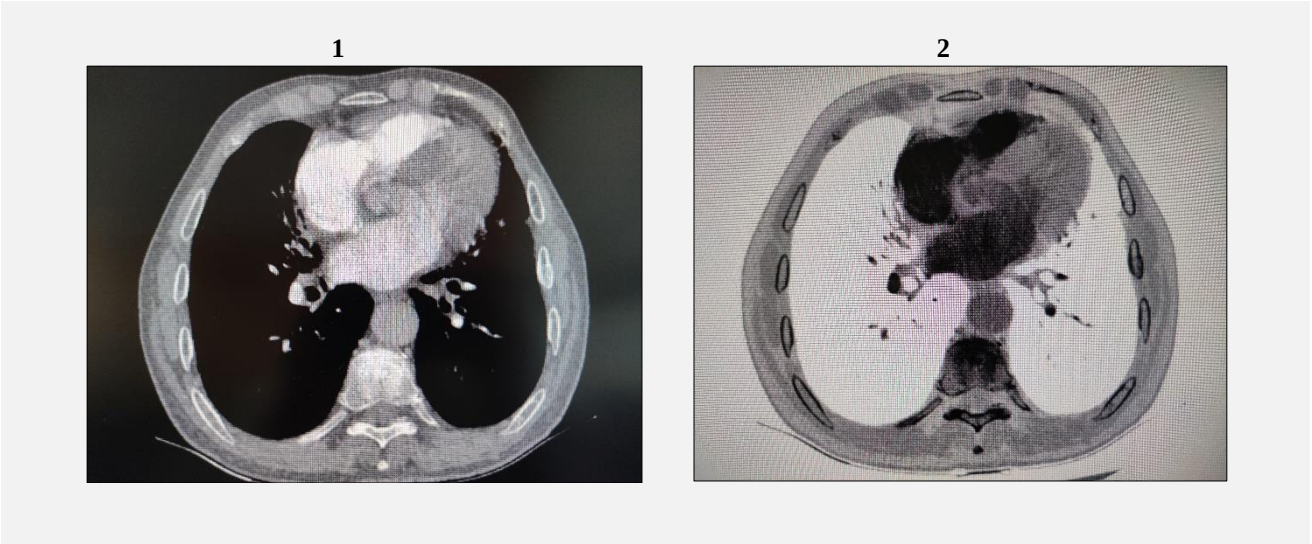

Figure 1 - 2. A pulmonary arteriogram suggests a filling defect is seen in the localized pulmonary artery fraction of the left lower lobe, and localized pulmonary artery branch thrombosis in the left lower lobe is considered.

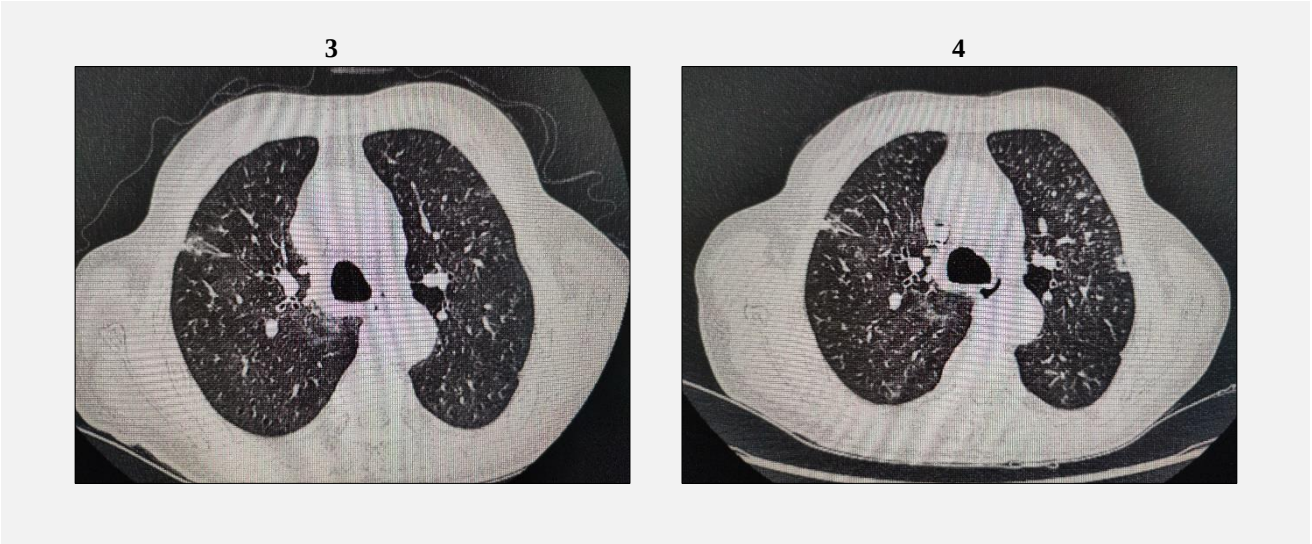

Figure 3 - 4. Diffuse visible multi-nodular high-density shadow in both lungs, inflammatory lesions in both lungs; after 10 days of anti-infection treatment, inflammatory lesions in both lungs progressed more than before, and diffuse multi-nodular high-density shadow in both lungs did not show significant changes.

tuberculosis infection needs to be guarded against due to its polymorphic, multifocal, and multi-calcified nature [6], especially during glucocorticoid therapy [7]. Mycobacterium tuberculosis infection most often presents with symptoms of tuberculosis toxicity, such as malaise, low-grade fever, and night sweats, and less frequently with symptoms of respiratory distress. Meanwhile, chest imaging usually shows alveolar infiltrates, cavitation, lymphadenopathy, and pleural effusion [8]. Eventually, in this case, the presence of Mycobacterium tuberculosis infection in the patient was clarified with the help of bronchoscopy.

The lesson learned from this patient is that we initially did not pay attention to the cause of the diffuse multiple nodular dense shadow presentation in both lungs and did not recognize that dyspnea may be due to a combination of etiologies. Early bronchoscopy and pathologic diagnosis should be improved in patients with dyspnea,

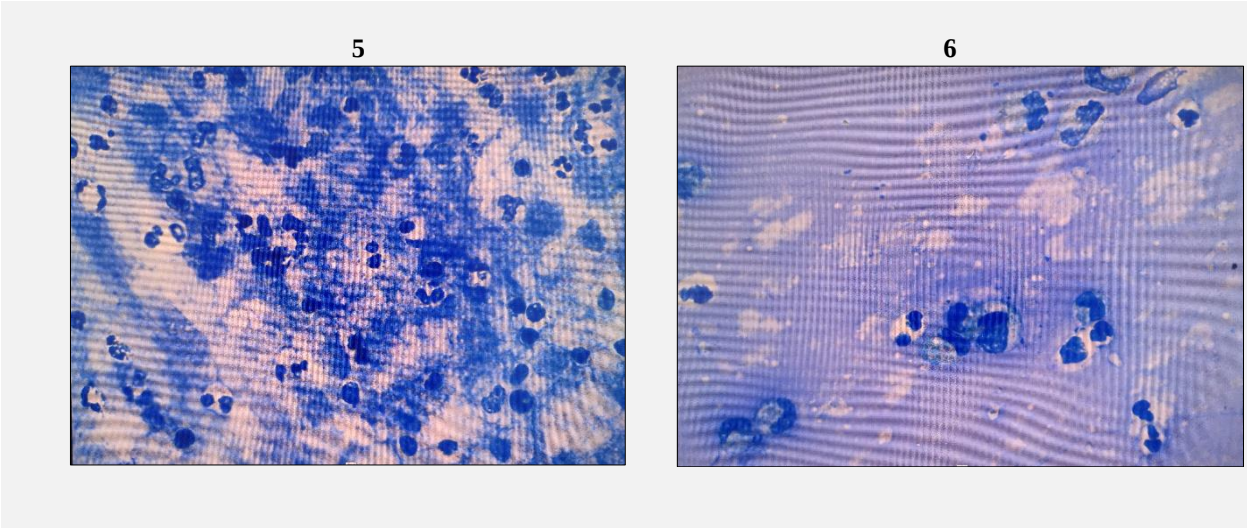

Figure 5 - 6. Antacid staining of the lavage fluid suggests a small number of antacid bacilli are visible.

NGS reported

Detection index	Number of detected sequences *	Relative abundance (%) #
Mycobacterium tuberculosis complex	5	0.77

*** - Number of detected sequences: refers to the number of sequences that can match the pathogen. The higher the number of detected sequences, the higher the confidence that the pathogen is detected in the specimen.**
 # - relative abundance: refers to the proportion of microorganisms in the same type of microorganisms detected in the entire specimen. The higher the abundance, the higher the proportion of the same type of microorganisms.

especially if symptomatic relief is not apparent with initial treatment.

CONCLUSION

In patients with dyspnea, it is crucial to find the causative agent and to promptly improve relevant examinations such as pulmonary arteriography and bronchoscopy, and if necessary, to make a definitive diagnosis by NGS.

Acknowledgment:
We would like to thank other members of the Department of Respiratory Medicine, Affiliated Hospital of the North China University of Technology for the constructive criticism.

Source of Support:
This work was supported by the Notice of Hebei Medical applicable technology tracking project plan in 2021 (gz2021057).

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

Declaration of Interest:
No conflicts of interest.

References:

1. Crawford F, Andras A, Welch K, Sheares K, Keeling D, Chappell FM. D-dimer test for excluding the diagnosis of pulmonary embolism. Cochrane Database Syst Rev 2016 Aug 5;2016(8): CD010864. (PMID: 27494075)

2. Shen JH, Chen HL, Chen JR, Xing JL, Gu P, Zhu BF. Comparison of the Wells score with the revised Geneva score for assessing suspected pulmonary embolism: a systematic review and meta-analysis. J Thromb Thrombolysis 2016 Apr;41(3):482-92. (PMID: 26178041)

3. Poletti V, Casoni G, Chilosi M, Zompatori M. Diffuse panbronchiolitis. Eur Respir J 2006 Oct;28(4):862-71. (PMID: 17012632)

4. Weinberger M, Lesser D. Diffuse panbronchiolitis: A progressive fatal lung disease that is curable with azithromycin, but only if diagnosed! Pediatr Pulmonol 2019 Apr;54(4):457-62. (PMID: 30609307)

5. Li H, Zhou Y, Fan F, et al. Effect of azithromycin on patients with diffuse panbronchiolitis: retrospective study of 51 cases. Intern Med 2011;50(16):1663-9. (PMID: 21841323)

6. Wang Y, Shang X, Wang L, et al. Clinical characteristics and chest computed tomography findings related to the infectivity of pulmonary tuberculosis. BMC Infect Dis 2021 Nov 27;21(1): 1197. (PMID: 34837990)

7. Dheda K, Barry CE 3rd, Maartens G. Tuberculosis. Lancet 2016 Mar 19;387(10024):1211-26. (PMID: 26377143)

8. Grozdanovic Z, Berrocal Almanza LC, Goyal S, et al. A Novel Reading Scheme for Assessing the Extent of Radiographic Abnormalities and Its Association with Disease Severity in Sputum Smear-Positive Tuberculosis: An Observational Study in Hyderabad/India. PLoS One 2015 Sep 18;10(9):e0138070. (PMID: 26381644)