A novel therapeutic strategy to close bronchopleural fistula related to *Mycobacterium chelonae* in elderly patients: two case reports and literature review

Xiaolong Liu[1,2], Zhihua Huang[3], Shaohua Luo[1], Shifang Yang[1], Junwei Huang[1], Pingping Chen[1], Qi Lin[1], Jian Wu[1,2]^

[1]Second Department of Geriatrics Respiratory Medicine, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangdong Provincial Geriatrics Institute, Guangzhou, China; [2]The Second School of Clinical Medicine, Southern Medical University, Guangzhou, China; [3]Department of Cardiology, Fuwai Hospital, National Clinical Research Center for Cardiovascular Diseases, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Correspondence to: Jian Wu, MD, PhD. Second Department of Geriatrics Respiratory Medicine, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangdong Provincial Geriatrics Institute, Guangzhou 510080, China. Email: sywujian@scut.edu.cn.

Background: *Mycobacterium chelonae* (*M. chelonae*) empyema complicated with bronchopleural fistula (BPF) remains a significant challenge in diagnosis and treatment and the clinical outcomes are often unsatisfactory, especially in elderly patients. There is a paucity data related to the management of the condition. This is the first well-documented report of the therapeutic experience with bronchoscopic closure of a bronchopleural fistula with empyema related to *M. chelonae* infection in the elderly patients.

Case Description: An 86-year-old non-smoking male with a history of diabetes mellitus, emphysema, and bronchiectasis, and a 72-year-old non-smoking male with two past surgeries for lung cancer, both presented with chronic fever, purulent expectoration, hemoptysis, and dyspnea, and were diagnosed with bronchopleural fistula associated with *M. chelonae* infection. Long-term antibiotic regimens, prolonged thoracic drainage, and endoscopic closure with biological glue were all unsuccessful. The culprit bronchus was identified precisely with the combined assistance of the instillation of methylene blue and the Chartis digital air leak monitoring system. Bronchoscopic interventional therapy was successfully performed using the Zephyr one-way endobronchial valve or the Amplatzer patent ductus arteriosus occluder. Finally, two patients succeeded in removing chest tube, and were able to conduct daily activities.

Conclusions: The successful bronchoscopic closure with the combined assistance of methylene blue and the Chartis digital air leak monitoring system provided valuable experience and novel strategy in dealing with BPF related to *M. chelonae* in the elderly and high-risk inoperable patients.

Keywords: *Mycobacterium chelonae* (*M. chelonae*); bronchopleural fistula (BPF); Zephyr endobronchial valve; Amplatzer occluder; case report

Submitted Apr 01, 2022. Accepted for publication May 19, 2022.
doi: 10.21037/atm-22-2130
View this article at: https://dx.doi.org/10.21037/atm-22-2130

Introduction

Rapidly growing mycobacteria (RGM) exists widely in the environment. RGM pulmonary diseases are mainly due to *Mycobacterium abscessus* and *M. fortuitum*. *M. chelonae* commonly causes skin and soft tissue infections, but is a rare pathogen of thoracic empyema complicated with bronchopleural fistula (BPF). Besides, there is a paucity of

^ ORCID: 0000-0003-0008-899X.

data related to the management of the condition. Once, surgical resection is considered a curative treatment, but is associated with a high mortality rate, reaching approximately 67% (1,2). Through a literature review, we found four similar case reports including 4 patients (3-6). All reported cases were treated with antibiotics, and 3 patients underwent open window thoracotomy, and 1 patient closed BPF with bronchoscopic biological glue occlusion successfully who was discharged from the hospital more quickly in all patients (6). Therefore, in addition to antibiotics and surgical resection, bronchoscopic closure of BPF related to *M. chelonae* with BPF may be another one novel and less-invasive strategy. This current case study describes two elderly patients who presented with *M. chelonae* empyema with BPF, who were successfully treated with bronchoscopic closure using the one-way endobronchial valve (EBV) or the Amplatzer patent ductus arteriosus (PDA) occluder, aided by methylene blue instillation and the Chartis digital air leak monitoring system. The result of our study provided clinical evidence for bronchoscopic closure to BPF related to *M. chelonae* in the elderly and inoperable patients. We present the following article in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-2130/rc).

Case presentation

This study was approved by the Medical Research Ethical Committee of Guangdong Provincial People's Hospital (No. GDREC2019219A). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Case one

An 86-year-old non-smoking man was admitted to Guangdong Provincial People's Hospital on July 5, 2018, due to fever, purulent expectoration, and dyspnea lasting for three months. He had a past medical history of diabetes mellitus, obsolete pulmonary tuberculosis, emphysema, bronchiectasis, and untreated rectal adenocarcinoma.

The chest computed tomography (CT) suggested right-sided hydro-pneumothorax and pneumonia (*Figure 1A*). The pleural effusion examined by metagenomic next generation sequencing (mNGS) revealed the presence of *M. chelonae*. He was therefore treated with sensitive antibiotics (amikacin plus ciprofloxacin), chest drainage, transbronchoscopic closure with 2 mL biological glue (Beijing Kangpaite Medical Equipment Co., Ltd., Beijing, China), and oxygen supplement. However, the pneumothorax and empyema did not resolve successfully. Due to his poor pulmonary function and deficient nutritional state, bronchoscopic one-way endobronchial valve (EBV) implantation was adopted as an ideal modality. First, the right upper lobe (RUL) was suspected as the target lobe as blue liquid flowed out from the RUL after instilling 20 mL methylene blue solution through the thoracic catheter. Second, under negative thoracic pressure drainage (–10 cmH_2O), the Chartis air leak monitoring system (American Pulmonx Inc) visually displayed an intense negative pressure, indicating that the B2 and B3 segments of the RUL had effective communication to the leak when the catheter tip was exposed to the fistula, with no bypass ventilation (*Figure 1B*). After measuring the bronchial lumen, we decided to implant two Zephyr EBVs (Emphasys Medical Inc, USA) at the opening of B2b (EBV-TS-5.5) and B3b (EBV-TS-4.0), respectively (*Figure 1C,1D*). The amount of air leak was reduced by approximately 50% by visual inspection of air bubbles in the water seal, and the Chartis system showed a typical decreasing breathing curve. No adverse events occurred after the procedure. However, due to the right empyema, the patient required repeated pleural lavage with sodium chloride solution through the chest tube. The air leakage finally resolved on September 22, 2018, and the chest tube was removed after three days. The patient was able to conduct daily activities after discharge. The whole process of diagnosis and treatment of BPF related to *M. chelonae* was outlined in *Figure 2*.

Case two

A 72-year-old non-smoking male presented with a persistent cough, purulent expectoration, and dyspnea for three months after he underwent a wedge-shaped resection of the RUL by video-assisted thoracoscopic surgery (VATS) for lung cancer ($pT_{1a}N_0M_0$, IA). He was initially misdiagnosed with pulmonary tuberculosis based upon sputum positive acid-fast bacilli and standard anti-tuberculosis treatments were commenced for six months.

After antibiotic treatment, his chest CT showed a new pulmonary mass (3.1 cm × 1.8 cm) in the right upper hilum,

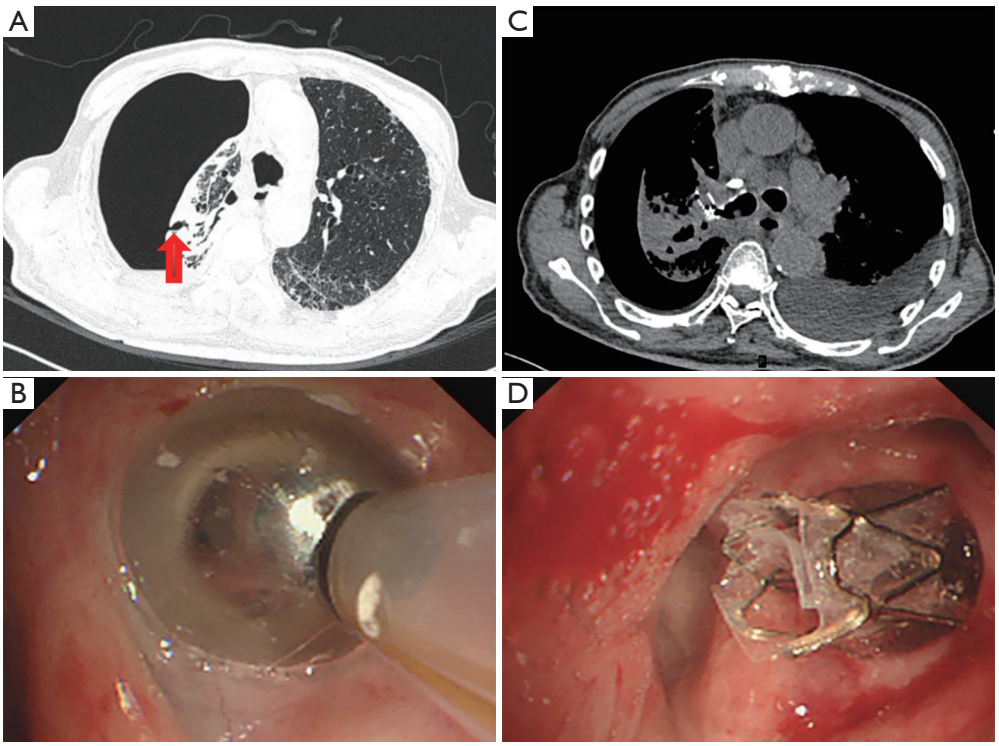

Figure 1 The chest CT scan and bronchoscopic view of BPF related to *M. chelonae* in the case one. The pulmonary window of the initial CT scan showing bilateral pneumonia pattern and right-side hydro-pneumothorax. The red arrow indicates a fistula in the right upper lobe (A). The bronchoscopic view of the Chartis balloon catheter (B). The mediastinal window of the CT scan showing EBVs in the right B2b and B3b segments one week after valve insertion (C). The bronchoscopic view of the EBV in the right B2b (D). CT, computed tomography; BPF, bronchopleural fistula; EBV, endobronchial valve.

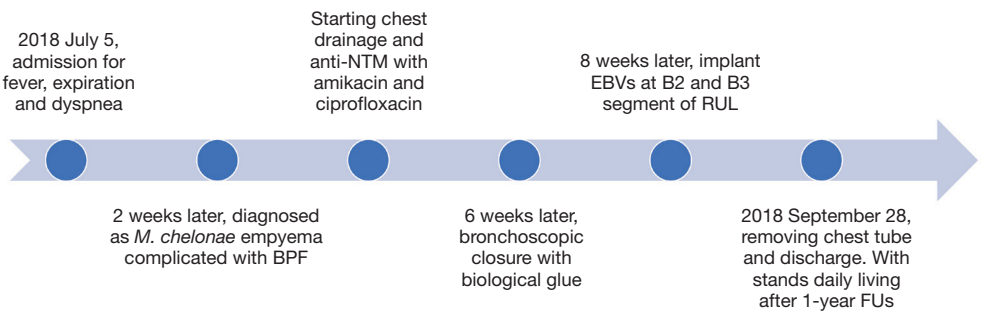

Figure 2 Timeline for diagnosis and therapy of BPF related to *M. chelonae* in case one. BPF, bronchopleural fistula; NTM, nontuberculosis mycobacteria; EBV, endobronchial valve; RUL, right upper lobe; FUs, follow-ups.

which was considered a new metastatic lesion of lung cancer. Smear samples obtained by endobronchial ultrasound-guided transbronchial fine-needle aspiration (EBUS-TBNA) confirmed the presence of cancer cells. His doctor advised him to undergo a pneumonectomy, and tissue histopathology revealed inflammatory granulomas in the mediastinal pleural membrane and an aggressive adenocarcinoma in the RUL of the lung ($rT_{2a}N_1M_0$, IIA). *M. chelonae* was confirmed in his lung lesion tissue by 16sRNA analysis. He was originally treated with amikacin and linezolid. Three months later, the chest CT showed an additional right hydro-pneumothorax (*Figure 3A*), and a chest tube was placed into the pleural

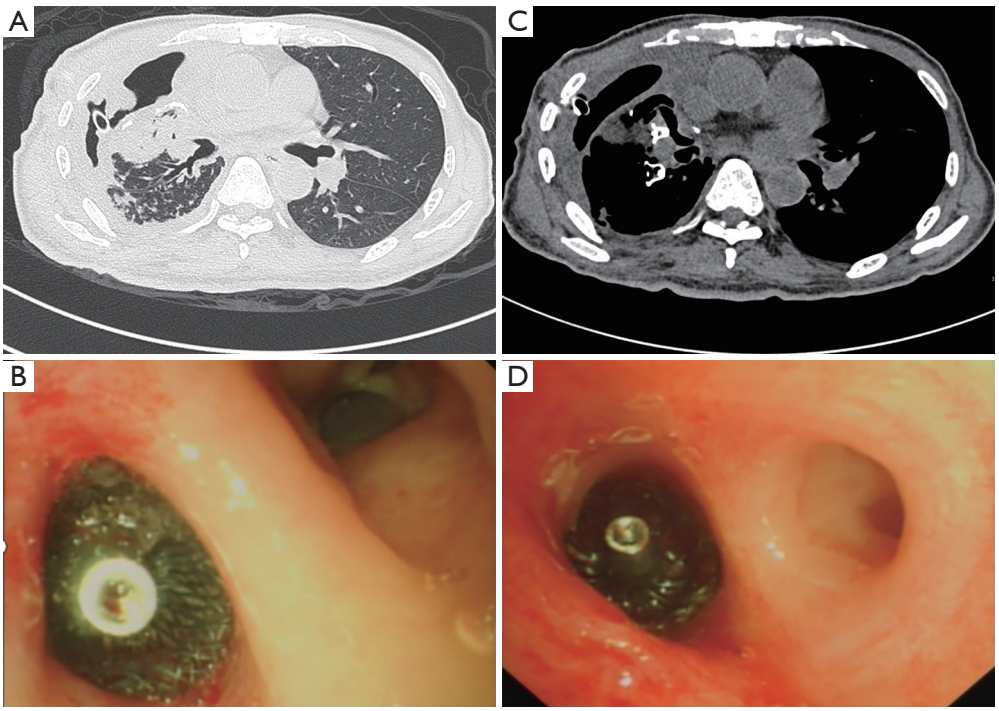

Figure 3 The chest CT scan and bronchoscopic view of BPF related to *M. chelonae* in the case two. The pulmonary window of the initial CT scan suggesting pneumonia, hydro-pneumothorax, and thoracic tube in the right lung (A). The mediastinal window of the CT scan showing two PDA occluders in the right B4 and B6 segments (B). A bronchoscopy view showing the two PDA occluders in the right B4a segment (C). A bronchoscopy view showing the two PDA occluders in the B6a+c (D). CT, computed tomography; BPF, bronchopleural fistula; PDA, patent ductus arteriosus.

cavity. However, a persistent air leak indicated a suspicious BPF. A multidisciplinary team evaluation was conducted involving a radiologist, physician, thoracic surgeon, and interventional pulmonologist. Finally, bronchoscopic interventional therapy was chosen as the patient was deemed inoperable. The suspected culprit bronchus was identified by instillation of methylene blue through a chest tube, and the Chartis monitoring system confirmed another fistulous tract located in the right B4a and B6a+c, with no bypass ventilation between them. The Amplatzer PDA device was used to manage the stump fistula. Using the 6F and 8F delivery systems, two PDA occluders (Heart RTM, Xianjian Technology (Shenzhen) Co., Ltd., China) were precisely released at the opening of the right B4a (XJFD0406) and B6a+c (XJFD0810) (*Figure 3B-3D*). No adverse event happened during the procedure.

Following this procedure, there was a dramatic reduction of air bubbles from the water-sealed bottle. His pleural drainage tube was removed successfully after 47 days. The patient's condition improved steadily and he continued on oral clarithromycin for 1 year after discharge. The whole process of diagnosis and treatment of BPF related to *M. chelonae* was outlined in *Figure 4*.

Literature review

To the best of our knowledge, to date, there have been no large-sample clinical trials to evaluate the therapeutic efficacy of applying bronchoscopic closure to BPF related to *M. chelonae*. The available reports include 5 studies with 6 patients (including the present study; *Table 1*). The underlying diseases were 2 cases of lung cancer, 1 case of esophageal cancer, 1 case of bronchiectasis, emphysema, and diabetes mellitus, and 3 cases with lobectomy. There were 3 males and 3 females, and the age of patients ranged from 39–86 years in all studies. All patients received antibiotic therapy, including clarithromycin. Two patients received open window thoracotomy, and three patients underwent endobronchial closure (including Gelfoam plug, EBV, and PDA occluder). Out of the 6 patients, 5 patients

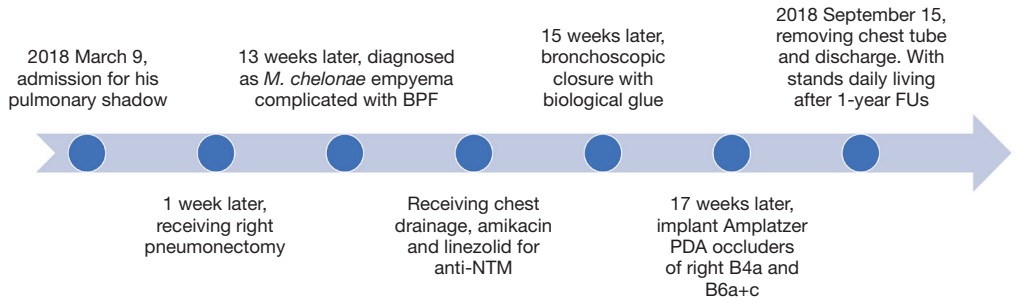

Figure 4 Timeline for diagnosis and therapy of BPF related to *M. chelonae* in case two. BPF, bronchopleural fistula; NTM, nontuberculosis mycobacteria; PDA, patent ductus arteriousus; FUs, follow-ups.

Table 1 Literature regarding M. chelonae empyema with bronchopleural fistula

Author, year (Ref.)	Patient's gender	Patient's age, years	Underlying disease	Therapy	Outcomes, adverse events
Opie JC, 1992 (3)	Female	64	Lung cancer, right upper lobectomy	Endobronchial closure (Gelfoam plug/thrombin), antibiotics	Successful, none
Takemoto N, 1996 (4)	Male	49	Esophageal cancer, right middle lobectomy	Open window thoracotomy antibiotics	Successful, none
Hsieh HC 2008 (5)	Female	53	None	Open window thoracotomy right middle lobectomy, antibiotics	Successful, none
Wali S, 2009 (6)	Female	39	Pulmonary tuberculosis	Clarithromycin, moxifloxacin and amikacin	Lost to follow-up, unknown
Case one	Male	86	Bronchiectasis, emphysema, diabetes mellitus	EBV, chest tube, antibiotics	Successful, none
Case two	Male	72	Lung cancer, right upper lobectomy	PDA occluders, chest tube antibiotics	Successful, none

Adverse events include bleeding, pneumothorax, tracheal tear, secondary infection, arrhythmia, etc. EBV, endobronchial valve; PDA, patent ductus arteriosus.

achieved successful fistula closures, and 1 patient was lost to follow-up. Firstly, our cases are different from four past reports, the patients in our study failed to close the BPFs by conservative antibiotics and chest tube drainage, and endobronchial biological glue administration. Secondly, our patients are elderly and impossible to tolerate surgery because of complicated underlying diseases, extremely terrible cardio pulmonary function and nutritional status. Thirdly, after evaluated by a multidisciplinary team, we innovatively applied bronchial interventional therapy to manage their BPF with empyema related to *M. chelonae* infection, and then one case was chosen EBVs and another with PDA occluders by tailoring patients condition carefully and judging comprehensively. Lastly but not least, we first reported a new approach to precisely locating the fistula, by combination with the advanced Chartis digital air leak monitoring system and conserve methods, such as CT scan and bronchoscopy view with methylene blue installation. Finally, the BPFs of our two patients has been solved completely and recovered quickly.

Discussion

RGM is widely distributed in the environment and can form colonies in less than one week. *M. abscessus* and *M. fortuitum* are the most common pathogens in pulmonary diseases related to RGM. However, *M. chelonae* empyema with BPF is rarely reported because *M. chelonae* commonly causes skin and soft tissue infections (7-9). A review of the relevant literatures revealed that advanced age, lobectomy, pulmonary tuberculosis, and immunosuppression are risk factors for acquiring these organisms. As *M. chelonae*

empyema complicated with BPF has rarely been reported, there is a paucity of data related to the management of the condition.

M. chelonae is characterized by high-level antimicrobial resistance and easy formation of biofilms, therefore it is a significant challenge to resolve *M. chelonae* empyema (10). In addition to underlying pulmonary diseases, patients with a deficiency of the interferon-gamma 1/2R-IL-12R-IL-23R pathway are also prone to non-tuberculosis mycobacterial infections. Persistent inflammation activated by *M. chelonae* infections can destroy lung tissues and induces BPF. Antibiotics are an important part of the therapeutic approach to *M. chelonae* empyema. Usually, *M. chelonae* is highly sensitive to tobramycin, clarithromycin, and linezolid, and moderately susceptible to imipenem and amikacin (11). Cefoxitin and imipenem are primarily recommended in the intensive phase (usually 3–4 months), while clarithromycin and amikacin are alternative drugs (12). According to guideline's recommendation, we chose clarithromycin plus amikacin to treat with the patients.

BPF is a pathological communication between the bronchial tree and pleural space. The principal etiologies include pneumonectomy, necrotizing pneumonia, tuberculosis, and advanced malignancy. Persistent air leak and empyema are the common clinical manifestations of BPF, severely decreasing a patient's quality of life and survival. The conventional treatments for BPF include conservative therapy, endoscopic techniques, and surgery (8). The American Thoracic Society (ATS) guideline (2017) recommends pneumonectomy as the curative treatment for empyema with BPF (13). Notably, an 18-month follow-up study showed that the Amplatzer occluder was effective in 96% of patients who cannot tolerate surgery (30/31) (14). A recent large case series study suggested that 80% of cases achieved removal of the chest tubes, and the median days of chest tube removal were shorter after the insertion of EBV (15). Therefore, bronchoscopic closure is a feasible and practical method to close the BPF.

In this case study, the BPF of neither patient could be closed by conservative drug treatment and bronchial bioglue. Considering the high surgical risks and the lack of any controlled studies offering alternative options, we innovatively applied endoscopic interventional therapy for *M. chelonae* empyema with BPF. Endoscopic intervention may be safer, more productive, and less invasive than surgery, especially for elderly patients with a declining condition. Our experiences suggested that two key steps are required to ensure successful endoscopic interventional therapy, including identifying the leak bronchus and selecting a suitable plugged material or device. Transbronchoscopic balloon exploration is the most common location method in clinical practice. However, it has some disadvantages including poor air seal and subjective judgment related to air leak (no objective data or charts to support), and the uncertainty regarding the abnormal communication in the trans-lobar segment. The Chartis system is mainly used for preoperative assessment of airway bypass ventilation. We applied the Chartis system to localize the target bronchus and predict postoperative efficacy. The Chartis system was combined with the negative pressure suction of closed thoracic drainage, and the target bronchus was identified according to the monitoring curve. We made a comprehensive judgement according to the three indicators, including breathing curve, airway pressure, and bubble overflow. Only when there is a single fistula and no bypass ventilation, will the system show a typical decreasing breathing curve, falling airway pressure curve, and the lack of air bubbles visible from the seal bottle. In our cases, the combination of CT scan and bronchoscopy view with the help of methylene blue installation and the Chartis digital air leak monitoring system was advantageous for precisely locating the fistula.

Considering case one with emphysematous regions and dynamic air trapping, we selected an one-way directional EBV because the patient might benefit from bronchoscopic lung volume reduction. In case two, the short length and large opening of the target bronchial lumen rendered the double-disc PDA occluder a more suitable plugging device because of its tight fixation with the bronchus. Furthermore, long-term effective antibiotic administration and chest tube drainage are the cornerstone therapies of BPF related to *M. chelonae* infection. Therefore, bronchoscopic intervention must be performed based on conventional thoracic drainage and antibiotic therapy. In addition, choosing the optimal endoscopic interventional option is crucial. The endoscopic device should be carefully tailored and chosen based on the size, position, and surrounding tissue of the fistula, the target bronchial characteristics, and the patient's underlying pulmonary diseases. Last, but not least, multidisciplinary team evaluation and comprehensive treatments are equally important. From all documented literatures, there were no adverse events in any of the three patients treated with endoscopic closure.

Conclusions

M. chelonae empyema complicated with BPF is a clinical

problem with high morbidity and mortality. These patients usually require long-term antibiotic regimen, thoracic drainage, and traditional surgery. This is the first well-documented report to demonstrate the therapeutic efficacy of the EBV or PDA occluder insertion, with the combined assistance of methylene blue and the Chartis digital air leak monitoring system for accurate positioning. This may be a novel, less invasive, and feasible option in the context of elderly, high-risk, inoperable patients.

Acknowledgments

The authors would like to thank the patients and their families, as well as the investigators of the Guangdong Provincial People's Hospital who were involved in this study. *Funding:* This study was supported by the National Natural Science Fund of China (No. 81970012), the Shanghai Wu Mengchao Medical Science Foundation of China (No. JJHXM-2019004), and the Key Research Projects of Science and Technology Plan of Guangdong Province of China (No. 81023072316). The funding bodies had no role in study design, collection, analysis, interpretation of data, or writing on the manuscript.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2130/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-2130/coif). All authors report that this study was supported by the National Natural Science Fund of China (No. 81970012), the Shanghai Wu Mengchao Medical Science Foundation of China (No. JJHXM-2019004), and the Key Research Projects of Science and Technology Plan of Guangdong Province of China (No. 81023072316). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Medical Research Ethical Committee of Guangdong Provincial People's Hospital (No. GDREC2019219A). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Mitchell JD. Surgical Treatment of Pulmonary Nontuberculous Mycobacterial Infections. Thorac Surg Clin 2019;29:77-83.
2. Inayama M, Shinohara T, Yoshida M, et al. Bronchopleural fistula following M. abscessus infection 11 years after lobectomy for lung cancer. Springerplus 2013;2:568.
3. Opie JC, Vaughn CC, Comp RA, et al. Endobronchial closure of a postpneumonectomy bronchopleural fistula. Ann Thorac Surg 1992;53:686-8.
4. Takemoto N, Kohiyama R, Tsuboi J, et al. A case of a patient with post-operative empyema due to Mycobacterium chelonae. Kyobu Geka 1996;49:301-5.
5. Hsieh HC, Lu PL, Chen TC, et al. Mycobacterium chelonae empyema in an immunocompetent patient. J Med Microbiol 2008;57:664-7.
6. Wali S. Mycobacterium chelonae empyema with bronchopleural fistula in an immunocompetent patient. Ann Thorac Med 2009;4:213-5.
7. Jones RS, Shier KL, Master RN, et al. Current significance of the Mycobacterium chelonae-abscessus group. Diagn Microbiol Infect Dis 2019;94:248-54.
8. Jones MM, Winthrop KL, Nelson SD, et al. Epidemiology of nontuberculous mycobacterial infections in the U.S. Veterans Health Administration. PLoS One 2018;13:e0197976.
9. Donohue MJ. Increasing nontuberculous mycobacteria reporting rates and species diversity identified in clinical

laboratory reports. BMC Infect Dis 2018;18:163.
10. Esteban J, García-Coca M. Mycobacterium Biofilms. Front Microbiol 2018;8:2651.
11. Akram SM, Rathish B, Saleh D. Mycobacterium Chelonae. In: StatPearls. Treasure Island (FL): StatPearls Publishing; September 20, 2021.
12. Dugan KC, Laxmanan B, Murgu S, et al. Management of Persistent Air Leaks. Chest 2017;152:417-23.
13. Shen KR, Bribriesco A, Crabtree T, et al. The American Association for Thoracic Surgery consensus guidelines for the management of empyema. J Thorac Cardiovasc Surg 2017;153:e129-46.
14. Fruchter O, El Raouf BA, Abdel-Rahman N, et al. Efficacy of bronchoscopic closure of a bronchopleural fistula with amplatzer devices: long-term follow-up. Respiration 2014;87:227-33.
15. Bermea RS, Miller J, Wilson WW, et al. One-Way Endobronchial Valves as Management for Persistent Air Leaks: A Preview of What's to Come? Am J Respir Crit Care Med 2019;200:1318-20.

Cite this article as: Liu X, Huang Z, Luo S, Yang S, Huang J, Chen P, Lin Q, Wu J. A novel therapeutic strategy to close bronchopleural fistula related to Mycobacterium chelonae in elderly patients: two case reports and literature review. Ann Transl Med 2022;10(10):615. doi: 10.21037/atm-22-2130

