Life-threatening *Mycobacterium intracellulare* pleuritis in an immunocompetent host

Case reports

Bo-Gun Kho, MD<sup>a</sup>, Young-Ok Na, MD<sup>a</sup>, Hwa Kyung Park, MD<sup>a</sup>, Jae-Kyeong Lee, MD<sup>a</sup>, Hyung-Joo Oh, MD<sup>a</sup>, Ha-Young Park, MD<sup>a</sup>, Tae-Ok Kim, MD<sup>a,b</sup>, Hong-Joon Shin, PhD<sup>a,b</sup>, Yong-Soo Kwon, PhD<sup>a,b</sup>, Yu-II Kim, PhD<sup>a,b</sup>, Sung-Chul Lim, PhD<sup>a,b</sup>

Abstract

**Rationale:** Nontuberculous mycobacteria (NTM)–associated pleuritis is a very rare disease. Here, we describe 2 cases of life-threatening *Mycobacterium intracellulare*-associated pleuritis in immunocompetent hosts.

**Patient concerns:** A 78-year-old man with sudden onset-onset dyspnea (case 1) and an 80-year-old man with cough, sputum and fever (case 2) presented to our emergency room.

**Diagnoses:** Both the patients were diagnosed with *Mycobacterium intracellulare*-associated pleuritis.

**Intervention:** In case 1, the patient underwent intubation with mechanical ventilation due to hypoxemic respiratory failure. Daily azithromycin, rifampin and ethambutol, and intravenous amikacin 3 times a week was administered. In case 2, the patient received daily azithromycin, rifampin and ethambutol, and intravenous amikacin 3 times a week.

**Outcomes:** In case 1, after receiving NTM treatment for 14 months, NTM-associated pleuritis was cured, with radiologic improvement. In case 2, however, bronchopleural fistula was developed. Despite tube drainage, air leak continued. The patient refused surgical management and eventually died of respiratory failure.

**Lessons:** Pleural effusion arising from NTM lung disease located in the subpleural area should be considered a possible cause of NTM-associated pleuritis. Drainage and a multidrug regimen are required to treat NTM, and surgical treatment should be considered when complications occur.

**Abbreviations:** NTM = nontuberculous mycobacteria, WBC = white blood cell.

**Keywords:** bronchopleural fistula, *Mycobacterium intracellulare*, pleuritis

1. Introduction

Nontuberculous mycobacteria (NTM) are a group of mycobacterium species other than *Mycobacterium tuberculosis* complex.

---

**Editor:** Maya Saranathan.

This study was supported by the National Research Foundation of Korea funded by the Korean Government (grant 2019R1F1A1060899).

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

<sup>a</sup> Department of Internal Medicine, Chonnam National University Hospital, Gwangju, Republic of Korea, <sup>b</sup>Chonnam National University Medical School, Gwangju, Republic of Korea.

<sup>*</sup> Correspondence: Hong-Joon Shin, Department of Internal Medicine, Chonnam National University Hospital, 42 Jebongro, Donggu, Gwangju 501-757, South Korea (e-mail: 99naussica@naver.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Kho BG, Na YO, Park HK, Lee JK, Oh HJ, Park HY, Kim TO, Shin HJ, Kwon YS, Kim YI, Lim SC. Life-threatening *Mycobacterium intracellulare* pleuritis in an immunocompetent host: case reports. Medicine 2021;100:51(e28342).

Received: 3 November 2021 / Received in final form: 25 November 2021 / Accepted: 1 December 2021

http://dx.doi.org/10.1097/MD.00000000000028342

---

**Mycobacterium leprae** and **Mycobacterium ulcerans.**<sup>[1]</sup> The most common spectrum of NTM disease is pulmonary disease accounting for about 90% of all NTM disease.<sup>[1]</sup> The incidence of NTM lung disease is increasing worldwide.<sup>[2–4]</sup> However, NTM-associated pleuritis remains very rare.<sup>[5–8]</sup> Here, we describe 2 cases of life-threatening *Mycobacterium intracellulare*-associated pleuritis in immunocompetent hosts.

2. Methods

This study was approved by the Institutional Review Board of the Chonnam National University Hospital (the number of approval: CNUH-EXP-2021-421). Written informed consent was obtained from each patient for publication of this case report and any accompanying images.

3. Case presentations

3.1. Case 1

A 78-year-old man presented to our emergency room with sudden-onset dyspnea. He was an ex-smoker with a 60 pack-year history. He also had a history of diabetes mellitus managed by medication and underwent spinal fusion surgery 10 years prior. He had recently undergone a bronchoscopic procedure to evaluate a cavitary lesion in the left lower lobe at a local clinic (Fig. 1A, B). He had taken antituberculous drugs empirically 7
days before presenting at the emergency room at the local clinic. He presented with a 1-day history of acute-onset fever, chills, purulent sputum, pleuritic chest pain, and dyspnea.

A physical examination revealed tachycardia at 120 beats/min. His blood pressure was 120/80 mm Hg, body temperature was 36.0°C, and respiratory rate was 28 breaths/min. A chest examination showed coarse crackles on the left lung.

The white blood cell (WBC) count was 9900/μL, with a neutrophil differential of 92.4%. The C-reactive protein level increased to 30.1 mg/dL (reference range, 0–0.6 mg/dL). Chest radiography and computed tomography revealed aggrading pneumonic consolidation and a cavity in the left lower lobe with a newly developed massive pleural effusion (Fig. 1C, D). On an arterial blood gas analysis, the partial pressure of oxygen was 97 mm Hg and partial pressure of carbon dioxide was 26 mm Hg through a face mask with 15 L/min of oxygen. The patient received tazobactam/piperacillin and underwent immediate pig-tail catheter insertion. A pleural fluid analysis revealed an exudate with a WBC count of 227700/mm³, neutrophil differential of 88%, lymphocyte differential of 10%, adenosine deaminase level of 179 IU/L, and pH of 5.0. The patient was admitted to the respiratory ward and continued treatment with antibiotics and drainage. However, on day 2, the patient was transferred to the intensive care unit and underwent intubation with mechanical ventilation due to acute hypoxic respiratory failure. We decided to insert a chest tube instead of a pig-tail catheter and change the antibiotics to meropenem and vancomycin.

On day 7, Mycobacterium intracellulare was identified at a local clinic in a specimen obtained via bronchial washing. The multidrug regimen consisting of daily azithromycin 250 mg, rifampin 600 mg, and ethambutol 800 mg and intravenous amikacin 1.0 g 3 times a week was administered to treat the M. intracellulare lung disease. A pleural fluid culture also revealed M. intracellulare. We conclude that the present empyema developed after rupture of the previous cavitary lung lesion associated with the M. intracellulare lung disease. We continued the anti-NTM treatment. Negative sputum culture conversion was achieved on day 27 of NTM treatment. On day 42, we removed the chest tube. On day 58, the patient was discharged home on long-term oxygen therapy. After 5 months of NTM treatment, azithromycin, rifampin, and ethambutol daily therapy were maintained without amikacin injections. The NTM treatment was finished after a total of 14 months (Fig. 2A). There was no evidence of NTM recurrence at 1 year after treatment completion (Fig. 2B).

### 3.2. Case 2

An 80-year-old man presented to our emergency room with a 5-day history of cough, sputum, and fever. He was an ex-smoker with a 30 pack-years history. He also had a history of hypertension treated with medication. Five months prior, he was diagnosed with *M. intracellulare* lung disease with a subpleural cavitary lesion in the right lower lobe (Fig. 3A, B). However, he refused treatment for the NTM lung disease.

His blood pressure was 100/60 mm Hg and body temperature was 37.5°C. His pulse rate was 83 beats/min and respiratory rate was 20 breaths/min. A chest examination showed coarse crackles on the right lung.

The WBC count was 18500/μL, with a neutrophil differential of 80.6%. The C-reactive protein level was increased to 11.0 mg/dL. Chest radiography and computed tomography revealed aggrading pneumonic consolidation and a cavity in the right lower lobe with a newly developed pleural effusion (Fig. 3C, D).

On the arterial blood gas analysis, the partial pressure of oxygen was 69 mm Hg and partial pressure of carbon dioxide was 25 mm Hg on room air.

The patient received tazobactam/piperacillin and underwent immediate thoracentesis. A pleural fluid analysis revealed an exudate with a WBC count of 2807/mm³, neutrophil differential of 39%, lymphocyte differential of 40%, adenosine deaminase 69.6 IU/L, and pH of 7.4. The patient was admitted to the respiratory ward and treatment with antibiotics and drainage was continued. The multidrug regimen consisting of daily azithromycin 250 mg, rifampin 600 mg, and ethambutol 800 mg and intravenous amikacin 1.0 g 3 times a week was administered to treat the *M. intracellulare* lung disease. A pleural fluid culture also revealed *M. intracellulare*. On day 11, a chest X-
Figure 3. Chest radiographs and computed tomography (CT) images of case 2. (A) and (B) Images obtained 5 months before presentation. (C) and (D) Images obtained at presentation to the emergency room. (A) Chest radiograph showing consolidations in the right lower lobe. (B) Chest CT images showing a subpleural cavitary lesion with perilobular consolidation in the right lower lobe. (C) Chest radiograph showing a pleural effusion with consolidation in the right hemithorax. (D) Chest CT image revealing an increased subpleural cavitary lesion and pleural effusion in the right hemithorax.

Figure 4. Chest radiographs showing (A) hydropneumothorax with pigtail catheter insertion in the right lung; and (B) hydropneumothorax with chest tube insertion in the right lung.

The pleuritis associated with NTM is rare. Ando et al reported that 15 cases (1.4%) of NTM pleuritis among 1044 patients with NTM lung disease. Park et al demonstrated 14 patients with NTM pleuritis in a 17-year retrospective study of the data of a single tertiary hospital. Naito et al and Yoon et al reported retrospective data of 12 patients over 15 years and 5 patients over 13 years in a single center each. The most common causative microorganism of NTM pleuritis is M. intracellulare. However, Ando et al reported that 9 of 15 patients with NTM pleuritis had M. avium infection. The infections in the 2 cases in this study were associated with M. intracellulare. The rate of treatment initiation due to the progression of NTM lung disease is higher in patients with M. intracellulare than in those with M. avium. Therefore, it is possible that M. intracellulare is a risk factor of the progression from NTM lung disease to pleuritis in cases of M. avium complex-associated lung disease. However, pleuritis associated with Mycobacterium abscessus complex, Mycobacterium chelonae, and Mycobacterium fortuitum has also been reported; therefore, further studies of the relationship between microorganisms and NTM pleuritis are required.

Although the mechanism of NTM pleuritis is unclear, 2 theories have been proposed: invasion from NTM lung disease to the pleura; and perforation of the NTM lung disease resulting in leakage into the pleural space. In this study, both cases had subpleural cavities before developing NTM pleuritis. After development of the pleural effusion, bronchopleural fistula occurred in case 2. These findings support the latter hypothesis that the pleuritis arose from perforation of the existing NTM lung disease.

The treatment regimens for M. avium complex-associated pleuritis have yet to be established. In this study, we treated the patients with a multidrug regimen consisting of azithromycin, rifampicin, and ethambutol and intravenous amikacin due to the advanced M. avium complex lung disease. Negative sputum culture conversion was achieved after 1 month (case 1) and 6 weeks (case 2) after the initiation of NTM treatment. Although the patient in case 1 required intubation with mechanical ventilation, the M. intracellulare diseases including lung disease and pleuritis were treated successfully without further complications. However, the patient in case 2 required a chest tube due to a complicated bronchopleural fistula. The patient in case 2 refused to undergo surgical treatment of the complicated bronchopleural fistula and eventually died of respiratory failure. Patients with NTM pleuritis often require surgical management. Naito et al reported that 7 of 12 patients with NTM-associated pleuritis required surgical management. Ando et al also reported that 6 of 15 patients with NTM-associated pleuritis required surgical treatment.

The treatment regimens for M. avium complex–associated pleuritis have yet to be established. In this study, we treated the patients with a multidrug regimen consisting of azithromycin, rifampicin, and ethambutol and intravenous amikacin due to the advanced M. avium complex lung disease. Negative sputum culture conversion was achieved after 1 month (case 1) and 6 weeks (case 2) after the initiation of NTM treatment. Although the patient in case 1 required intubation with mechanical ventilation, the M. intracellulare diseases including lung disease and pleuritis were treated successfully without further complications. However, the patient in case 2 required a chest tube due to a complicated bronchopleural fistula. The patient in case 2 refused to undergo surgical treatment of the complicated bronchopleural fistula and eventually died of respiratory failure. Patients with NTM pleuritis often require surgical management. Naito et al reported that 7 of 12 patients with NTM-associated pleuritis required surgical management. Ando et al also reported that 6 of 15 patients with NTM-associated pleuritis required surgical treatment.

5. Conclusion

Pleural effusion arising from NTM lung disease located in the subpleural area should be considered the possible cause of NTM-associated pleuritis. Drainage and multidrug regimen for NTM treatment are required, and surgical treatment should be considered in cases with complications.


Author contributions

Conceptualization: Hong-Joon Shin.
Data curation: Bo-Gun Kho, Young-Ok Na, Hwa Kyung Park, Jae-Kyeong Lee, Hyung-Joo Oh.
Formal analysis: Ha-Young Park, Tae-Ok Kim, Yong-Soo Kwon, Yu-Il Kim, Sung-Chul Lim.
Funding acquisition: Hong-Joon Shin.
Resources: Young-Ok Na, Hwa Kyung Park, Jae-Kyeong Lee, Hyung-Joo Oh, Ha-Young Park, Tae-Ok Kim.
Supervision: Yong-Soo Kwon, Yu-Il Kim, Sung-Chul Lim.
Validation: Yong-Soo Kwon, Yu-Il Kim, Sung-Chul Lim.
Writing – original draft: Bo-Gun Kho.
Writing – review & editing: Bo-Gun Kho, Hong-Joon Shin.

References

[1] Daley CL, Iaccarino JM, Lange C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. Eur Respir J 2020;56:1–43.
[2] Hoefsloot W, van Ingen J, Andrejak C, et al. The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples: an NTM-NET collaborative study. Eur Respir J 2013;42:1604–13.
[3] Kendall BA, Winthrop KL. Update on the epidemiology of pulmonary nontuberculous mycobacterial infections. Semin Respir Crit Care Med 2013;34:87–94.
[4] Kwon YS, Koh WJ. Diagnosis of pulmonary tuberculosis and nontuberculous mycobacterial lung disease in Korea. Tuberc Respir Dis (Seoul) 2014;77:1–5.
[5] Naito M, Maekura T, Kurahara Y, et al. Clinical features of nontuberculous mycobacterial pleurisy: a review of 12 cases. Intern Med 2018;57:13–6.
[6] Ando T, Kawashima M, Matsui H, et al. Clinical features and prognosis of nontuberculous mycobacterial pleuritis. Respiration 2018;96:507–13.
[7] Park S, Jo KW, Lee SD, Kim WS, Shim TS. Clinical characteristics and treatment outcomes of pleural effusions in patients with nontuberculous mycobacterial disease. Respir Med 2017;133:36–41.
[8] Yoon HJ, Chung MJ, Lee KS, Kim JS, Park HY, Koh WJ. Bronchopleural fistula with hydro pneumothorax at CT: diagnostic implications in mycobacterium avium complex lung disease with pleural involvement. Korean J Radiol 2016;17:295–301.
[9] Wen P, Wei M, Xu YR, Dong L. Clinical relevance and characteristics of nontuberculous mycobacterial pleuritis. Jpn J Infect Dis 2020;73:282–7.
[10] Moon SM, Jhun BW, Baek SY, et al. Long-term natural history of noncavitary nodular bronchiectatic nontuberculous mycobacterial pulmonary disease. Respir Med 2019;151:1–7.
[11] Koh WJ, Jeong BH, Jeon K, et al. Clinical significance of the differentiation between Mycobacterium avium and Mycobacterium intracellulare in M avium complex lung disease. Chest 2012;142:1482–8.
[12] Fabbian F, De Giorgi A, Pala M, Fratti D, Contini C. Pleural effusion in an immunocompetent woman caused by Mycobacterium fortuitum. J Med Microbiol 2011;60:1375–8.
[13] Hsieh HC, Lu PL, Chen TC, Chang K, Chen YH. Mycobacterium chelonae empyema in an immunocompetent patient. J Med Microbiol 2008;57:664–7.
[14] Fairhurst RM, Kubak BM, Shpiner RB, Levine MS, Pegues DA, Ardehali A. Mycobacterium abscessus empyema in a lung transplant recipient. J Heart Lung Transplant 2002;21:391–4.
[15] Kotani K, Hirose Y, Endo S, Yamamoto H, Makihara S. Surgical treatment of atypical Mycobacterium intracellulare infection with chronic empyema: a case report. J Thorac Cardiovasc Surg 2005;130:907–8.
[16] Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175:367–416.