


CASE REPORT

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Mycobacterium abscessus ssp. *abscessus* infection progressing to empyema from vertebral osteomyelitis in an immunocompetent patient without pulmonary disease: a case report

Naaki Kadota¹, Tsutomu Shinohara^{2*} , Hiroyuki Hino³, Yuichiro Goda⁴, Yoshiro Murase⁵, Satoshi Mitarai⁵ and Fumitaka Ogushi¹

Abstract

Background: Pleural involvement by non-tuberculous mycobacteria (NTM) in patients without distinct pulmonary disease is extremely rare. Vertebral osteomyelitis (VO) with or without pulmonary disease is also a rare clinical presentation of NTM infection, and pleural spread of NTM from VO has not been reported.

Case presentation: A 63-year-old woman was admitted to our hospital with back pain persisting for 4 months and a 2-day history of fever and right chest pain. The patient was initially treated as right-sided empyema due to general bacteria. However, after removal of the chest tube, a previously overlooked paravertebral lesion was observed on CT. MRI confirmed VO at T7/8. *Mycobacterium abscessus* ssp. *abscessus* was detected in both the thoracic cavity and the paravertebral lesion. Both VO and the paravertebral abscess were improved by antimycobacterial treatment.

Conclusion: VO of the thoracic spine due to non-tuberculous mycobacterial infection should be considered as a cause of pleuritis or empyema without pulmonary disease, especially in patients with back pain.

Keywords: *Mycobacterium abscessus* ssp. *abscessus*, Vertebral osteomyelitis, Empyema

Background

Mycobacterium abscessus (*M. abscessus*) ssp. *abscessus*, a rapidly growing species of non-tuberculous mycobacteria (NTM), is well-known as a pathogen of the skin, soft tissues, bone, and lungs [1–3]. NTM, especially *M. avium-intracellulare* complex (MAC), occasionally causes pleuritis or empyema, probably due to direct spread from pulmonary lesions [4–9]. However, pleural involvement without distinct pulmonary disease is extremely rare, with only a few cases in the literature, and primary pleural disease due to *M. abscessus* ssp. *abscessus* has not been reported [10–13].

Vertebral osteomyelitis (VO) with or without pulmonary disease is also a very rare clinical presentation of NTM infection, including that caused by *M. abscessus* complex [14–18]. Approximately half of all VO develops in immunocompetent patients and most frequently affects the thoracic spine [14]. According to a recent hypothesis, “locus minoris resistentiae” after noninvasive trauma may be a risk factor for VO, i.e., macrophages containing NTM migrate to the site of injury and release the mycobacteria to initiate a new focus of infection [16]. However, pre-disposing trauma or surgery is not reported in 85% of patients with VO [14]. Here we report a very unusual case of *M. abscessus* ssp. *abscessus* infection that presented as empyema without distinct pulmonary disease and was found to arise from VO.

* Correspondence: shinohara.tsutomu.kg@mail.hosp.go.jp

²Department of Clinical Investigation, National Hospital Organization Kochi Hospital, 1-2-25 Asakuranishimachi, Kochi 780-8077, Japan
Full list of author information is available at the end of the article



Case report

A 63-year-old woman was admitted to our hospital with back pain persisting for 4 months and a 2-day history of fever and right chest pain. On admission, her height and weight were 154 cm and 50 kg, respectively. She had no history of other diseases, including autoimmune disease, diabetes, bronchiectasis, old healed tuberculosis, trauma, or acupuncture. The patient had visited two other hospitals, where contusion of the thoracic spine had been diagnosed by MRI (two months before admission) and contrast CT (three weeks before admission) (Fig. 1a, b), despite no history of trauma. She had received symptomatic therapy with an anti-inflammatory agent from both hospitals, but her back pain had persisted.

Initial laboratory data included a white blood cell count of 7580/ μ l (85.0% neutrophils) and a C-reactive protein of 8.26 mg/dl. CT showed a right-sided pleural effusion (Fig. 1c). Right pleuritis was diagnosed and the patient was treated with ampicillin/sulbactam for 11 days, but this was not effective (Fig. 1d). She subsequently underwent thoracoscopic curettage followed by drainage of pus from the pleural cavity for 7 days using 22 and 24 Fr double lumen trocars, and administration of cefoperazone/sulbactam for the same period (Fig. 1e). General bacterial culture of pus obtained at surgery was negative, but culture for acid-fast bacteria (mycobacteria growth indicator tube (MGIT) system; BACTEC MGIT 960) proved to be positive after the 7-day treatment period. The pathogen was identified as *M. abscessus*

complex by DNA-DNA hybridization [19], and was confirmed to be *M. abscessus* ssp. *abscessus*, but not *M. abscessus* ssp. *massilense* or *M. abscessus* ssp. *bolletii* [20], by multiplex PCR [21] and *rpoB* sequence analysis [22]. Since there was no previous report of primary empyema due to *M. abscessus* ssp. *abscessus* and the patient had no underlying disease suggesting a source of infection, the result was considered to represent contamination and further treatment was not provided. However, CT performed one month later revealed progression of a previously overlooked paravertebral lesion to involve the lung (Fig. 1f). *M. abscessus* ssp. *abscessus* was detected from lavage fluid of the paravertebral lesion recovered by bronchoscopic examination. Two months after admission (5 weeks after initial detection of *M. abscessus* ssp. *abscessus*), treatment with imipenem/cilastatin (IPM/CS: 1 g/day i.v.), amikacin (AMK: 400 mg/day i.v.), and clarithromycin (CAM: 800 mg/day p.o.) was initiated based on a diagnosis of VO due to *M. abscessus* ssp. *abscessus*, with paravertebral abscess caused by direct spread. An antibiotic susceptibility test was performed with air-dried microplates containing serial dilutions of antimicrobial agents and modified Middlebrook 7H9 broth [23], revealing that the minimum inhibitory concentration (MIC) of CAM for the pathogen was 0.25 μ g/ml on day 3 and 1.0 μ g/ml on day 14. These data indicated that the pathogen remained susceptible to CAM (MIC \leq 2.0 μ g/ml on days 3 and day 14) and did not develop inducible resistance (susceptible on day 3 with

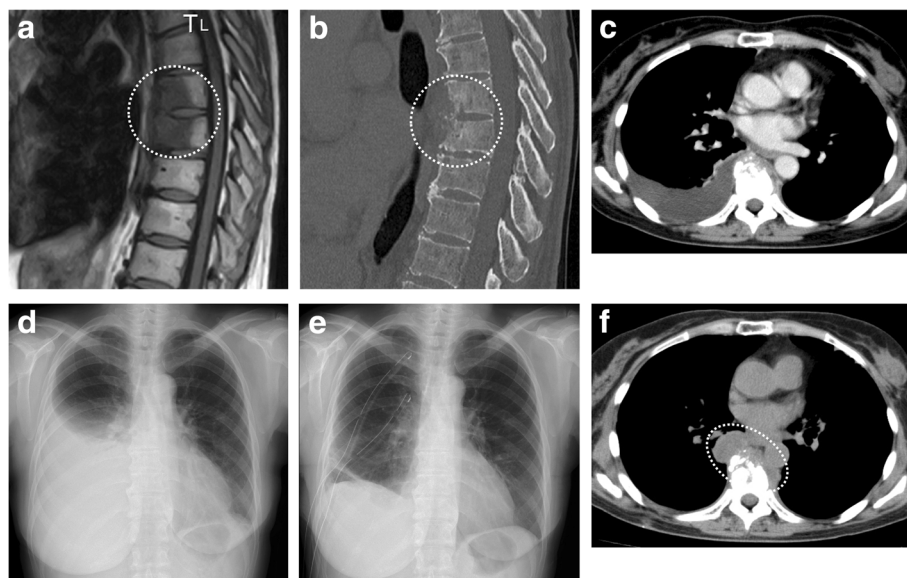


Fig. 1 Imaging findings before antimycobacterial treatment (**a** T1-weighted spinal MRI obtained 2 months before admission, **b** spinal CT obtained 3 weeks before admission, **c** enhanced chest CT scan on admission, **d** chest X-ray film after treatment with ampicillin/sulbactam for 11 days, **e** chest X-ray film during chest drainage and administration of cefoperazone/sulbactam following thoracoscopic curettage, **f** chest CT scan one month after chest tube removal). Spinal MRI and CT detected a T7/8 vertebral lesion (circled). Chest drainage achieved satisfactory re-expansion of the right lung. After removal of the chest tube, a paravertebral lesion was detected on CT (circled)

MIC ≥ 8.0 $\mu\text{g/ml}$ at day 14), according to the Clinical Laboratory Standards Institute Guideline [24, 25].

After continuation of treatment for three months, both the MRI-confirmed VO and the paravertebral abscess showed improvement (Fig. 2a, b, d, e, g, h), so she was switched to oral antibiotic therapy (faropenem (FRPM) 600 mg/day, levofloxacin (LVFX) 500 mg/day, and CAM 800 mg/day). After that, further improvement was observed and the antimycobacterial treatment was completed within 2 years (Fig. 2c, f, i). No other combination therapy was administered during this period. No evidence of recurrence has been detected during follow-up for 4 months after the end of treatment.

Discussion and conclusions

In patients with pleural involvement alone, the main pathway by which NTM reaches the thoracic cavity is thought to be direct discharge of an undetectable subpleural caseous focus into the pleural space [10]. However, early *M. abscessus* complex pulmonary disease is generally of the nodular bronchiectatic type, so a subpleural caseous focus is an uncommon incipient lesion of *M. abscessus* complex infection compared to MAC infection [26]. In our patient, the VO was considered to be the initial focus of infection for the following reasons. First, empyema occurred after vertebral abnormality was detected on imaging studies at previous hospitals. Second,

M. abscessus ssp. *abscessus* was not only isolated from the thoracic cavity, but also from the paravertebral abscess. The reason for non-recurrence of empyema was considered to be postoperative pleural adhesion induced by thoracoscopic curettage and subsequent drainage. Third, although vertebral biopsy was not performed, the paravertebral abscess and vertebral lesion both improved simultaneously with antimycobacterial treatment, suggesting that VO was also caused by *M. abscessus* ssp. *abscessus* infection. According to a review of 13 cases of pyogenic spondylitis with exudative pleural effusion, *Staphylococcus aureus* was the major pathogen [27]. To the best of our knowledge, this is the first reported case of NTM with a similar clinical presentation to those cases. Although there was no clear history of pre-disposing trauma, “locus minoris resistentiae” may have been the mechanism of underlying VO, since our patient had no peripheral pulmonary lesion.

Her treatment (IPM/CS 1 g/day, AMK 400 mg/day and CAM 800 mg/day followed by FRPM 600 mg/day, LVFX 500 mg/day and CAM 800 mg/day) was selected on the basis of drug sensitivity data for *M. abscessus* ssp. *abscessus* obtained in Japanese patients and a report on a patient successfully treated with this regimen [3, 28, 29]. Standard criteria have not been established for terminating treatment of *M. abscessus* ssp. *abscessus* infection, but the patient preferred to stop medication when the lesion

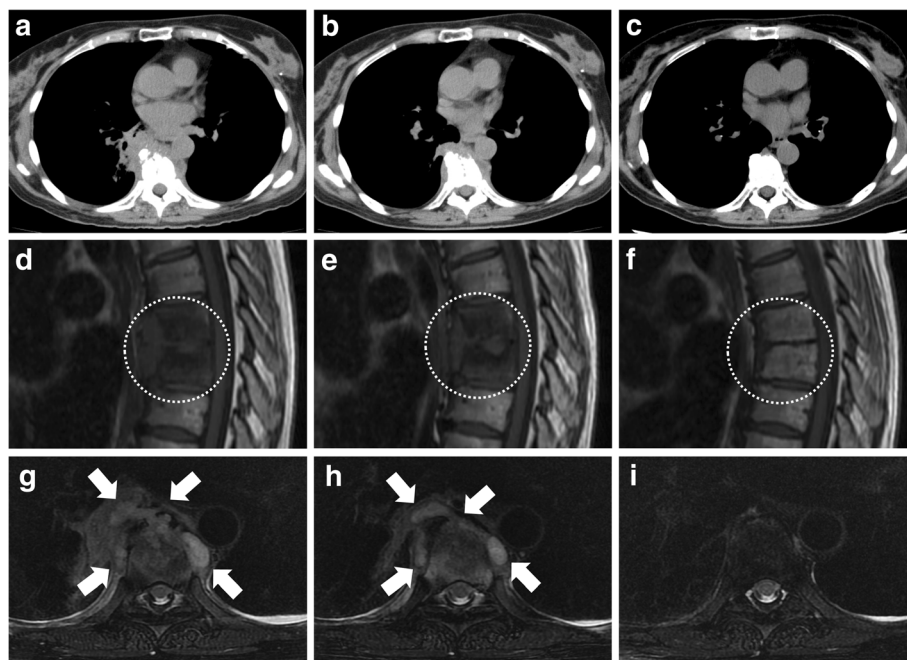


Fig. 2 Chest CT scans (a–c) and spinal MRI (d–f T1-weighted, g–i fat-suppressed T2-weighted) obtained after initiation of antimycobacterial treatment (a, d and g at 1 month, b, e and h at 3 months, c, f and i at 2 years). Both the VO (bone destruction on CT and low signal on T1-weighted MRI (circled)) and the abscess (paravertebral lesion on CT and high signal on fat-suppressed T2-weighted MRI (arrow)) improved gradually over 2 years

almost resolved on imaging. In recent years, it has been suggested that inducible and acquired resistance to CAM are the main causes of treatment-refractory *M. abscessus* ssp. *abscessus* pulmonary disease [25, 30–32]. Inducible macrolide resistance (susceptible on day 3 but resistant on day 14) is a natural trait of *M. abscessus* spp. *abscessus* due to ribosomal methyl transferase gene *erm(41)*. However, T/C polymorphism occurs at position 28 of *erm(41)* and C28 strains usually lose *erm(41)* function, resulting in susceptibility to macrolides [32]. Although genetic analyses were not performed, the isolate from our patient was susceptible and did not show inducible resistance to CAM. On the other hand, acquired macrolide resistance develops during treatment, and is associated with mutations of the *rml* gene region encoding the peptidyl-transferase domain of the 23S rRNA [25, 32]. Because no acid-fast bacteria were detected in our patient after the start of macrolide treatment, it is unknown whether there was a change in susceptibility of *M. abscessus* ssp. *abscessus* to CAM. However, the good clinical course of our patient makes it unlikely that acquired resistance to CAM developed during the treatment period.

Delayed diagnosis of spinal disease may lead to neurologic complications. Accordingly, VO of the thoracic spine due to NTM infection should be considered as a cause of pleuritis or empyema in patients without pulmonary disease, especially when back pain is present.

Abbreviations

AMK: Amikacin; CAM: Clarithromycin; FRPM: Faropenem; IPM/CS: Imipenem/cilastatin; LVFX: Levofloxacin; MAC: *Mycobacterium avium-intracellulare* complex; MIC: Minimum inhibitory concentration; NTM: Non-tuberculous mycobacteria; VO: Vertebral osteomyelitis

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Availability of data and materials

All data supporting our findings is contained within the manuscript.

Authors' contributions

NK drafted the initial manuscript. TS edited and submitted the manuscript. HH and YG were involved in diagnosing and treating the patient. YM and SM performed molecular genetic studies. FO was the attending physician throughout the disease. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval to report this case was not required.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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Author details

¹Division of Pulmonary Medicine, National Hospital Organization Kochi Hospital, 1-2-25 Asakuranishimachi, Kochi 780-8077, Japan. ²Department of Clinical Investigation, National Hospital Organization Kochi Hospital, 1-2-25 Asakuranishimachi, Kochi 780-8077, Japan. ³Division of Thoracic Surgery, National Hospital Organization Kochi Hospital, 1-2-25 Asakuranishimachi, Kochi 780-8077, Japan. ⁴Division of Orthopaedic Surgery, National Hospital Organization Kochi Hospital, 1-2-25 Asakuranishimachi, Kochi 780-8077, Japan. ⁵Department of Mycobacterium Reference and Research, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, 3-1-24 Matsuyama, Kiyose, Tokyo 204-8533, Japan.

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