CASE REPORT

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Environmental intervention for two cases of non-tuberculous mycobacterial disease

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ABSTRACT

Non-tuberculous *Mycobacterium avium* complex (MAC) disease is caused by inhalation of water or soil dust containing MAC bacteria. Treatment of MAC disease should include not only drug treatment, usually a three-drug regimen consisting of a macrolide, ethambutol, and a rifamycin, but also environmental intervention. However, there is no standardized approach to environmental evaluation or remediation of potentially harmful exposures from potting soils in home or workplace environments for patients with non-tuberculous mycobacterial infection. We present two patients with MAC disease who were positive for anti-MAC antibodies but had no culturable mycobacteria in sputum. One patient discontinued gardening, and the other patient moved her many indoor plants outside. Both patients subsequently had decreased sputum, and subsequent chest computed tomography showed decreased ground-glass opacities, consolidation, and small nodules. Environmental intervention may therefore be sufficient treatment for mild MAC disease.

Keywords: soil microbe, non-tuberculous mycobacterial infection (NTM), non-tuberculous *Mycobacterium avium* complex (MAC), environmental intervention, non-drug therapy

Abbreviations:
CT: computed tomography
MAC: *Mycobacterium avium* complex
NTM: Non-tuberculous mycobacteria

INTRODUCTION

Non-tuberculous mycobacteria (NTM) are widely distributed in water and soil in the natural environment.[1] Transmission of NTM from the environment to humans occurs through the inhalation of NTM from water aerosols or soil dust.

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Pulmonary NTM disease increased from 2–4 cases per 100,000 person-years before 2000 to 14.7 cases per 100,000 person-years in 2014. The incidence of pulmonary *Mycobacterium avium* complex (MAC) disease, which can be caused by either *M. avium* or *M. intracellulare*, was especially notable compared with *M. kansasii* and *M. abscessus* disease (13.1, 0.6, and 0.5 cases per 100,000 person-years, respectively).[2] The ratio of pulmonary *M. avium* disease to MAC was higher in the northern and eastern parts of Japan, whereas the ratio of pulmonary *M. intracellulare* disease to MAC was higher in the southern and western parts of Japan.[2]

Guidelines from the American Thoracic Society/European Respiratory Society/European Society of Clinical Microbiology Infectious Disease/Infectious Diseases Society of America (ATS/ERS/ESCMID/IDSA) suggest a three-drug regimen consisting of a macrolide, ethambutol, and a rifamycin to treat MAC disease.[3] The goal of treatment includes both clinical and radiologic improvement and achievement of negative sputum cultures whilst limiting treatment-associated adverse effects. Retrospective studies have reported sputum conversion rates of 75–86% with macrolide-containing regimens,[4,5] and 54–87% after 12 to 24 months of a multidrug regimen.[6]

Continuing treatment for 15 months or more after sputum conversion reduces the relapse rate.[7] To reduce the risk of death, the total treatment period for MAC disease should be at least 18 months.[8] It is important to follow patients undergoing long-term treatment for MAC for adverse effects. Although multidrug therapy is effective in sputum conversion, the long treatment period and high patient burden due to the side effects of the drugs[9] causes 13.5% of patients to discontinue treatment.[10]

Treatment of MAC disease should include not only drug treatment but also environmental intervention,[11] because most reinfections come from repeated environmental exposures. An effort should be made by susceptible patients to reduce environmental exposures to NTM, which can be found in house dust[12]; garden soils[13,14]; water sources such as showerheads,[15] sink faucets,[16] and hot tubs[17]; continuous positive airway pressure machines[18]; and humidifiers.[19] Environmental interventions are to remove and clean showerheads, remove any humidifiers, and avoid dusts from potting soils by wetting the potting soil or wearing a mask.[20] However, there is no standardized approach to environmental evaluation or remediation of potentially harmful exposures from potting soils in home or workplace environments for patients with NTM.

In this report, we describe two cases of clinically diagnosed pulmonary MAC disease. These cases were managed without drug therapy because environmental guidance regarding soil was considered useful.

CASE PRESENTATION

Case 1

A 67-year-old woman presented at our hospital with a 7-month history of cough and sputum. An abnormality on chest X-ray had been detected during a medical checkup at her workplace in October of the previous year, but she did not undergo a medical examination because she had no symptoms. Her sputum and cough began the following April, and she visited our hospital in November. Appendicitis surgery was her only notable medical history. She had never experienced pneumonia, tuberculosis, or asthma, but she was an ex-smoker of 19 pack-years. Her occupation was nursing care. One of the most characteristic features of her life history is that she enjoys gardening and grew vegetables in her field. Her bath is not a circulatory system. At the first visit, she was 156.0 cm tall, weighed 40.0 kg, and had a body mass index (BMI) of 16.4. Her temperature was 36.0 °C, heart rate was 82 beats/min, blood pressure was 151/71 mmHg, and oxygen saturation (SpO2) was 96% in room air. Breath sounds were heard as coarse crackles in the bilateral anterior thoracic regions. A blood test showed 10,400 white blood cells/μL, C-reactive protein 2.32 mg/dL, blood sedimentation rate 74 mm/h (normal range <10–15 mm/h), 91.0 mm in 120 min (normal range <25–40 mm/h), anti-MAC antibody 4.7 U/mL (normal range <0.7 U/mL), and tuberculosis polymerase chain reaction (PCR) was negative. A chest X-ray at her first hospital visit showed consolidation and small nodules present in the right and left upper and middle lung fields (Figure 1). Chest computed tomography (CT) showed consolidation, ground-glass opacities (GGO), and nodules in the right and left upper lobes (Figure 2a, b). There was a thin-walled cavity at the periphery of the lingular segment of the left lung (Figure 2c). Bronchiectasis was present in the left upper lobe (Figure 2a), right middle lobe, lingular segment of the left lung, and left lower lobe (Figure 2d). The images showed a tree-in-bud appearance in the middle lobe (Figure 2c, d). Sputum was found in the dilated bronchi (Figure 2d).

We suspected NTM and examined a sputum mycobacterial culture test four times on different days, and the cultures were negative all four times, so no pharmacological intervention for MAC disease was indicated. We suggested that she discontinue gardening, growing vegetables, and other activities in the soil and clean her bathroom and showerhead. After she stopped gardening, her sputum and cough gradually decreased and disappeared. Her chest CT 1 year after the environmental intervention showed that the consolidation and nodules in the right and left upper (Figure 3a, b) and lower (Figure 3c, d) lobes had decreased. Some consolidation had changed to GGO (Figure 3a) since the pre-intervention CT (Figure 2a, b). The walls of the dilated bronchi in the middle lobe and lingular segment became thinner and the granular opacities decreased (Figure 3d). The thin-walled cavity shadow seen on the CT scan in the previous year had disappeared (Figure 3c).

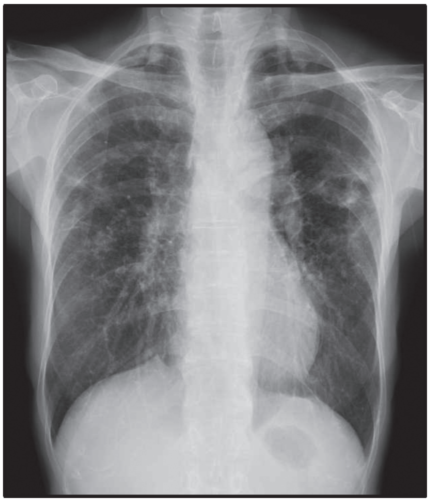

Fig. 1 Chest radiography on first presentation to the hospital in the patient in Case 1
Consolidation and small nodules are present in the right and left upper and middle lung fields.

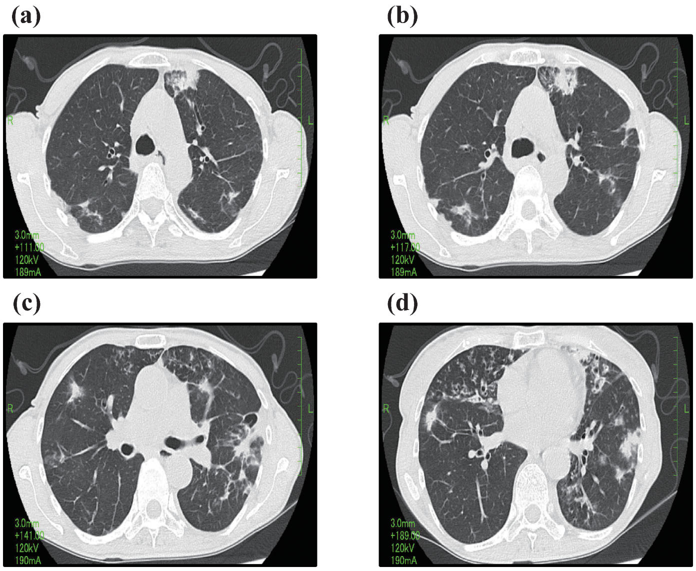

Fig. 2 Computed tomography of the chest during the first hospital visit of the patient in Case 1
Upper lobes (a, b); lower lobes (c, d). Consolidation, ground-glass opacities, and nodules are present in the right and left upper lobes (a, b). There is a thin-walled cavity at the periphery of the lingular segment of the left lung (c). Bronchiectasis is present in the left upper lobe (a) and in the middle lobe, lingular segment of left lung, and left lower lobe (d). The images show a tree-in-bud appearance in the middle lobe (c, d). Sputum can be seen in the dilated bronchi (d).

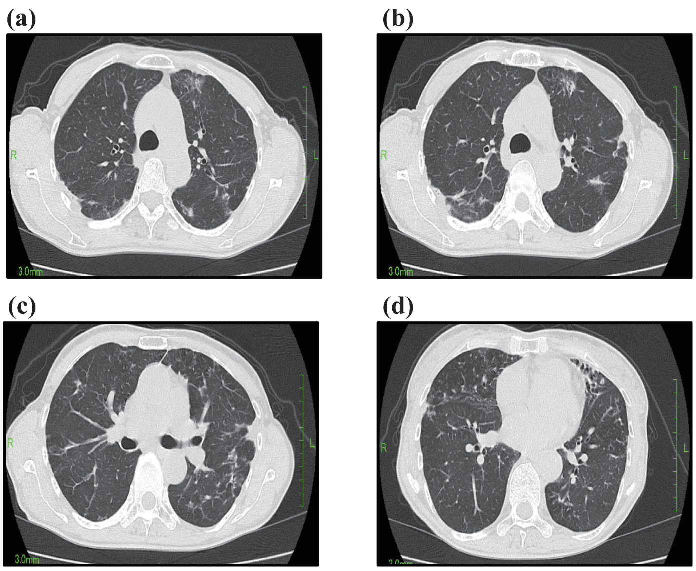

Fig. 3 Computed tomography of the chest 1 year after environmental intervention in the patient in Case 1
Upper lobes (a, b); lower lobes (c, d). Ground glass opacities and nodules are present in the right and left upper lobes (a, b). The thin-walled cavity shadow seen on the CT scan the previous year has disappeared (c), and the consolidation has shrunk to be barely visible. Bronchodilation is evident in the middle lobe and lingular segment, but there is only a small amount of sputum in the bronchi (d).

Case 2

The patient was a 72-year-old woman with a history of hypertension and hyperlipidemia who had experienced chronic sputum and cough for several years. She did not have a circulatory bath but did enjoy working in her garden and had 16 pots of houseplants in her bedroom.

In September, she had an increase of sputum and was treated with 100 mg of sitafloxacin hydrate for ten days in a clinic, but the sputum did not decrease, and she had consolidation in her left lung fields on chest X-ray. She was referred to our hospital in same month. At presentation, she was 158.0 cm tall and weighed 53.0 kg, giving a BMI of 21.2. Her temperature was 36.6 °C, heart rate was 75/min, blood pressure was 158/88 mmHg, and SpO2 was 95% in room air. We confirmed coarse crackles among her chest sounds.

A chest X-ray showed nodules and linear opacities in the right middle lung field, consolidation in the right lower lung field, and GGO in the left lower lung field (Figure 4). Atelectasis had formed in the peripheral lingular area of the left lung. Blood findings were as follows: white blood cells 10,800/μL, C-reactive protein 0.57 mg/dL, blood sedimentation rate 37.0 mm/h (>10–15 mm) and 61.0 mm/2h (>25–40 mm), anti-MAC antibody 2.9 U/mL, and tuberculosis PCR was negative. Chest CT images at the time of initial examination showed consolidation in contact with the pleura in the right upper lobe (Figure 5a), GGO and consolidation in the middle lobe and lingular area (Figure 5b, c), dilated bronchi (Figure 5c) and a nodular shadow in the right middle lobe (Figure 5d), and atelectasis in the left lingular segment (Figure 5d). We suspected NTM, but two sputum mycobacterial culture tests were negative.

We recommended that she move all 16 pots of indoor plants outside as an environmental intervention to treat NTM, which she promptly did. Immediately after the environmental intervention, she noticed a decrease in sputum production. After 2 weeks, her sputum disappeared, and none could be collected for a third culture.

A CT exam 7 months after the environmental intervention showed that the consolidation in the upper lobe and in the middle and lingular segments that had been seen on CT at the time of the initial examination had disappeared (Figure 6a-d), as had the atelectasis in the left lingular segment (Figure 6d). Slight granular shadows were observed in the middle lobe and lingular region (Figure 6d). The patient has been followed up by her primary care physician and her symptoms have not flared up again.

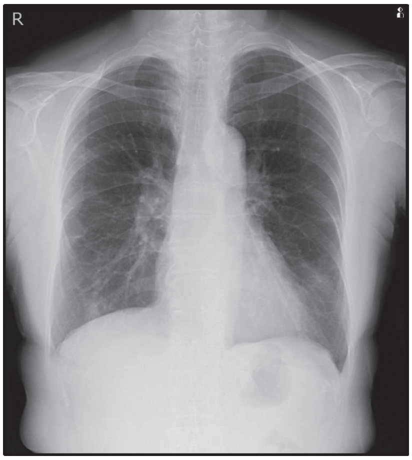

Fig. 4 Chest radiography on first presentation to the hospital of the patient in Case 2
Nodules and linear opacities are present in the right middle lung field, consolidation in the right lower lung field, and ground glass opacities in the left lower lung field.

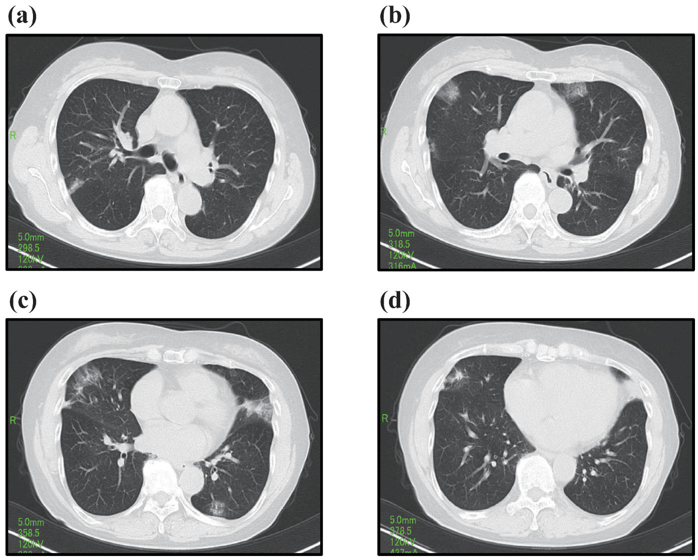

Fig. 5 Computed tomography of the chest during the first hospital visit of the patient in Case 2
Upper lobes (a, b); lower lobes (c, d). Consolidation is visible in contact with the pleura in the right upper lobe (a), ground glass opacities and consolidation in the middle lobe and lingular area (b, c), dilated bronchi (c) and a nodular shadow in the right middle lobe (d), and atelectasis in the left lingular segment (d).

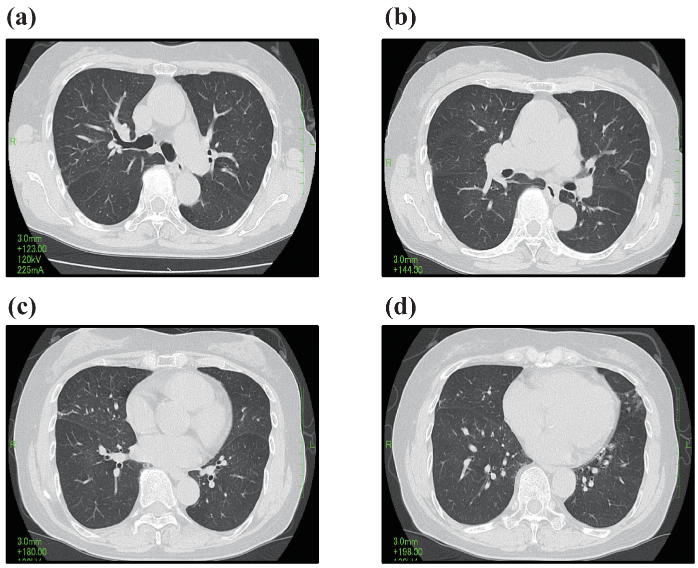

Fig. 6 Computed tomography of the chest 7 months after environmental intervention in the patient in Case 2
Upper lobes (a, b); lower lobes (c, d). Consolidation is visible in the upper and lower lobe but has disappeared from the middle and lingular segments where it had been seen on CT at the time of the initial examination 7 months earlier (a–d). Atelectasis in the left lingular segment had also disappeared (d). Slight granular shadows can be seen in the middle lobe and lingular region (d).

Written informed consent was obtained from both subjects for the publication of these case reports.

DISCUSSION

Clinical practice guidelines for NTM from ATS/ERS/ESCMID/IDSA suggest that a bacteriological diagnosis must meet one of the following three criteria[9]: First, at least two sputum specimens are culture positive. Second, at least one bronchial lavage fluid is positive. Finally, at least one bronchoalveolar lavage fluid or sputum culture is positive in addition to tissue findings such as granuloma formation on a transbronchial lung biopsy or lung biopsy. The diagnosis must meet all of the clinical, imaging, and bacteriological criteria provided in the guidelines.[3,9] These cases we described were culture negative and did not meet the bacteriological criteria. However, anti-MAC antibodies were positive in both patients. Although anti-MAC antibodies are not included in the diagnostic criteria, they have a very high specificity, with a cutoff value of 0.7, and are useful for definitive diagnosis.[21]

If the MAC antibody titer is high (>10 U/mL), the probability of a positive culture is high in bronchial washings, but if the antibody titer is low (<5 U/mL), the positive culture rate is low.[22] In these cases, the antibody titers were low, and we consider that it was difficult to confirm positive cultures, including by bronchoscopy.

M. avium and a variety of other *Mycobacterium* species are present in the environment. *M. avium, M. intracellulare*, and *M. chelonae* have been recovered from aerosols produced by potting soil.[13] *M. avium* and *M. intracellulare* were detected in only 0.6% and 1.8% of air samples, respectively, but in 34.6% and 43.6% of soil samples, indicating that soil is a large source of exposure.[23] MAC is also more frequently detected in soil from gardens, potted plants, agricultural soil, and other sources than in water-related areas such as showerheads and bathrooms. Some reports have shown that *M. intracellulare* is more common than *M. avium*, but others have shown that it is about the same.[23,24] There are reports that the risk of developing *M. avium* increases with long-term exposure to soil for more than 6 years in agriculture,[25] and that patients with MAC disease were more likely to have been exposed to soil two or more times than patients with bronchiectasis who did not have MAC disease.[26] There are warnings that wearing a mask is essential in occupations where there is exposure to soil.[13]

After a diagnosis of pulmonary MAC disease, the two most common options are initiation of drug therapy or follow-up (watchful waiting). Nearly a quarter of patients with pulmonary MAC disease remain free of exacerbations after 3 years of follow-up[27]; in data restricted to bronchiectasis of the nodular type, about half of patients remain stable after an average follow-up of 32 months.[28] The initial choice of follow-up is not associated with adverse outcomes, and it is not necessary to initiate drug therapy in all patients. Characteristics of patients whose clinical findings improve with follow-up include younger age, higher BMI, fewer systemic symptoms, more localized extent of disease, and negative sputum smear specimens at initial presentation.[27]

However, the recurrence rate of pulmonary MAC disease is high even after standard treatment with medication, with a report showing that 30%–50% of those who were once cured of the disease experienced a recurrence.[5] There are two causes of recurrence: re-infection by a different organism, and relapse due to the growth of bacteria remaining in the body.

Among patients with MAC treated with triple therapy, most of those who relapse after cessation of treatment are reinfected with a different organism, and there is a significantly higher incidence of soil exposure in relapsed cases, especially after the start of treatment.[5] Some reports also indicate that treatment success is higher in patients with less post-treatment soil exposure.[29]

Thus, reinfection is a major factor in relapse, and reducing exposure to NTM may reduce the risk of post-treatment infection and relapse.[10]

In this study, we suggest that in cases of pulmonary NTM disease that are anti-MAC antibody positive but have negative sputum cultures and low disease activity, subjective symptoms and imaging findings may improve after soil-related environmental intervention. Thus, proactive environmental remediation may be a useful treatment option for pulmonary MAC disease.

CONFLICT OF INTEREST

No author has any conflict of interest to disclose.

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