

Mycobacterium chimaera: a case report from Italy

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Abstract

Mycobacterium chimaera is an environmental non-tuberculous mycobacterium belonging to *Mycobacterium avium* complex (MAC). It has been widely known to be associated with disseminated infection after cardiac surgery, related to heater-cooler units used

during these procedures. Although *M. chimaera* seems to be a less virulent species compared to *M. avium* and *M. intracellulare* among MAC, several cases of *M. chimaera* lung infections have been reported in settings of chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis, malignancy, or immunosuppression. Here, we present an Italian case report in association with newly diagnosed COPD.

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Introduction

Mycobacterium chimaera is an environmental non-tuberculous mycobacterium belonging to the *Mycobacterium avium* complex (MAC), first isolated and identified in 2004 [1]. It is a ubiquitous mycobacterium, mainly present in water, soil, and dust. *M. chimaera*'s infections were reported worldwide and linked to an outbreak associated with heater-cooler devices utilized during cardio-surgery procedures in 2013 [2]. The first case of *M. chimaera* infection in Italy, as part of this global outbreak, was described in December 2016 in a woman with a history of cardiac surgery who developed disseminated infection and vertebral osteomyelitis [3]. Although *M. chimaera* seems to be a less virulent species compared to *M. avium* and *M. intracellulare* among MAC, it can also affect people with underlying pulmonary affections [4], such as those presenting a history of chronic obstructive pulmonary disease (COPD) [5]. In fact, the association between non-tuberculous mycobacterial pulmonary disease (NTM-PD) and COPD can worsen the evolution of COPD and increase mortality. Furthermore, the use of inhaled corticosteroids is considered a risk factor for the development of NTM-PD [6].

Case Report

An 84-year-old woman presented to the Respiratory Rehabilitation Unit Clinic in IRCCS Maugeri on March 6th, 2023, complaining of worsening dyspnea at rest, productive cough, weight loss, and lack of appetite over the previous 6 months. As regards her past medical history, she never smoked and had no work exposure to inhalants. She also reported multiple annual bronchitic exacerbations requiring antibiotic therapy. It is worth mentioning that chronic respiratory failure developed in 2020 when long-term oxygen therapy was started. Regarding other non-respiratory comorbidities, she suffered from not hemodynamically significant bilateral carotid atheroma, arterial hypertension, deficiency anemia, anxious-depressive syndrome, and an allergy to iodine.

At presentation, she denied a previous history of cardio-thoracic surgery, recent travels, and contact with birds or wild animals. Blood pressure was 120/80 mmHg, heart rate was 90 beats per minute, respiration rate was 18 breaths per minute, her oxygen saturation was 92% in O₂ 1 L/min, temperature was 36°C, weight was 50 kg, and the body mass index (BMI) was 19.5 kg/m². Arterial

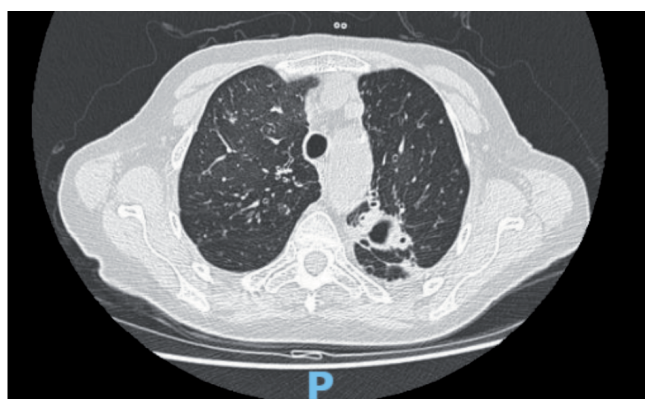
blood test on supplemental oxygen (1 L/min) documented partially compensated chronic hypercapnic respiratory failure.

Blood tests were all in range according to the patient's age, except for iron deficiency anemia and vitamin D lack, which were promptly supplemented. QuantiFERON test and HIV test were negative. No other immunosuppressive conditions were found. Lung function tests were performed, and she was diagnosed with COPD: forced expiratory volume in 1 second (FEV-1) was 0.47 L (27% of predicted), forced vital capacity (FVC) was 0.60 L (26%), FEV-1/FVC ratio was 46.8%, residual volume was 3.62 L (163%), and total lung capacity was 97%. It was first diagnosed with COPD GOLD 4 category, class E. Her Medical Research Council Questionnaire (mMRC) was 3, while the COPD assessment test (CAT) was 20. According to functional tests (global spirometry), multidimensional questionnaires (modified Medical Research Council dyspnea scale and CAT), and GOLD 2023 guidelines [7], the patient was started on triple closed inhalator therapy.

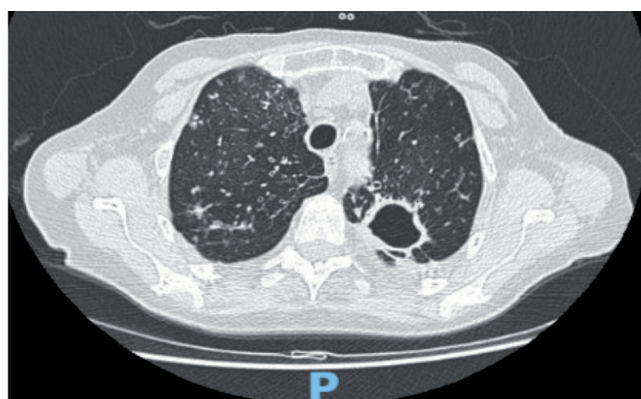
She also performed a 6-minute walking test while supplemented firstly with 1 L/min, then with 2 L/min, reaching a borderline oxygen saturation of 89%. A chest X-ray showed a left-sided apical opacity, confirmed by high-resolution computed tomography, which highlighted a 3 cm diameter pulmonary cavitation in the left lung apex. Additionally, patchy reticulonodular opacities, emphysema, and multiple bronchiectasis spread all over the lungs were found (Figures 1 and 2). The images led to the diagnosis of cavitary pneumonia, so blood cultures and sputum cultures were performed.



Figure 1. Chest x-ray posterior-anterior view, on initial presentation, illustrating left-sided apical opacity.



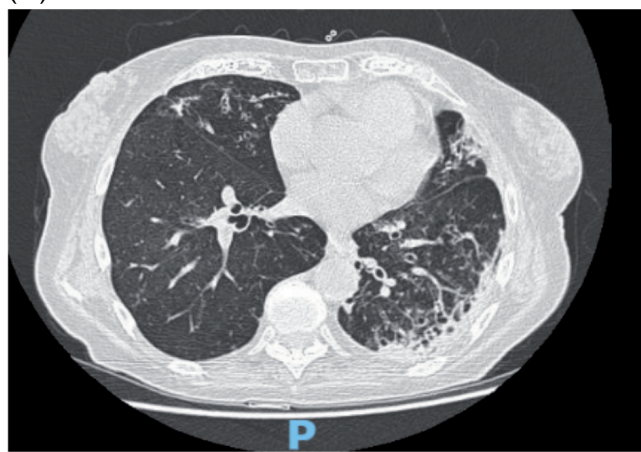
(a)



(b)



(c)



(d)

Figure 2. High-resolution computed tomography of the thorax showing a 3 cm diameter pulmonary cavitation in the left lung apex surrounded by emphysema and several bronchiectasis as shown by different slices in panels a-d, moving from the apex to the bottom.

Sputum samples were negative for acid-fast bacilli at the microscopic examination, and PCR testing for *M. tuberculosis* was also negative. Bacterial and fungal culture tests were negative. Samples were cultured on solid and liquid media for almost 5 weeks, and mycobacteria were identified in >2 separate sputum samples. Species identification was performed, and finally, *M. chimaera* was isolated. All samples were susceptible to macrolides and aminoglycosides. Blood cultures were negative. According to the ATS/ERS/ESCMID/IDSA Clinical Practice Guidelines published in 2020 [8], the patient was diagnosed with NTM-PD.

Beyond that, although a diagnosis was made, the patient needed further follow-up to ensure a global resolution of her acute condition. Nocturnal non-invasive mechanical ventilation (NIMV) was started, and oxygen titration at rest and on exertion was optimized with a prompt improvement in respiratory failure. Respiratory physiotherapy techniques tailored to the patient's needs were implemented, with a progressive benefit on mucus-ciliary clearance throughout cyclical sessions with high-flow nasal cannula (HFNC) oxygen therapy and expiratory flow accelerator techniques. The patient was also taught how to perform inhalation techniques properly and manage the NIMV and HFNC devices to get more confidence and autonomy. As for the pulmonary rehabilitation (PR) program, strength training was performed through bodyweight exercises, while the physical reconditioning to effort was performed with interval training by using a stationary cycle ergometer and reaching a daily load of 15 Watts for 30 minutes with a constant load mode. She was discharged with mMRC 2 and CAT 2. Because of a weight loss history and borderline BMI, the patient was also followed by a dietary counsellor. Additionally, a psychological support program was implemented, with both group and individual counseling sessions.

She was finally directed to the Regional Tuberculosis Reference Center, Villa Marelli Institute, Niguarda Hospital, Milan. In May 2023, she was started on a multidrug regimen with a combination of rifampicin, ethambutol, and azithromycin. During the follow-up, a progressive reduction of respiratory symptoms and radiological improvement was noted. Progressive cavitation reduction, weight gain, and respiratory improvements were obtained in the first 4 months of treatment, as shown in Figure 3 and Table 1.

Discussion

M. chimaera is part of the MAC, as are the two more common species, *M. avium* and *M. intracellulare*, and several other closely related mycobacteria. Initially, *M. chimaera* was misreported as *M. intracellulare* because molecular genetic standard tools in clinical microbiological laboratories did not differentiate MAC members.

Like other non-tuberculous mycobacteriosis (NTMs), *M. chimaera*'s distribution in human isolates depends on several factors, such as the geochemical characteristics of the environment; its

prevalence is less than 2% in bronchiectasis patients, as shown by Suska *et al.* in Italy [9]. Literature provides sufficient evidence associating *M. chimaera* as the infectious organism in patients undergo-

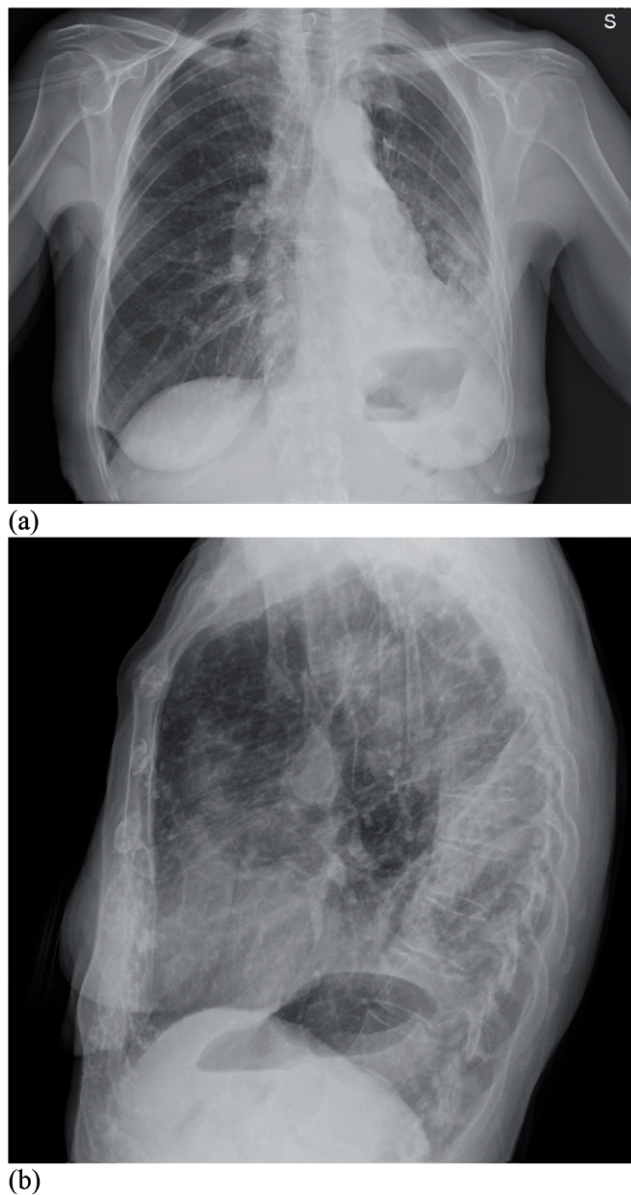


Figure 3. (a) Chest x-ray posterior-anterior and (b) later-lateral views on follow-up (after 4 months) presentation, illustrating improvement of left-sided apical opacity.

Table 1. Respiratory, radiological, and biometrical parameters at admission and follow-up.

Variables	Admission	Follow-up
CAT	20	2
mMRC	3	2
pO ₂ (in 1 L/min)	66.6 mmHg	72.2 mmHg
pCO ₂ (in 1 L/min)	68.8 mmHg	47.6 mmHg
Weight	50 kg	52 kg
Radiological findings	3 cm left-sided apical cavitation	Reduction of left-sided apical cavitation

CAT, chronic obstructive pulmonary disease assessment test; mMRC, modified Medical Research Council; pO₂, partial pressure of oxygen; pCO₂, partial pressure of carbon dioxide.

ing cardiac surgery (specifically, surgeries utilizing heater-cooler units) [10], but there are still a few cases described in patients with underlying pulmonary infections. Two case reports by Bills *et al.* in 2009 and Miskoff *et al.* in 2018, described a similar case of a patient with a history of COPD and smoking [5,11]. In addition, a case of cavitory *M. chimaera* with isolation of *Candida parapsilosis* in sputum was recently presented by Robinson *et al.* in 2022 [6]. Azzarà *et al.* reported the first case of NTM-PD due to *M. chimaera* in an oncologic patient receiving immune checkpoint inhibitors [12]. Our patient did not undergo surgical procedures and was not immunocompromised, but was first diagnosed with COPD and bronchiectasis. Moreover, the patient was started on inhaled corticosteroids a few days before the diagnosis of NTM-PD, suggesting that it did not contribute as a risk factor [13]. Although transmission of NTM-PD occurs predominantly *via* water and soil, other less common transmission routes exist, such as several hobbies or job-related activities (farming), dusty environments, heater-cooler devices, war contexts, natural disasters, or migration. These alternative routes can be handled by using respiratory protective equipment also for domestic or recreational activities, by adopting prophylaxis measures, and by limiting situations of social hardship [14]. To the best of our knowledge, this is one of the few cases describing *M. chimaera* infection in the Italian scenario. *M. chimaera* infection could be more common and more virulent than expected in chronic respiratory diseases such as COPD, as described also by Tortoli *et al.* [1]. Interestingly, our case shows a positive effect of combining rehabilitation and pharmacological-specific treatment [8]. In fact, along with pharmacological therapy, the patient was trained to strengthen her respiratory muscles through respiratory physiotherapeutic techniques. In addition, mucus clearance was improved, using oscillating positive expiratory pressure devices and high-frequency chest wall oscillation, as recommended by Sharma *et al.* and by O'Neill *et al.* [14,15]. To reduce breathlessness and fatigue, the patient followed an interval training program, interspersing high-intensity exercise with rest periods or lower-intensity exercise. As explained by Spruit *et al.*, interval training and continuous training appear to be equally effective in COPD and may be a useful alternative for symptom-limited individuals who cannot tolerate high-intensity continuous training [16].

Indeed, due to the reported association between low BMI and increased mortality in advanced COPD and NTM-PD, the patient was also supported by a dietary counselor who planned food fortification and vitamin supplementation to gain an ideal weight in 3 months and to promote an anti-inflammatory effect with reduced tissue damage [17].

Beyond that, considering that up to 40% of persons with COPD have depression or anxiety, especially in those using supplemental oxygen [18], and this comorbidity is also described in NTM-PD patients, medical staff should timely identify symptoms and program intervention [15]. Considering all these aspects, during rehabilitation, our patient attended individual and collective psychotherapy counseling to improve psychological symptoms.

Regarding the specific pharmacological treatment, a multidrug regimen composed of rifampicin, ethambutol, and azithromycin was started as suggested in guidelines for cavitory NTM-PD due to MAC [8]. The duration of the therapy is at least 12 months after sputum conversion. Even though indicated in NTM-PD's treatment guideline, in our case, amikacin could not be started because of the patient's age and comorbidities.

Nowadays, there are few studies specifically assessing the role of PR in patients with NTM-PD. In the narrative review by Youssefnia *et al.* [19], it is elicited that, since NTM-PD pharmaco-

logical treatment has a low percentage of success, in addition to reducing exposures to the NTM and treating it with antibiotics, there are ancillary treatment measures that can help in maximizing treatment outcomes, such as airway clearance, physical and PR, nutritional support [19]. Other evidence relies on similar studies on diseases resembling NTM-PD, such as bronchiectasis and tuberculosis [15,17].

Finally, it has been demonstrated that combined chemotherapy and supervised PR can be provided safely and improve health-related quality of life and physical function in NTM-PD. Omatsu *et al.* recommend that combined chemotherapy and PR be considered for treating NTM-PD according to the patient's condition [20]. Besides that, further investigations should be done to better understand the best personal and tailored approach for every patient.

Conclusions

We presented the case of an immunocompetent patient with advanced pulmonary *M. chimaera* infection with undiagnosed COPD and bronchiectasis. The patient underwent multiple interventions, firstly by stabilizing the COPD, then by building a tailored PR program, starting a multidrug regimen, and investigating comorbidities such as undernutrition and psychological aspects. The objective improvements in respiratory, radiological, and biometrical parameters observed after a few months suggest that the involvement of a multidisciplinary team may favor patient management.

In summary, NTM is interesting for the following reasons: i) diversity of mycobacteria – NTM encompasses various mycobacterial species with unique characteristics. This diversity is intriguing from a scientific and epidemiological perspective as it requires understanding different species, their growth habits, transmission routes, and clinical manifestations, especially for *M. chimaera*; ii) emerging diseases – NTM has been gaining increasing attention due to the rising number of reported cases worldwide, especially among people with chronic lung conditions or immunodeficiencies. This makes NTM an issue of growing relevance in the medical and epidemiological fields.

Research and awareness on this topic are essential for addressing the challenges associated with NTM. For the future, it could be far-sighted to carry out longitudinal studies about NTM-PD tracking infections in COPD by developing management strategies for these patients.

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