Nontuberculous Mycobacterial Infection: Focus on Pulmonary Disease

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Abstract

- **Objective:** To review the clinical features, diagnosis, and management of nontuberculous mycobacterial (NTM) infection.
- **Methods:** Literature review in the context of clinical cases
- **Results:** NTM species are mycobacterial species other than those belonging to the *Mycobacterium tuberculosis* complex and *M. leprae*. Radiographic findings of NTM lung disease vary and depend on the species but can usually be separated into a predominately fibrocavitary or fibronodular/nodular pattern with or without bronchiectasis. The diagnosis of NTM lung disease requires microbiologic confirmation. The decision to treat should consider potential risks of benefits for the individual patient based on symptomatic, radiographic, and microbiologic criteria as well as underlying systemic or pulmonary immune status. *M. avium* complex (MAC) is the most common of the nontuberculous mycobacteria that causes disease in humans. Clinical syndromes of pulmonary MAC disease include a primary form in healthy nonsmokers and a secondary form in patients with underlying lung disease. Macrolides are the mainstay of treatment.
- **Conclusion:** NTM infection has variable manifestations. Management strategies must be individualized based on degree of involvement, goal of therapy, and risk-benefit ratio.

Nontuberculous mycobacteria (NTM) are ubiquitous in the environment and have been recovered from tap and natural water sources, soil, and food products [1–3]. Mycobacteria have been isolated from body surfaces or secretions without causing apparent disease and are often considered as contaminants or colonizers with no clinical significance. However, with increased awareness and modern and more rapid microbiologic methods for detecting the presence of NTM in a clinical setting where comorbid pulmonary and nonpulmonary conditions may exist, their clinical significance has now been recognized. NTM species are mycobacterial species other than those belonging to the *Mycobacterium tuberculosis* complex and *M. leprae*. More than 130 NTM species have been identified, but since infection caused by NTM is not reportable, the incidence is unknown. U.S. laboratory surveys in the 1980s reported that approximately 60% of recovered mycobacterial species were NTM [4], the most common being *M. avium*, followed by *M. fortuitum* and *M. kansasii*. This percentage may also include the high incidence of disseminated *M. avium* complex (MAC) disease in patients with AIDS. However, it has been observed that there is increased isolation and prevalence of many species of NTM in several geographic areas, such as in the southeast United States and in the other parts of the world. The clinical significance of this observation is unclear [5–8].

This article reviews the clinical features, diagnosis, and management of NTM infection in general, focusing on the characteristics of *M. kansasii*, rapidly growing mycobacteria (RGM), and disseminated infection. Subsequently, the clinical features and management of MAC pulmonary disease (MAC-PD) are reviewed.

CASE 1 PRESENTATION

A 67-year-old male smoker with a past history of *M. tuberculosis* infection treated completely in the 1970s presents to the emergency department with cough and shortness of breath. Physical examination reveals a thin man with hyperresonance on lung examination and crackles in the left apex. Chest radiograph reveals an old *M. tuberculosis* scar with fibrocystic disease and a cavitary opacity in the left upper lobe (Figure 1). Pulmonary function tests document moderate obstructive airway dysfunction. HIV test is negative. Sputum smears are positive for acid-fast bacilli. Culture determines that the organism is not *M. tuberculosis*, and repeat cultures identify moderate growth of *M. kansasii*. 
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Are there any distinguishing features of NTM infection?

Clinical Characteristics

The clinical characteristics of NTM are variable and can be broadly divided into 5 groups [9–12]:

(1) Progressive pulmonary disease, which is caused primarily by MAC and *M. kansasii*

(2) Superficial lymphadenitis, especially cervical lymphadenitis, seen primarily in children and typically caused by MAC, *M. scrofulaceum*, or in some cases *M. malmoense*

(3) RGM, typically seen with skin and soft tissue infection and usually acquired via direct inoculation. Three clinically relevant species of RGM can be identified by culture within a week: *M. fortuitum*, *M. chelonae*, and *M. abscessus*.

(4) NTM infection occurring in transplant patients (ie, lung, hematopoetic stem cell) or those otherwise immunocompromised or undergoing immune modulation therapy [12,13]

(5) Disseminated NTM, usually seen in AIDS and severely immunocompromised patients and typically caused by MAC and *M. kansasii* [14,15]

*Mycobacterium kansasii* Infection

*M. kansasii* is a slow-growing photochromogen NTM based on growth characteristics on culture and pigmentation when exposed to light. *M. kansasii* is a common cause of NTM pulmonary disease in the United States, second only to MAC [10]. On radiography, *M. kansasii* lung disease closely resembles typical tuberculosis (ie, cavitary infiltrates in upper lung zones). Older age, male sex, smoking history, and underlying lung disease (eg, chronic obstructive pulmonary disease) are common clinical features. Other risk factors include malignancy, use of immunosuppressive drugs, alcohol abuse, pneumoconiosis, and HIV infection. Affected patients tend to present in their fifth decade of life or later, with an approximate 3:1 male predominance [1]. Certain occupational groups are at increased risk, including miners, welders, sandblasters, and painters. Some patients, however, have no risk factor other than their geographic area of residence, such as the southeast United States and parts of England and Wales [16]. *M. kansasii* can cause disseminated disease in immunocompromised hosts, such as patients with AIDS [17].

Infection Caused by Rapidly Growing Mycobacteria and Other NTM

RGM typically manifest in skin, soft tissue, and bone, but the role of RGM as pulmonary pathogens is unclear. Underlying diseases associated with RGM include previously treated mycobacterial disease, coexistent MAC cystic fibrosis, malignancies, and gastroesophageal disorders. *M. abscessus* is the third most commonly identified respiratory NTM and accounts for the majority (80%) of RGM respiratory isolates seen [9]. Other NTM (not RGM) reported to cause lung disease as well as affect the skin, bone, and joints include *M. simiae*, *M. xenopi*, and *M. malmoense* [18].

Disseminated NTM Disease

Disseminated NTM disease is associated with very low CD4+ lymphocyte counts in approximately 5% of patients with HIV infection [17,19–21]. Although disseminated NTM disease is rarely seen in immunosuppressed patients without HIV infection, it has been reported in renal or cardiac transplant patients, patients who use chronic corticosteroids, and those with leukemia. More than 90% of infections are caused by MAC, but other potential pathogens include *M. kansasii*, *M. chelonae*, *M. abscessus*, and *M. haemophilum* [1,10,14,15,22]. Although seen less frequently with the advent of highly active antiretroviral therapy (HAART), disseminated infection can develop progressively from an apparently indolent or localized infection or a respiratory or gastrointestinal source [19]. Symptoms of disseminated infection (specifically MAC-associated disease) are nonspecific and include fever, night sweats, abdominal tenderness, weight loss, and hepatosplenomegaly [14].

Radiographic Features

The radiographic findings of NTM lung disease vary and
Case-based review

depend to some extent on the species. Findings can usually be separated into a predominantly fibrocavitary or fibronodular or nodular pattern with or without bronchiectasis. Cavitary disease in the upper lung zones, similar to pulmonary tuberculosis, is seen in approximately 90% of patients with *M. kansasii* infection and in approximately 50% of those with MAC infection (Figure 2). On chest radiography, cavities caused by NTM have relatively thinner walls with less satellite lesions than those caused by *M. tuberculosis* [18,23–25]. Nodules and bronchiectasis are usually present within the same lobe and occur most frequently in the right middle lobe and lingula and are seen best on a computed tomography (CT) scan. The nodular and/or bronchiectatic radiographic pattern is seen more in MAC disease but can also be seen with other NTM pathogens, including *M. abscessus, M. simiae*, and *M. kansasii* [26,27]. Pleural effusions are uncommon in NTM infection.

- Are there diagnostic criteria for NTM lung disease?
- Does diagnosis of NTM lung disease require microbiologic confirmation? Are skin tests helpful?

**Table.** Criteria for Diagnosing Nontuberculous Mycobacterial Lung Disease

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Microbiologic</th>
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<td>Pulmonary symptoms, chest radiograph showing nodular or cavitary opacities, or high-resolution CT demonstrating multifocal bronchiectasis with multiple small nodules</td>
<td>Positive culture results from at least 2 separate expectorated sputum samples. If the results are not diagnostic, consider repeat sputum AFB smears and cultures</td>
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<td>AND</td>
<td>OR</td>
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<td>Exclusion of other diagnoses (eg, tuberculosis, fungal disease, malignancy), although it must be recognized that these conditions may coexist</td>
<td>Positive culture result from at least 1 bronchial wash or lavage</td>
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**Microbiologic**

Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) and 1 or more sputum or bronchial washings that are culture-positive for NTM

Expert consultation should be obtained when NTM are recovered, are infrequently encountered, or usually represent environmental contamination

Patients with suspected nontuberculous mycobacterial lung disease but who do not meet diagnostic criteria should be followed until the diagnosis is established or excluded


**Diagnosis**

American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) criteria for diagnosing NTM lung disease are shown in the Table [10]. These criteria best apply to MAC, *M. kansasii*, and *M. abscessus* but are clinically applied to other NTM respiratory pathogens.

Because of the nonspecific symptoms and lack of diagnostic specificity of chest imaging, the diagnosis of NTM lung disease requires microbiologic confirmation. Specimens sent to the laboratory for identification of NTM must be handled with care to prevent contamination. Transport media and preservatives should be avoided, and transportation of the specimens should be prompt. These measures will

Figure 2. Chest radiograph demonstrating cavitary opacities in both lung fields with volume loss on the right side.
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prevent bacterial overgrowth. Further, yield of NTM may be affected if the patient has used antibiotics, such as macrolides and fluoroquinolones, prior to obtaining the specimen.

NTM should be identified at the species level [10]. The preferred staining procedure in the laboratory is the fluorochromes method. Specimens should be cultured on both liquid and solid media. Some species require special growth conditions and/or lower incubation temperatures and other identification methods, such as DNA probes, polymerase chain reaction genotyping nucleic acid sequence determination, and high-performance liquid chromatography, may have to be employed. Species-specific skin test antigens are not commercially available and are not helpful in the diagnosis of NTM disease because of cross-reactivity of *M. tuberculosis* and some NTM. However, increased prevalence of NTM sensitization based on purified protein derivative testing has been noted in a recent survey, which is consistent with an observed increase in the rates of NTM infections, specifically MAC, in the United States [28].

RGM usually grow within 7 days of subculture, and the laboratory time to culture is a helpful hint. The majority of NTM grow within 2 to 3 weeks. Recognizing the morphology of mycobacterial colony growth may also be helpful in identification. Further, in a clinical setting, knowledge of conditions associated with NTM infection or specific phenotypes of patients (eg, thoracic anomalies, cystic fibrosis) can lead to a better recognition of suspected NTM infection [29]. The presence of NTM infection should be considered in the differential in a symptomatic patient with a chronic pulmonary infiltrate with or without a cavity.

- Are there special considerations in the management of NTM?
- How should this patient's *M. kansasii* pulmonary infection be treated?

Management

Making the diagnosis of NTM lung disease does not necessitate the institution of therapy. The decision to treat should be weighed against potential risks and benefits to the individual patient based on symptomatic, radiographic, and microbiologic criteria as well as underlying systemic or pulmonary immune status. Close observation is indicated if the decision is made not to treat. If treatment for NTM is initiated, comprehensive management includes long-term follow-up with periodic bacteriologic surveillance, watching for drug toxicity and drug-drug interactions, ensuring adherence and compliance to treatment, and managing comorbidity.

Generally, pulmonary disease progresses slowly, but lung disease attributed to RGM can result in respiratory failure. Thus, RGM should be recognized as a possible cause of chronic mycobacterial lung disease, especially in immunocompromised patients, and respiratory isolates should be assessed carefully [10,17]. Identification and drug susceptibility testing are essential before initiation of treatment of RGM. Treatment may include a combination of injectable aminoglycosides, imipenem, or cefoxitin and oral drugs such as a macrolide (eg, clarithromycin, azithromycin), doxycycline, fluoroquinolones, trimethoprim-sulfamethoxazole, or linezolid. If there is an identifiable skin or subcutaneous site or evidence of local disease, surgical debridement or resection of localized disease combined with multidrug clarithromycin-based therapy offers the best chance for a cure [10].

- What additional considerations are important in this case?

As per Clinical and Laboratory Standards Institute guidelines, routine susceptibility testing of *M. kansasii* isolates is recommended for rifampin only, as treatment failure is generally associated with rifampin-resistant strains. Treatment of *M. kansasii* pulmonary disease is a regimen of daily isoniazid (300 mg/day), rifampin (600 mg/day), and ethambutol (15 mg/kg/day), and patients should be treated until culture-negative on therapy for 1 year [10]. In patients receiving HAART, rifabutin should be substituted for rifampin, at modified doses and while monitoring for drug-drug interactions [10]. Use of fluoroquinolones and macrolides in rifampin-resistant cases lacks clear evidence.

Based on this patient's underlying history of chronic obstructive pulmonary disease and smoking as well as the characteristics of the lesion, other coexisting conditions such as a malignancy or fungal disease must be ruled out. The diagnostic criteria for the treatment of NTM underscore the importance of this approach [10].

Case 1 Resolution

CT is performed and results suggest an aspergilloma. The patient undergoes bronchoalveolar lavage and biopsy to rule out malignancy, and the results are consistent with inflammation. The patient is initially placed on 4-drug antituberculosis therapy, rifampin, isoniazid, ethambutol, and pyrazinamide, until the specific diagnosis is established and *M. kansasii* is cultured and identified. Drug treatment is then deescalated to rifampin, isoniazid, and ethambutol because pyrazinamide is not effective against *M. kansasii*. The patient shows symptomatic improvement;
However, repeated chest radiographs remain relatively unchanged over a period of a year.

**CASE 2 PRESENTATION**

A 42-year-old female nonsmoker woman with no past medical problems except seasonal allergic rhinitis and “colds and flu-like illness” once or twice a year is evaluated for a chronic lingering cough with occasional sputum production. The patient denies any other chronic symptoms and is otherwise very active, participating in a very rigorous regular exercise program. Physical examination reveals no specific pulmonary abnormalities, a body mass index of 22 kg/m², and mild pectus excavatum. Chest radiograph is unremarkable, but a CT scan of the chest reveals minimal nodular and cylindrical bronchiectasis in both lungs (Figure 3). No previous radiographs are available for comparison. The patient is HIV-negative. Sputum tests reveal normal flora and fungus, and an acid-fast bacilli smear is negative. Later sputum culture for mycobacteria grows a scanty growth of MAC in 1 specimen.

- What are the initial considerations in a patient who presents with MAC infection?
- Should treatment be initiated in this patient?

**Clinical Considerations**

MAC includes 2 species: *M. avium* and *M. intracellulare*. These organisms are genetically similar and generally not differentiated in the clinical microbiology laboratory. Among NTM, MAC is the most common cause of pulmonary disease worldwide [1–5].

Patients with NTM lung disease, especially *M. avium*, appear to have similar clinical characteristics and body types, including lean build, scoliosis, pectus excavatum, and mitral valve prolapse [29,30]. The mechanism by which this body morphotype predisposes to pulmonary mycobacterial infection is not defined, but ineffective mucociliary clearance is a possible explanation. Evidence suggests that some patients may be predisposed to NTM lung disease because of preexisting bronchiectasis. Some potential etiologies for bronchiectasis in this population include gastroesophageal reflux with chronic aspiration, α₁ antitrypsin deficiency, and cystic fibrosis [30,31].

Although robust data are lacking, the widespread impression is that the frequency of pulmonary MAC disease (MAC-PD) may be increasing. Pulmonary disease caused by MAC may take on 1 of several clinically different forms, ranging from asymptomatic “colonization” or persistent minimal infection, endobronchial involvement, progressive pulmonary disease with radiographic and clinical deterioration, hypersensitivity pneumonitis, or persistent, overwhelming mycobacterial growth, often in an underlying damaged lung either due to chronic obstructive lung disease or pulmonary fibrosis [10,11,32–34].

Various clinical syndromes of MAC-PD are recognized. These include:

- Disseminated MAC disease, which occurs primarily in patients with more advanced HIV disease (CD4+ count typically < 50 cells/μL) [31,32]. Clinically, disseminated MAC manifests as intermittent or persistent fever, constitutional symptoms with organomegaly and organ-specific abnormalities (eg, anemia, neutropenia from bone marrow involvement, adenopathy, hepatosplenomegaly), and elevations of liver enzymes or lung infiltrates from pulmonary involvement. With the advent of aggressive HAART and the use of prophylactic antibiotics, the incidence of disseminated MAC infection has decreased.

- The traditionally recognized presentation of MAC-PD, which is a male smoker in his late 40s or 50s with a chest radiograph showing apical fibrocavitary lung disease. If left untreated or in cases of resistant infection or erratic treatment, this form of disease is generally progressive and can result in extensive cavitary lung destruction and respiratory failure [32,33].

- Pulmonary disease in postmenopausal, nonsmoking, white women (known as Lady Windermere...
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syndrome), which may also present radiographically with nodular and interstitial infiltrates frequently involving the right middle lobe or lingula but tends to have a much slower progression than cavitary disease [26,34]. Even with this more indolent form of disease, progression can occur. In these cases, high-resolution CT may demonstrate multiple, small peripheral pulmonary nodules centered on the bronchovascular tree and peripheral tubular or cylindrical bronchiectasis. The radiographic term “tree-in-bud” has been used to describe what may reflect inflammatory changes, including bronchiolitis. Patients may also have other pathogens isolated from culture, including Pseudomonas aeruginosa, Staphylococcus aureus, and occasionally other NTM such as M. abscessus or M. chelonae.

• Hypersensitivity pneumonitis, which was initially described as a consequence of exposure to hot tubs. This presentation mimics allergic hypersensitivity pneumonitis with respiratory symptoms and culture/tissue identification of MAC or sometimes other NTM. It is unclear whether hypersensitivity pneumonitis is an inflammatory process, an infection, or both, and opinion regarding the need for specific antibiotic treatment is divided [10,11,35]. However, avoidance of exposure is recommended.

Treatment Considerations

The diagnosis of MAC is most readily established by culture of blood, bone marrow, respiratory secretions/fluid, or tissue specimens from suspected sites of involvement. Shedding of MAC into the respiratory secretions in patients with nodular bronchiectatic disease as compared with those with fibrocavitary form of the disease may be intermittently positive with variable colony counts [36]. Therefore, prior to the advent of high-resolution CT, isolation of MAC from the sputum of such patients was frequently dismissed as colonization; hence, the composite criteria of symptoms and radiographic and microbiologic correlation is essential to categorize the disease and decide need for therapy. In the absence of evidence of any clinical, radiologic, or mycobacterial progression of disease, clinical surveillance without initiating specific anti-MAC therapy is a reasonable option [10].

Case 2 Continued

After approximately 2 months of observation and nonspecific symptomatic treatment, the patient’s chronic symptoms continue. She now develops intermittent hemoptysis. Repeat sputum studies reveal moderate growth of M. avium. A follow-up CT scan shows progression of disease with an increase in the “tree-in-bud” pattern (Figure 4).

• What treatment protocols are recommended? What is the importance of macrolide-based treatment regimens?

Treatment Regimens

As per the ATS/IDSA statement [10], macrolides form the mainstay of treatment for MAC-PD. Macrolides have an increased concentration in the lung, and, when used for treatment of MAC-PD, there is a strong correlation between in vitro susceptibility, in vivo (clinical) response [37,38], and their immunomodulating effects [39]. Macrolide-containing regimens have demonstrated efficacy in patients with MAC-PD [40,41]; however, macrolide monotherapy should be avoided to prevent the development of resistance.

The newer macrolides have had a significant impact on the treatment of MAC-PD. Prior to the advent of these agents, treatment with multidrug regimens, usually including rifampin, ethambutol, and isoniazid, achieved initial sputum conversion rates of only 50% to 70%, with 20% to 30% relapse rates [10]. After determining that the patient requires therapy and whether suppressive or aggressive therapy should be initiated, the standard recommended treatment for MAC-PD includes [10,32]:

• For most patients with nodular/bronchiectatic disease, a thrice-weekly regimen of clarithromycin (1000 mg) or azithromycin (500 mg), rifampin (600 mg), and ethambutol (25 mg/kg) is recommended.
• For patients with fibrocavitary MAC-PD or severe nodular/bronchiectatic disease, a daily regimen of clarithromycin (500–1000 mg) or azithromycin (250 mg), rifampin (600 mg) or rifabutin (150–300 mg), and ethambutol (15 mg/kg), with consideration of 3 times/week amikacin or streptomycin early in therapy, is recommended.

• Treatment of disseminated MAC disease should include clarithromycin (1000 mg/day) or azithromycin (250 mg/day) and ethambutol (15 mg/kg/day) with or without rifabutin (150–350 mg/day). The duration of therapy depends upon resolution of signs and immune reconstitution.

• Prophylaxis for disseminated MAC disease should be given to HIV-infected adults with a CD4+ count less than 50 cells/μL. Azithromycin 1200 mg/week or clarithromycin 1000 mg/day have proven efficacy, and rifabutin 300 mg/day is also effective but less well tolerated.

• For MAC hypersensitivity pneumonitis, avoidance of exposure is the mainstay of management. In some cases, steroids are used with or without a short course of anti-MAC therapy (ie, clarithromycin/azithromycin, rifampin, ethambutol).

Case 2 Continued

The patient is treated with clarithromycin, rifampin, and ethambutol for 1 year with sputum conversion after 9 months. In the later part of her treatment, she experiences decreased visual acuity. Treatment is discontinued prematurely after 1 year due to drug toxicity and continued intolerance to drug therapy. She remains asymptomatic for 8 months and then begins to experience mild to moderate hemoptysis with increasing cough and sputum production associated with postural changes during exercise. Physical examination overall remains unchanged. Three sputum results reveal heavy growth of MAC, and the CT scan of the chest shows a cavitary lesion in the left upper lobe along with the nodular bronchiectasis (Figure 5).

• What are the management options at this stage?

Based on this patient’s continued symptoms, progression of radiologic abnormalities, and current culture growth, she requires retreatment. With the adverse effects associated with ethambutol during the first round of therapy, the drug regimen needs to be modified. Several considerations are relevant at this stage. Relapse rates range from 20% to 30% after treatment with a macrolide-based therapy [10,41]. Obtaining a culture sensitivity profile is imperative in these cases. Of note, in ideal cases, treatment should not be discontinued altogether, and instead the toxic agent should be removed from the treatment regimen. In this case, the patient could have continued on a 2-drug regimen of clarithromycin and rifampin.

Reinfection with multiple genotypes may also occur after successful drug therapy but is primarily seen in MAC patients with nodular bronchiectasis [36,42]. Patients who have failed previous therapy, even those with macrolide-susceptible MAC isolates, are less likely to respond to subsequent therapy. Data suggest that intermittent medication dosing is not effective for patients with severe or cavitary disease or in those who have failed previous therapy [43]. In this case, treatment should include a daily 3-drug therapy, with an injectable thrice-weekly aminoglycoside. Other agents such as fluoroquinolones and linezolid may have to be tried. Clofazimine, cycloserine, and ethionamide are sometimes used but their efficacy is unproven. Pyrazinamide and isoniazid have no activity against MAC.

Treatment Failures and Drug Resistance

Patients are considered treatment failures if they have not had response (microbiologic, clinical, or radiographic) after 6 months of appropriate therapy or achieved conversion of sputum to culture-negative after 12 months of appropriate therapy [10]. Multiple factors can interfere with the successful treatment of MAC-PD, including medication nonadherence, medication side effects or intolerance, lack of response to a medication regimen, or the emergence of a macrolide-resistant or multidrug-resistant strain [32,33,44]. Treatment failure may also be drug-related, due to poor drug penetration into the organism.
the damaged lung tissue and subtherapeutic tissue levels or drug-drug interactions leading to suboptimal drug levels. Further, factors identified as contributing to the poor response to therapy include poor compliance, cavitary disease, previous treatment for MAC-PD, and a history of chronic obstructive lung disease or bronchiectasis [43].

- Is surgery an option in this case?

Surgery is an option in selected cases as part of adjunctive therapy along with anti-MAC therapy based on mycobacterial sensitivity. Surgery is used as either a curative approach or a “debulking” measure [10]. When present, clearly localized disease, especially in upper lobe, lends itself best to surgical intervention. Surgical resection of a solitary pulmonary nodule due to MAC in addition to concomitant medical treatment is recommended. Surgical intervention should be considered early in the course of the disease, because it may provide a cure without the prolonged treatment and its associated problems, and approach may lead to early sputum conversion. Surgery should also be considered in patients with macrolide-resistant or multidrug-resistant MAC or in those who cannot tolerate the side effects of therapy, provided that the disease is focal and limited. Patients with poor preoperative lung function have poorer outcomes than those with good lung function, and postoperative complications arising from treatment, especially with a right-sided pneumonectomy, tend to occur more frequently [32,33,45].

Case 2 Resolution

The patient is restarted on therapy with clarithromycin, rifampin, and moxifloxacin. She has a good clinical response.

CONCLUSION

NTM is ubiquitous in the environment, and NTM infection has variable manifestations, especially in patients with no recognizable immune impairments. Management strategies must be individualized based on degree of involvement, goal of therapy, and risk-benefit ratio. In diffuse pulmonary disease, drug treatment remains difficult, secondary to medication side effects and high failure rates. When a localized source of infection is identified, especially in RGM disease, surgical treatment may be needed. The importance of appropriately determining which patients require close surveillance and no specific antimicrobial therapy or specific treatment with recognition of comorbidity and relapses cannot be overemphasized.
25. Shitrit D, Baum GL, Priess R, et al. Pulmonary Mycobacterium avium complex pulm-