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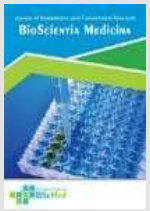

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Rare Presentation of Non-Tuberculous Mycobacteria: A Case of Lung Infection with Pleural Effusion

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A B S T R A C T

Background: Non-tuberculous mycobacteria (NTM) are environmental organisms that can cause pulmonary infections, particularly in individuals with predisposing conditions. While NTM lung disease is increasingly recognized, pleural effusion as a complication remains uncommon, posing diagnostic and therapeutic challenges. This case emphasizes the importance of a high index of suspicion, comprehensive microbiological investigations, and bronchoscopy in the diagnosis of NTM lung disease with pleural effusion. **Case presentation:** We present the case of a 55-year-old male farmer with a history of smoking, who presented with progressive dyspnea, cough, and constitutional symptoms. Initial investigations suggested tuberculosis, but sputum tests were negative. Chest imaging revealed a right pleural effusion and cavitary lung lesions. Pleural fluid analysis showed an exudative pattern with elevated adenosine deaminase (ADA) but negative for acid-fast bacilli. Bronchoscopy with bronchoalveolar lavage culture yielded Mycobacterium other than tuberculosis (MOTT). The patient was diagnosed with NTM lung disease complicated by pleural effusion and initiated on multidrug therapy. **Conclusion:** This case highlights the diagnostic challenges of NTM lung disease, particularly when presenting with pleural effusion. A high index of suspicion, comprehensive microbiological investigations, and bronchoscopy are crucial for accurate diagnosis. Prompt initiation of appropriate multidrug therapy is essential for optimal outcomes.

1. Introduction

The landscape of pulmonary infections has witnessed a significant shift in recent decades, with the increasing prevalence of Non-Tuberculous Mycobacteria (NTM) lung disease emerging as a formidable global health challenge. NTM also referred to as atypical mycobacteria or mycobacteria other than tuberculosis (MOTT), are ubiquitous environmental organisms found in soil and water sources.[1] While these organisms have long been recognized, their clinical significance has gained prominence as the incidence of NTM lung disease has steadily risen, even surpassing tuberculosis in certain regions.[2] The reasons behind this epidemiological transition are multifaceted, encompassing factors such as heightened awareness, improved diagnostic capabilities, and potentially, environmental and host-related susceptibilities.[3] NTM comprise a vast and heterogeneous group of over 190 recognized species, each with distinct microbiological characteristics and pathogenic potential.[4] The most frequently encountered NTM species associated with pulmonary infections include the *Mycobacterium avium* complex (MAC), *M. kansasii*, and *M. abscessus*.[5] These organisms, while generally less virulent than *Mycobacterium tuberculosis*, can cause significant morbidity and mortality, particularly in susceptible individuals.[6] NTM lung disease predominantly affects

individuals with pre-existing structural lung diseases such as chronic obstructive pulmonary disease (COPD), bronchiectasis, or prior tuberculosis, which provide a fertile niche for NTM colonization and subsequent infection.[7] Additionally, immunocompromised individuals, including those with HIV infection or undergoing immunosuppressive therapy, are at an elevated risk due to impaired host defenses.[8] The clinical presentation of NTM lung disease is often insidious and nonspecific, characterized by chronic cough, sputum production, fatigue, weight loss, and occasionally, hemoptysis.[9] These symptoms can mimic those of tuberculosis, leading to diagnostic challenges and potential delays in appropriate treatment initiation.[10]

The diagnosis of NTM lung disease necessitates a meticulous and comprehensive approach, integrating clinical, radiological, and microbiological investigations. Sputum culture remains the gold standard for diagnosis, enabling the isolation and identification of the causative NTM species.[1] However, sputum culture may yield negative results in some cases, particularly in the early stages of disease or in the presence of comorbidities such as bronchiectasis.[2] Bronchoscopy with bronchoalveolar lavage emerges as a valuable diagnostic tool, allowing for direct sampling of the lower respiratory tract and enhancing the sensitivity of NTM detection.[3] Molecular diagnostic techniques, such as polymerase chain reaction (PCR), have also revolutionized the field, enabling rapid and accurate identification of NTM species, even in culture-negative cases.[4] While NTM lung disease primarily manifests with pulmonary symptoms and radiological abnormalities, pleural effusion as a complication is relatively infrequent, occurring in a minority of cases.[5] The exact mechanisms underlying the development of NTM-related pleural effusion remain elusive, but potential pathways include direct extension from pulmonary foci, hematogenous spread, or lymphatic dissemination.[6]

The clinical presentation of NTM-related pleural effusion is often subtle, with patients experiencing dyspnea, chest discomfort, or cough.[7] Pleural fluid analysis typically reveals an exudative pattern with lymphocytic predominance and elevated adenosine deaminase (ADA) levels, mirroring the findings in tuberculous pleural effusion.[8] However, the absence of acid-fast bacilli on smear microscopy and culture distinguishes NTM-related pleural effusion from its tuberculous counterpart.[9] The treatment of NTM lung disease is intricate and often protracted, requiring multidrug regimens tailored to the specific NTM species and disease severity.[10] Macrolides, such as azithromycin or clarithromycin, form the cornerstone of therapy for MAC lung disease, often combined with rifampicin and ethambutol.[1] The optimal duration of treatment for NTM lung disease with pleural effusion is not well established, but guidelines recommend continuing therapy for at least 12 months after sputum culture conversion.[2] Adherence to treatment regimens is paramount, as NTM are inherently resistant to many conventional antibiotics, and prolonged therapy is often required to achieve a cure.[3] Moreover, close monitoring for adverse drug reactions is essential, as the medications used in NTM treatment can have significant side effects.[4] This case emphasizes the importance of a high index of suspicion, comprehensive microbiological investigations, and bronchoscopy in the diagnosis of NTM lung disease with pleural effusion.

2. Case Presentation

The patient in this report is a 55-year-old male, residing in a rural area and employed as a farmer and herdsman. He presented to the hospital with a chief complaint of worsening shortness of breath that had intensified over the two days prior to admission. The dyspnea was persistent, exacerbated by exertion, and accompanied by a cough. The patient reported experiencing shortness of breath for the past week, prompting a visit to the emergency department of a specialized pulmonary hospital. A chest X-ray performed at that time led to his referral to our tertiary care center for further management. The patient's medical history revealed a cough productive of white sputum for two months, intermittent fever for one

month, and night sweats and decreased appetite with associated weight loss of 3 kg (approximately 5% of body weight) over the past three months. He denied hemoptysis, chest pain, hoarseness, or difficulty swallowing. The patient had a significant smoking history, having smoked 16 cigarettes per day for 35 years, but had quit three months prior to presentation. He had no prior history of tuberculosis or other chronic medical conditions. On physical examination, the patient appeared moderately ill and was fully conscious and cooperative. Vital signs included a blood pressure of 110/70 mmHg, heart rate of 88 beats per minute, respiratory rate of 26 breaths per minute, temperature of 36.7°C, and oxygen saturation of 95% on 3 liters per minute of supplemental oxygen via nasal cannula. His body mass index (BMI) was within the normal range. Chest examination revealed asymmetry, with the right side of the chest appearing more prominent than the left. Respiratory movements on the right side were lagging compared to the left. Palpation demonstrated decreased tactile fremitus on the right. Percussion elicited dullness over the right lower chest from the sixth rib downwards, while the left side was resonant. Auscultation revealed bronchovesicular breath sounds with crackles over the right upper chest up to the sixth rib, and diminished breath sounds below that level. The left lung fields exhibited normal bronchovesicular breath sounds without adventitious sounds. Initial laboratory investigations, including complete blood count, coagulation profile, blood glucose, electrolytes, liver function tests, renal function tests, hepatitis B surface antigen, and HIV antibody, were all within normal limits. A chest X-ray performed on admission showed a right-sided pleural effusion and infiltrates in the right lung field.

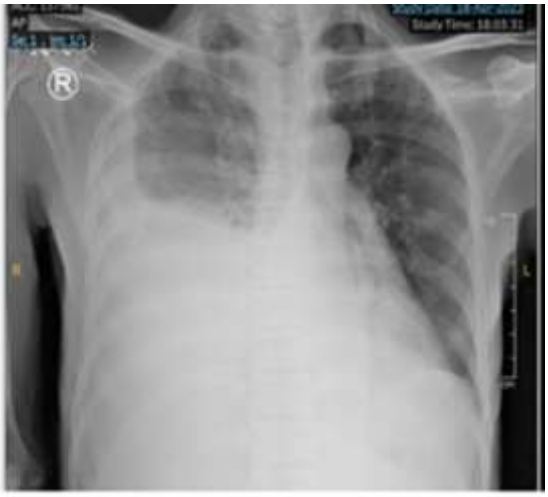

Figure 1. Chest X-ray performed on admission showed a right-sided pleural effusion and infiltrates in the right lung field.

Based on the initial presentation and chest X-ray findings, the working diagnosis was right pleural effusion with suspected pulmonary tuberculosis. However, other potential diagnoses, including lung cancer, were considered. Further imaging with chest ultrasound demonstrated a hypoechoic pleural effusion. Thoracentesis was performed, draining 1250 ml of serous fluid. Post-thoracentesis chest X-ray showed improvement in the pleural effusion but revealed cavitary lesions and infiltrates in the right lung. Pleural fluid analysis revealed an exudative effusion with a predominance of lymphocytes, suggestive of a chronic process. Adenosine deaminase (ADA) level in the pleural fluid was elevated at 43 U/L. Cytological examination of the pleural fluid was negative for malignancy, and acid-fast bacilli (AFB) smear and culture were negative. Sputum samples were also sent for AFB smear microscopy, culture, and

cytology. AFB smear microscopy was negative, and cytology showed no evidence of malignancy. However, GeneXpert MTB/RIF assay on sputum was negative for Mycobacterium tuberculosis. To further investigate the underlying cause of the pulmonary and pleural abnormalities, bronchoscopy was performed. Bronchoscopic examination showed hyperemic mucosa in the right upper lobe. Bronchoalveolar lavage (BAL) was performed, and the BAL fluid was sent for AFB smear microscopy, culture, fungal culture, and cytology. AFB smear microscopy of the BAL fluid was positive, and culture yielded growth of MOTT. Fungal culture was negative, and cytology showed no evidence of malignancy.

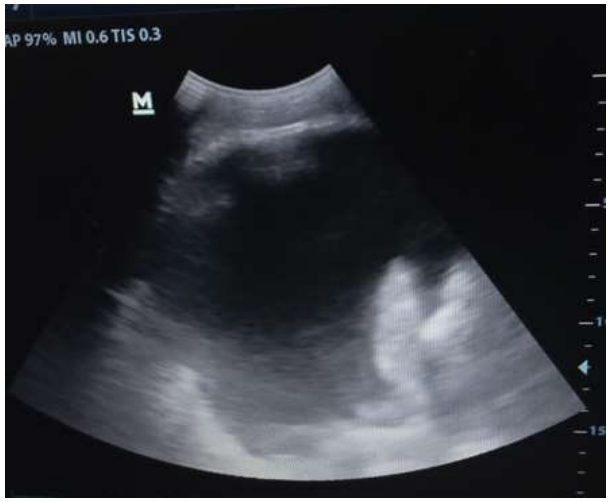

Figure 2. Chest ultrasound demonstrated a hypoechoic pleural effusion.

Figure 3. Thoracentesis was performed, draining 1250 ml of serous fluid.

Based on the collective clinical, radiological, and microbiological findings, the patient was diagnosed with non-tuberculous mycobacterial (NTM) lung disease complicated by pleural effusion. The specific NTM species was not identified due to limitations in laboratory facilities. The patient was initiated on multidrug therapy with rifampicin, ethambutol, and azithromycin, targeting the most common NTM species, MAC, and considering the presence of cavitary lung lesions. One month after initiating treatment, the patient reported significant improvement in symptoms, including resolution of fever and weight gain of 1 kg. Follow-up chest X-ray showed partial resolution of the pleural effusion and cavitary lesions. Sputum culture remained negative for NTM. The patient continued on multidrug therapy for a total of 12 months after sputum culture conversion. Regular monitoring for clinical response, adverse effects, and sputum culture was performed. At the end of treatment, the patient remained asymptomatic with complete resolution of the pleural effusion and significant improvement in lung lesions on imaging.

3. Discussion

The case presented underscores the intricate diagnostic challenges inherent to non-tuberculous mycobacterial (NTM) lung disease, particularly when it manifests with the added complexity of pleural

effusion. The clinical and radiological presentation of NTM lung disease often mirrors that of tuberculosis (TB), a far more prevalent and widely recognized infectious disease, especially in regions where TB remains endemic. This mimicry can lead to misdiagnosis, potentially delaying the initiation of appropriate treatment and adversely impacting patient outcomes. The clinical manifestations of NTM lung disease are protean and nonspecific, encompassing both respiratory and systemic symptoms. Chronic cough is often the most prominent symptom, typically productive of mucopurulent or purulent sputum. The chronicity of the cough, often lasting for weeks or months, can be a distinguishing feature from acute respiratory infections. Shortness of breath can occur due to the underlying lung damage caused by NTM infection, such as bronchiectasis or fibrosis. The severity of dyspnea can vary depending on the extent of lung involvement. Coughing up blood can be a concerning symptom, although it is less common in NTM lung disease compared to TB. It can occur due to the erosion of blood vessels within the areas of lung inflammation or cavitation. Chest pain can be present but is usually not a dominant feature. It may be pleuritic in nature, associated with inflammation of the pleura, or may be a dull ache related to the underlying lung pathology. A low-grade fever is often present, particularly in the presence of active infection. The fever may be intermittent or persistent and is often accompanied by other constitutional symptoms. Profuse sweating during sleep is a common symptom, reflecting the systemic inflammatory response to the infection. Unintentional weight loss can occur due to decreased appetite, malabsorption, or increased metabolic demands associated with chronic infection. Generalized weakness and fatigue are often reported, contributing to the overall decline in functional status.[9-11]

These clinical manifestations closely resemble those of pulmonary TB, which also presents with chronic cough, dyspnea, hemoptysis, chest pain, fever, night sweats, weight loss, and fatigue. This significant overlap in symptomatology can create diagnostic confusion, particularly in settings where TB is prevalent. The radiological findings in NTM lung disease further contribute to the diagnostic challenges, as they can closely resemble those seen in TB. Cavities, or air-filled spaces within the lung parenchyma, are a hallmark of both NTM and TB. These cavities can be thin-walled or thick-walled and may be associated with surrounding areas of consolidation or infiltration. Both NTM and TB can cause the formation of nodules and infiltrates within the lungs. These can be solitary or multiple and may exhibit varying patterns of distribution. Bronchiectasis, or abnormal dilation of the bronchi, is a common finding in NTM lung disease, particularly in those with underlying lung conditions. It can also be seen in TB, although less frequently. While pleural effusion is more commonly associated with TB, it can also occur in NTM lung disease, as exemplified in the presented case. The presence of pleural effusion can further complicate the diagnostic process and necessitate additional investigations. The radiological similarities between NTM and TB can make it difficult to differentiate between the two based on imaging alone. This underscores the importance of obtaining a thorough clinical history, performing appropriate microbiological tests, and considering the epidemiological context when evaluating patients with suspected pulmonary infections.[10-12]

The presence of pleural effusion in the context of NTM lung disease introduces an additional layer of diagnostic complexity. Pleural effusion, while more commonly associated with TB, can also occur in NTM lung disease, albeit less frequently. This can lead to initial misdiagnosis and delays in appropriate treatment. The pathogenesis of NTM-related pleural effusion is not fully elucidated but is thought to involve direct extension from pulmonary foci, hematogenous spread, or lymphatic dissemination. The pleural fluid analysis in NTM-related pleural effusion often reveals an exudative pattern with a predominance of lymphocytes and elevated ADA levels, similar to tuberculous pleural effusion. However, AFB smear microscopy and culture of pleural fluid are often

negative, as was the case in our patient. The presence of pleural effusion necessitates additional diagnostic procedures, such as thoracentesis and pleural biopsy, to rule out other potential causes, including malignancy, parapneumonic effusion, and other infectious etiologies. In cases where sputum cultures are negative or inconclusive, bronchoscopy with BAL may be necessary to obtain adequate samples for microbiological diagnosis of NTM lung disease.[11-13]

Given the overlapping clinical and radiological features of NTM and TB, a high index of suspicion is crucial for the timely diagnosis of NTM lung disease, particularly when presenting with pleural effusion. Clinicians should consider NTM lung disease in the differential diagnosis of patients with chronic respiratory symptoms, especially in those with predisposing conditions or epidemiological risk factors. A detailed clinical history, including exposure to potential environmental sources of NTM, underlying lung conditions, and immune status, is essential. Thorough physical examination and appropriate imaging studies should be performed. Microbiological investigations, including sputum culture and, if necessary, bronchoscopy with BAL, are critical for confirming the diagnosis. The case presented in this report serves as a poignant reminder of the diagnostic challenges posed by NTM lung disease, particularly when accompanied by pleural effusion. The clinical and radiological mimicry of TB can lead to misdiagnosis and delays in appropriate treatment. A high index of suspicion, comprehensive microbiological investigations, and bronchoscopy are vital for accurate diagnosis. Prompt initiation of appropriate multidrug therapy is essential for optimal outcomes in patients with NTM lung disease, even in the presence of pleural effusion.[12-14]

The occurrence of pleural effusion in the context of non-tuberculous mycobacterial (NTM) lung disease is an infrequent but increasingly recognized clinical scenario that significantly adds to the complexity of diagnosis and management. The underlying mechanisms that lead to the accumulation of fluid within the pleural space in NTM infections are multifaceted and not yet fully elucidated. However, several potential pathways have been proposed, each contributing to the intricate pathophysiology of this condition.The most intuitive and perhaps the most common mechanism for NTM-related pleural effusion is the direct extension of infection from adjacent pulmonary parenchyma. NTM organisms, having established a foothold within the lung tissue, can progressively infiltrate and erode through the visceral pleura, the delicate membrane lining the lungs. This breach allows the mycobacteria to gain access to the pleural cavity, triggering an inflammatory response. The ensuing inflammation leads to increased vascular permeability and the leakage of fluid, proteins, and inflammatory cells into the pleural space, culminating in the formation of a pleural effusion. The likelihood of direct extension is influenced by several factors, including the virulence of the NTM species, the extent of lung involvement, and the host's immune response. Cavitary lung lesions, a hallmark of certain NTM infections, particularly those caused by *M. kansasii* and MAC, are often located in close proximity to the pleura, increasing the risk of direct pleural invasion. The presence of bronchiectasis, another common manifestation of NTM lung disease, can also facilitate the spread of infection to the pleura due to the structural abnormalities and impaired mucociliary clearance associated with this condition. While less frequent than direct extension, hematogenous dissemination of NTM organisms can also lead to pleural involvement. In this scenario, mycobacteria gain entry into the bloodstream from a primary pulmonary focus or, less commonly, from an extrapulmonary source. Once in the circulation, NTM can seed the pleura, initiating an inflammatory cascade and subsequent effusion. Hematogenous spread is more likely to occur in individuals with disseminated NTM disease, a severe manifestation characterized by widespread involvement of multiple organ systems. Risk factors for disseminated NTM disease include underlying immunocompromising conditions, such as HIV infection or immunosuppressive therapy, and advanced age.[13-15]

The lymphatic system plays a crucial role in immune surveillance and clearance of pathogens, including mycobacteria. However, it can also serve as a conduit for the spread of infection. NTM organisms within the lung parenchyma can be taken up by lymphatic vessels and transported to regional lymph nodes. In some cases, the infection can overwhelm the lymph nodes and extend into the pleural space via lymphatic channels, leading to pleural effusion. Lymphatic dissemination is often associated with NTM infections that exhibit a predilection for lymphatic involvement, such as those caused by *M. scrofulaceum* and *M. avium* subspecies *hominissuis*. The presence of hilar or mediastinal lymphadenopathy in imaging studies can suggest lymphatic spread and raise the possibility of pleural involvement. The host's immune response to NTM infection plays a pivotal role in the development and progression of pleural effusion. A robust immune response can effectively contain the infection and prevent pleural involvement. However, in individuals with impaired immunity, the mycobacteria can evade host defenses and spread to the pleura. The immune response to NTM is complex and involves both innate and adaptive components. Macrophages, key players in the innate immune system, engulf and attempt to destroy the mycobacteria. However, NTM has evolved mechanisms to survive and replicate within macrophages, leading to persistent infection and chronic inflammation. The adaptive immune response, mediated by T lymphocytes, is crucial for controlling NTM infection. T cells recognize NTM antigens and orchestrate a cellular immune response aimed at eliminating the mycobacteria. However, in immunocompromised individuals, T cell function may be impaired, allowing the infection to progress and potentially involve the pleura.[14-16]

The multifactorial nature of NTM-related pleural effusion underscores the diagnostic challenges associated with this condition. The clinical presentation is often nonspecific, with symptoms such as cough, dyspnea, and chest pain, which can mimic other respiratory conditions, including tuberculosis. Radiological findings, such as pleural effusion and cavitary lung lesions, can raise suspicion for NTM infection, but definitive diagnosis relies on microbiological confirmation. Sputum culture remains the gold standard for diagnosing NTM lung disease, but bronchoscopy with BAL may be necessary in cases of negative sputum cultures or when pleural effusion is present. Pleural fluid analysis can provide valuable clues, with an exudative pattern, lymphocytic predominance, and elevated ADA levels being suggestive of NTM infection. However, AFB smear microscopy and culture of pleural fluid are often negative, necessitating further investigations, such as BAL or pleural biopsy, for definitive diagnosis. The treatment of NTM lung disease with pleural effusion requires a multidisciplinary approach, involving pulmonologists, infectious disease specialists, and thoracic surgeons. Multidrug therapy tailored to the specific NTM species is the mainstay of treatment, with the duration of therapy extending for at least 12 months after sputum culture conversion. In cases of persistent or recurrent pleural effusion despite adequate medical therapy, surgical intervention may be considered. Decortication, a procedure to remove the thickened pleura, can improve lung function and reduce symptoms. Pleurectomy, the complete removal of the pleura, may be necessary in cases of trapped lung or extensive pleural involvement.[15-17]

The identification of the specific Non-Tuberculous Mycobacteria (NTM) species causing an infection is of paramount importance in guiding effective treatment decisions. The reason for this lies in the inherent variability in susceptibility patterns exhibited by different NTM species to various antimicrobials. In essence, not all NTM species respond equally to the same antibiotics. Some species may be intrinsically resistant to certain drugs, while others may acquire resistance through genetic mutations or horizontal gene transfer. Therefore, administering an antibiotic without knowing the specific NTM species involved is akin to shooting in the dark - it may or may not hit the target. The consequences of mismatched antibiotic therapy can be severe. In the best-case scenario, the chosen antibiotic may be ineffective, leading to

treatment failure and disease progression. This not only prolongs the patient's suffering but also increases the risk of complications and transmission. In the worst-case scenario, the antibiotic may exert selective pressure, favoring the survival and proliferation of resistant strains. This can lead to the emergence of multidrug-resistant NTM, which are notoriously difficult to treat and pose a significant public health threat. The gold standard for NTM species identification is molecular techniques, such as polymerase chain reaction (PCR) and DNA sequencing. These methods offer high accuracy and resolution, allowing for the identification of even closely related species and subspecies. However, these techniques are often expensive, require specialized equipment and expertise, and may not be readily available in resource-limited settings. In such settings, where molecular identification is not feasible, clinicians may resort to empiric treatment based on the most prevalent NTM species in the region. This approach is based on the assumption that the infecting NTM species is likely to be one of the common ones encountered in the local population. While this approach may be pragmatic, it is not without its limitations.[16-18]

Firstly, the prevalence of NTM species can vary significantly across different geographical regions and even within the same region over time. Relying on outdated or inaccurate epidemiological data can lead to inappropriate treatment choices. Secondly, even within the same species, there can be considerable strain-level variation in drug susceptibility. Therefore, empiric treatment may not be effective against all strains of the presumed NTM species. Furthermore, empiric treatment carries the risk of overtreatment or undertreatment. Overtreatment with broad-spectrum antibiotics can lead to unnecessary side effects and promote the development of antibiotic resistance. Undertreatment, on the other hand, can result in treatment failure and disease progression. Therefore, while empiric treatment may be a necessary compromise in resource-limited settings, it should be viewed as a temporary measure until definitive species identification can be achieved. Efforts should be made to improve access to molecular diagnostic tools in these settings, as this will enable more targeted and effective treatment of NTM infections. In addition to species identification, drug susceptibility testing (DST) is another crucial aspect of guiding treatment decisions. DST involves exposing the isolated NTM strain to various antibiotics in the laboratory to determine its susceptibility or resistance. This information helps clinicians select the most effective drugs for the individual patient, maximizing the chances of treatment success and minimizing the risk of adverse events. However, DST for NTM is not as standardized or widely available as it is for Mycobacterium tuberculosis. There are challenges in culturing and isolating NTM, and the interpretation of DST results can be complex due to the lack of established breakpoints for many NTM species and drugs. Despite these challenges, DST should be performed whenever possible, especially in cases of treatment failure, relapse, or suspected drug resistance. In resource-limited settings, where DST may not be readily available, clinicians may need to rely on expert consultation and published susceptibility data to guide treatment choices. The identification of the specific NTM species and, ideally, DST are critical for optimizing treatment decisions in NTM lung disease. While empiric treatment may be necessary in resource-limited settings, efforts should be made to improve access to molecular diagnostic tools and DST to enable more targeted and effective therapy. A multidisciplinary approach involving clinicians, microbiologists, and infectious disease specialists is essential for the successful management of NTM lung disease.[17-19]

The optimal duration of therapy for NTM lung disease with pleural effusion remains an area of ongoing investigation and debate within the medical community. The current standard of care, as reflected in the guidelines, advocates for a continuation of treatment for a minimum of 12 months following the conversion of sputum cultures to negative. This recommendation stems from the understanding that

NTM infections, particularly those involving the lungs and pleura, can be indolent and challenging to eradicate completely. The extended treatment duration aims to ensure the complete elimination of the mycobacteria, thereby minimizing the risk of relapse or treatment failure. The rationale behind the 12-month benchmark is rooted in clinical experience and observational studies, which have suggested that shorter treatment durations may be associated with higher rates of recurrence. However, it is important to acknowledge that the evidence base for this recommendation is not as robust as that for other aspects of NTM treatment. The relative paucity of randomized controlled trials specifically addressing the optimal duration of therapy for NTM lung disease with pleural effusion underscores the need for further research in this area. The decision to continue treatment beyond 12 months should be individualized, taking into account various factors such as the specific NTM species involved, the severity of the disease, the patient's clinical response to therapy, and the presence of any comorbidities or complications. For instance, patients with more extensive lung involvement, cavitary lesions, or persistent symptoms may warrant a longer duration of treatment to achieve complete eradication of the infection. Close monitoring of the patient's clinical response and adverse effects throughout the treatment course is paramount. This includes regular assessments of symptoms, chest imaging, and sputum cultures. The frequency of monitoring may vary depending on the individual patient's circumstances and the treating physician's judgment. However, it is generally recommended that sputum cultures be performed monthly until two consecutive negative cultures are obtained, followed by less frequent monitoring thereafter.[16-18]

In addition to clinical and microbiological monitoring, it is crucial to be vigilant for potential adverse effects associated with the multidrug regimens used in NTM treatment. These can include hepatotoxicity, visual disturbances, ototoxicity, and gastrointestinal upset, among others. Early detection and management of these adverse effects can help to ensure patient safety and adherence to therapy. Despite optimal medical management, some patients with NTM lung disease and pleural effusion may experience persistent or recurrent pleural fluid accumulation. In such cases, surgical intervention may be considered as an adjunct to medical therapy. Decortication, which involves the removal of the thickened pleural peel, and pleurectomy, which entails the resection of the parietal pleura, are the two main surgical options available. The rationale behind surgical intervention is to facilitate lung re-expansion, improve lung function, and alleviate symptoms associated with the pleural effusion. Decortication is typically preferred in cases where the lung is trapped by a thick, organized pleural peel, while pleurectomy may be more suitable for patients with diffuse pleural thickening or recurrent effusions. However, the role of surgery in the management of NTM-related pleural effusion remains a subject of debate. While some studies have reported favorable outcomes with surgical intervention, others have raised concerns about potential complications and the lack of robust evidence supporting its efficacy. The decision to pursue surgery should be made on a case-by-case basis, carefully weighing the potential benefits against the risks. Factors to consider include the patient's overall health status, the severity of symptoms, the response to medical therapy, and the expertise of the surgical team. The optimal duration of therapy for NTM lung disease with pleural effusion is not well defined, and current guidelines recommend continuing treatment for at least 12 months after sputum culture conversion. Close monitoring for clinical response and adverse effects is essential. Surgical intervention may be considered in cases of persistent or recurrent pleural effusion despite adequate medical therapy, but its role remains controversial and requires further research.[19,20]

4. Conclusion

NTM lung disease with pleural effusion is a rare but increasingly recognized entity. A high index of suspicion, comprehensive microbiological

investigations, and bronchoscopy are crucial for accurate diagnosis. Prompt initiation of appropriate multidrug therapy is essential for optimal outcomes. Further research is needed to elucidate the pathogenesis and optimal management of NTM-related pleural effusion.

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