Nontuberculous Mycobacterial Pneumonia: Radiologic and Clinical Correlation in an Infant Presenting with Respiratory Distress

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Abstract

Nontuberculous mycobacterium (NTM) is a distinct group of organisms presenting with lymphadenitis and pulmonary infection as the common manifestations among pediatric population. The diagnosis of pulmonary NTM disease is based on clinical manifestations, radiologic findings and microbiologic culture.

This is a report of a confirmed case of NTM pneumonia in a 13-week old infant who presented with poor weight gain and tachypnea. Chest radiographs at the time of admission showed consolidation of the right upper and both lower lobes and hilar lymphadenopathy. The chest CT scan showed necrotizing pneumonia as well as enlarged and matted lymph nodes reflective of primary progressive tuberculosis with advanced lymph node and lung disease. The diagnosis of *Mycobacterium abscessus* pneumonia was confirmed after 6 weeks of confinement through a positive gastric aspirate culture and speciation for *M. abscessus*. Household screening tests revealed that a grandparent whose sputum tested positive for *M. abscessus*. The patient received amikacin, cefoxitin, and clarithromycin based on the results of the culture and sensitivity. The patient received the antibiotic treatment for one year, and underwent quarterly gastric aspirate AFB smear and culture. The patient responded to the treatment and had no recurrence after 1 year.

This case report highlights the difficulty of establishing the diagnosis of NTM infection that requires a high index of suspicion and multiple tests and procedures to isolate the causative agent. Radiographic features are very similar to those seen in complicated tuberculosis infection. The clinical manifestations and imaging features that characterize NTM and mycobacterium tuberculosis will aid in timely diagnosis and treatment of the disease.

Introduction

Mycobacterium tuberculosis (TB) accounts for around 95 percent of mycobacterial infections. Nontuberculous mycobacterium (NTM) also known as atypical mycobacterium or mycobacterium other than tuberculosis (MOTT) accounts for the remaining 5 percent of disease (2). NTM is a distinct group of organisms with more than 150 catalogued species (3). The notable increase in number of cases of NTM for the past 30 to 40 years has been attributed to improved detection rates and the increase in opportunistic infections brought about by the HIV-AIDS pandemic.

Pulmonary infections, lymphadenitis, skin and soft tissue infections are among the major diseases associated with NTM infection (3). In the pediatric population the annual incidence rate of NTM was estimated to be 0.77 cases per 100,000 children. Lymphadenitis is the most common manifestation in children, followed by pulmonary disease (4).

This case report will discuss an unusual case of nontuberculous mycobacterial pneumonia in an infant. The clinical presentation and the key imaging features will be highlighted to help distinguish NTM from TB pneumonia.

Case Presentation

A 13-week old female infant was admitted to a tertiary medical center in the Philippines for rapid breathing and notable weight loss. Patient was born full term with a birth weight of 2.95 kg without perinatal complications. Pure breastfeeding was supplemented with virgin coconut oil (1 ml given 5-7x a day) and dibencozide due to poor weight gain. At age 13 weeks, the patient was noted to have fast breathing with no fever, cough or colds. On pediatric consult, the body weight was 3.65 kg, and the infant had good suck and clear breath sounds.

Initial chest x-ray showed consolidation at the right upper and both lower lobes. Lateral view demonstrated lobulated soft tissue densities reflective of hilar lymphadenopathy [see Fig. 1].

Physical examination on admission showed a patient in moderate respiratory distress with a respiratory rate of 70 per minute and a heart rate of 124 per minute while on oxygen inhalation via nasal cannula at 1 li/min. Body temperature was 36.2°C and oxygen saturation was 95% at room air. Breath sounds were clear on auscultation. The working impression was bilateral pneumonia for which intravenous cefuroxime was started.
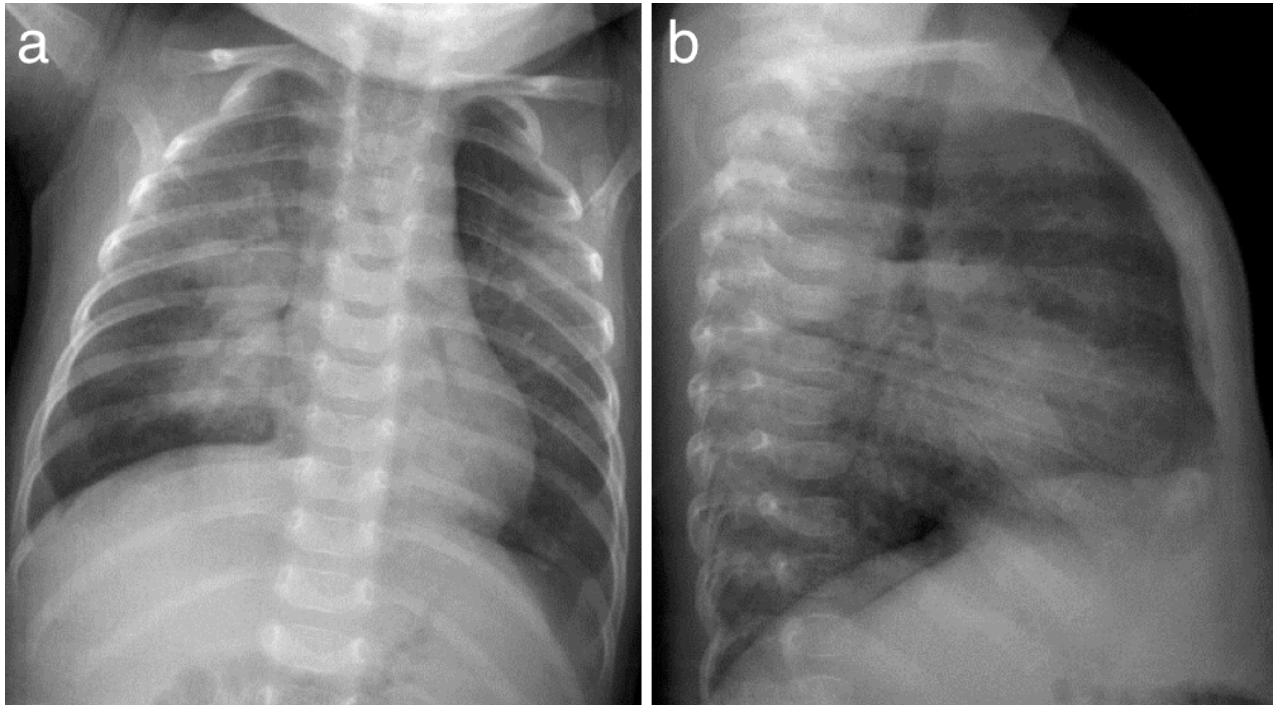
Fig. 1 Chest AP view (a) on admission showing consolidation of the right upper and both lower lobes. Lateral view (b) showed lobulated soft tissue densities suggestive of hilar lymphadenopathy.
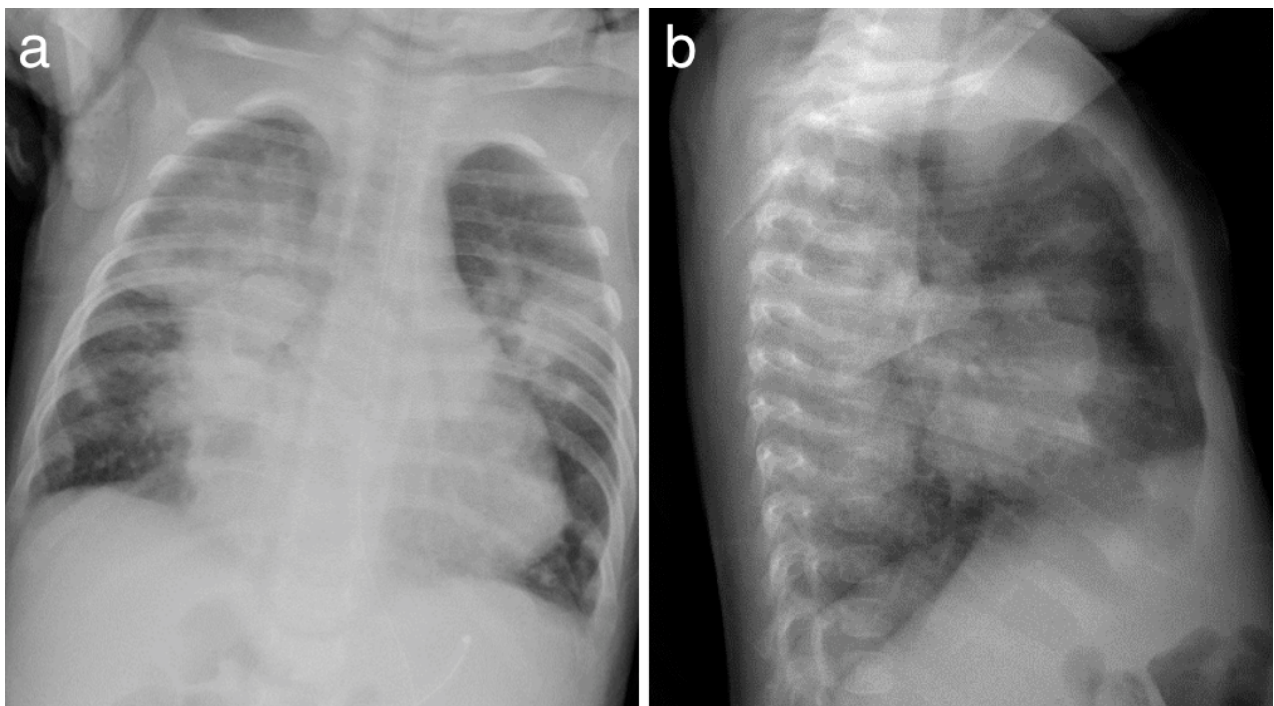

Fig. 2 Follow-up chest x-ray a week after initial radiograph shows progression in extent and degree of consolidation at upper and lower lobes. Lateral view (b) demonstrates better defined margins of the lobulated soft tissue densities reflective of hilar lymphadenopathy.

On the 3rd hospital day, the patient showed no appreciable improvement. At this point, the differential diagnoses included afebrile pneumonia syndrome, pulmonary tuberculosis, lipoid aspiration pneumonia and a congenital lung defect. Oral erythromycin was added. A repeat chest x-ray a week after initial radiograph was done which [see Fig. 2] revealed progression in extent and degree of the pulmonary disease.

One out of three gastric aspirate AFB smears was positive for AFB. Contact tracing of family members showed that 3 grandparents had chest x-ray findings that were suspicious for tuberculosis. Anti-TB medications (isoniazid, rifampicin, pyrazinamide and ethambutol) were then given to the patient.

Chest CT scan revealed bibasal consolidation pneumonia and multiple hilar lymphadenopathy [see Fig. 3]. Necrotizing pneumonia was also observed at the bilateral lung bases.
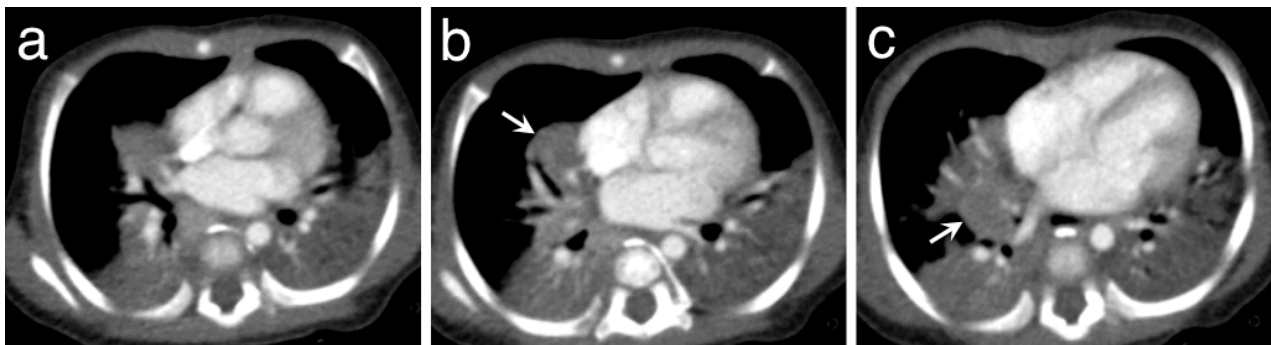

Fig. 3 Initial contrast-enhanced CT images of the chest in mediastinal window show bibasal lung consolidation, hilar lymphadenopathy (arrows), and necrotizing pneumonia at the bilateral lung bases.

The patient underwent fiberoptic bronchoscopy. Bronchial washings grew *Enterobacter cloacae* that was sensitive to amikacin and meropenem. Subsequently, the gastric aspirate culture results were positive for *Mycobacterium abscessus* on the 41st day of confinement. The anti-TB medications were then discontinued, and the patient was shifted to IV amikacin and cefoxitin and oral clarithromycin.

The other tests performed showed negative results for cystic fibrosis and ciliary dyskinesia. An initial immunologic panel showed significantly decreased CD3, CD4 and CD8 counts. A repeat testing done after 6 weeks showed normal counts so that primary immunodeficiency was ruled out in this case.

The culture and sensitivity tests showed that *M. abscessus* in this case was sensitive to amikacin, cefoxitin and clarithromycin. By the 58th hospital day, the patient became stable, afebrile, with good weight gain. She was discharged with oxygen supplementation. The three antibiotics were administered at home for one year. Gastric aspirate AFB smear and cultures were performed every 3 months, and these turned out negative for NTM. The respiratory rate and the patient's body weight gradually returned to normal.

Repeat chest CT done a year later [see Fig. 4] demonstrated marked improvement in the pulmonary parenchymal consolidation/necrotizing pneumonia and hilar lymphadenopathy.
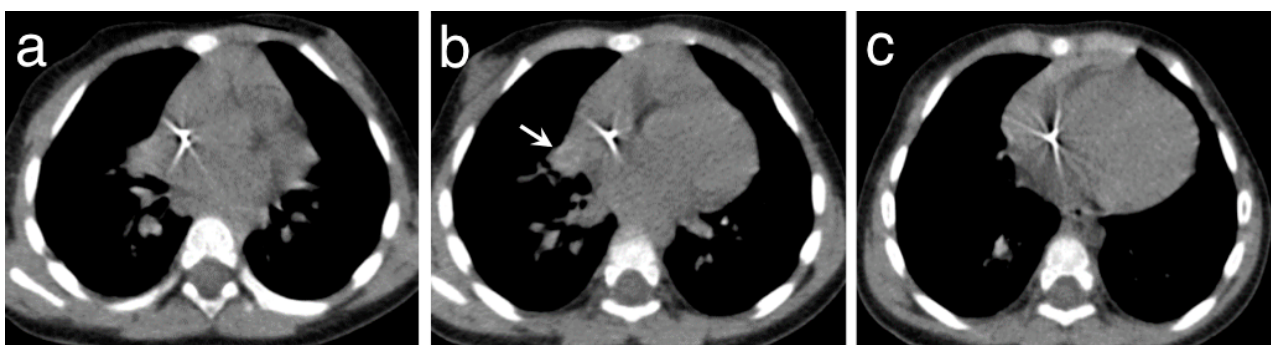
Fig. 4 Follow-up plain axial chest CT images in mediastinal window show resolution of the parenchymal consolidation, decrease in size of the hilar lymphadenopathy (arrow), and resolution of the necrotizing pneumonia at the bases.

Discussion

Epidemiology and Pathogenesis

NTM are ubiquitous organisms found in soil, water and air. The major mode of transmission for NTM is presumably by droplet inhalation. NTM infections are associated with immunosuppressive states or when the host defenses are impaired such as in HIV, cystic fibrosis, ciliary dyskinesia, pulmonary alveolar proteinosis and esophageal motility disorders.

NTM has been classified initially into groups based on the rate of growth and the production of pigment. This classification however, has low clinical significance when compared to newer molecular detection techniques that are capable of identifying specific species within few hours (6,11). The most common NTM isolated globally are *Mycobacterium avium complex* (MAC), *M. abscessus*, *M. kansasii, M.chelonae* and *M.fortuitum* (7).

Clinical Features

The American Thoracic Society (ATS) and the infectious Disease Society of America (IDSA) published a joint statement to establish uniform diagnostic criteria for NTM pulmonary disease (see Table I). This includes clinical symptoms, radiological manifestations and microbiologic cultures with exclusion of other etiologies (7). NTM demonstrates an indolent course with mild and non-specific signs such as chronic productive cough and fatigue. Fever and sweats are less frequent compared to TB disease. Weight loss, wasting and hemoptysis are uncommon and when present signifies advanced disease (6). Since the respiratory tract can be colonized with NTM without disease, it is necessary that clinical assessment be performed prior to a diagnosis of NTM disease. The disease is confirmed by culture growth of NTM from one bronchoalveolar lavage, two sputum samples or culture from respiratory tissue demonstrating granulomatous histopathology.

Table I American Thoracic Society Diagnostic Criteria for Nontuberculous Mycobacterial Lung Disease (Adapted from the Official ATS/IDSA Statement 2006)	The minimum evaluation of a patient suspected of nontuberculous mycobacterial (NTM) lung disease should include the following: 1. Chest radiograph, or in the absence of cavitation, chest high-resolution CT scan (HRCT) 2. Three or more specimens for acid fast bacilli (AFB) 3. Exclusion of other disorders, such as Tuberculosis (TB)
	Clinical Criteria: 1. Pulmonary symptoms, nodular or cavitary opacities on chest radiograph, or HRCT scan that shows multifocal bronchiectasis with multiple small nodules 2. Appropriate exclusion of other diagnoses
	Microbiologic Criteria: 1. Positive culture results from at least two separate expectorated sputum samples. 2. Positive culture results from at least one bronchial wash or lavage 3. Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histopathologic features and one or more sputum or bronchial washings that are culture positive for NTM 4. Expert consultation should be obtained when NTM are recovered that are either infrequently encountered or that usually represent environmental contamination 5. Patients who are suspected of having NTM lung disease but who do not meet the diagnostic criteria should be followed until the diagnosis if firmly established or excluded 6. Making the diagnosis of NTM lung disease does not, per se, necessitate the institution of therapy, which is a decision based on potential risks and benefits of therapy for individual patients

Imaging Clues

Five different types of Nontuberculous Mycobacterium Infection:

Classic or cavitary type
- most common form
- predominantly upper lobe
- cavitation
- tree-in-bud like nodules
- cavitations usually smaller than pulmonary TB
- calcified pulmonary nodules and mediastinal lymph node less frequent than pulmonary TB

Non-classic or bronchiectatic
- symmetric and cylindrical bronchiectasis
- more common in middle lobe and lingula
- atelectasis, mediastinal lymph nodes and cavitations uncommon

NTM with immunosupression
- reticulonodular opacities, mediastinal and hilar lymphadenopathies
- no significant features to distinguish it from TB

NTM associated with achalasia
- reticulo-nodular or airspace filling opacities like aspiration pneumonia

Hypersensitivity pneumonitis
- ground-glass centrilobular nodules, diffuse ground-glass opacities, consolidations and air trapping on expiratory examination

The current drug of choice for the treatment of pulmonary M. abscessus infection would be multidrug regimens that include clarithromycin. There are no drug regimens of proven or predictable efficacy for treatment of M. abscessus lung disease. Multidrug regimens may result in symptomatic improvement and regression of disease. A 12-month period of negative sputum cultures while on multidrug therapy (amikacin, cefoxitin, and a macrolide) may be a reasonable goal for treatment (7). The patient underwent gastric aspirates every 3 months for 1 year while on multidrug treatment with amikacin, cefoxitin, and clarithromycin. Cultures have been negative since his discharge from the hospital.

Pulmonary Imaging Features

Chest x-ray is the primary imaging modality that describes the parenchymal and lymph node involvement in a patient affected with tuberculosis. Further evaluation can be performed with a chest CT scan to elucidate the details of the bronchial lumina whether luminal compromise or bronchiectasis is present, the presence of nodules, consolidation, atelectasis, cavity, or possibly necrotic changes in mediastinal and hilar lymph nodes.

Yuan and colleagues (8) have recommended CT imaging criteria that may be used in differentiating features of tuberculous mycobacterial infection from nontuberculous mycobacterial infection (see Table II).

Table II CT features that differentiate Tuberculous Mycobacterial infection from Nontuberculous Mycobacterial infection

CT of Tuberculous Mycobacterial Infection	CT of Nontuberculous Mycobacterial Infection
Thick walled cavity (> 3 cm)	Thin walled cavity (< 3 cm)
Pulmonary consolidation	Small parenchymal nodules
Patchy and reticular infiltrates	Lymph node calcification
Atelectasis	
Mediastinal and hilar lymph nodes	
Lymph node calcification	
Pleural effusion	

(Adapted from article: Yuan MK, Chang CY, Tsai PH, et al. Comparative chest computed tomography findings of non-tuberculous mycobacterial lung diseases and pulmonary tuberculosis in patients with acid fast bacilli smear-positive sputum. BMC Pulmonary Medicine, 2014; 14:65 http://www.biomedcentral.com/1471-2466/14/65)

Miller classified pulmonary NTM infection according to its clinical presentation and imaging manifestations as a) classical (cavitary), b) non-classical (bronchiectatic), c) associated with immunosupression, d) achalasia like symptoms and e) nodules or masses in asymptomatic individuals (9). Tuberculosis and nontubercular mycobacterial disease have similar imaging features and may be indistinguishable solely on the basis of imaging manifestations (9).

Classic infection is the most common form of NTM disease with imaging features similar to post primary pulmonary tuberculosis. The radiological features are cavitations, ill-defined linear and nodular opacities predominantly at the upper lobes. Endobronchial spread of the NTM disease from the cavities is common and results in tree-in-bud like centrilobular nodules adjacent to the disease foci. Bronchiectatic and cicatricial atelectasis are also seen at the upper lobes. The lower lobe involvement is uncommon (9).

CT scan demonstrates cavities, which are usually smaller and thin-walled when compared with tuberculosis. The mean size of the cavities are less than 2.5 cm. Pleural effusion, calcified pulmonary nodules and mediastinal lymph nodes (or Ranke's complex) are less common in pulmonary NTM (10,11).   The NTM disease process demonstrates relatively slower course than active pulmonary tuberculosis. Pleural thickening adjacent to the parenchymal disease is more pronounced in NTM disease ~~as~~ compared to tuberculosis; however basal pleural disease is rare when compared with tuberculosis. *Mycobacterium avium complex* (MAC) is the most common organism responsible for NTM disease and commonly seen in elderly patients with preexisting lung disease like COPD.

Non-classic infection or bronchiectatic form of NTM disease is seen usually in elderly women without history of coexisting lung disease. Chronic cough may be the only clinical manifestation in majority of the patients. Lady Windermere Syndrome is associated with nontuberculous mycobacterial disease in women who chronically suppress their cough where there is voluntary cough suppression, leading to aspiration and entrapment of MAC infected secretions. The imaging features of the non-classic form of NTM disease are usually symmetric and cylindrical bronchiectasis, more common in the lingula and middle lobe with bronchiolitis in the form of tree-in-bud like nodules. Atelectasis, cavitations and mediastinal lymphadenopathy are uncommon (10, 11). The more common involvement of the middle lobe and the lingula may help in the diagnosis of the NTM disease as these are unlikely in TB.

Nontuberculous mycobacterial disease is seen with immunosupression state in both HIV and non-HIV patients. The disease manifests in HIV patients with low CD4 counts (less than 100 cells/mm^5) and are usually associated coexisting infections like pneumocystis, cytomegalovirus, and fungal infection (10). This overlapping diseases makes difficult to identify the only imaging features NTM disease in this group of patients.

MAC is the most common NTM organism associated with HIV infection and usually presents with disseminated disease. The pertinent imaging feature is mediastinal lymphadenopathy and less likely miliary nodules, pleural effusion and air space opacities. The other organisms associated with HIV infections are *M. kansasii* and *M. xenopi* with imaging features similar to disseminated Tubercular disease (TB).

NTM has been also reported to be associated with deglutition disorders like achalasia, stroke, and Parkinsonism. The organisms often isolated here are *M. fortuitum* and *M. chelonae*. The imaging manifestations are either reticulo-nodular or air space filling opacities like aspiration pneumonia with no definite lobar predominance (11). Pulmonary NTM may manifest as nodules or masses in asymptomatic individuals. MAC are the most common isolated organism. (10, 11).

There are few reported cases of hypersensitivity pneumonitis secondary to NTM disease. These organisms were also isolated from household waters. Imaging manifestations are ill-defined, ground-glass centrilobular nodules, diffuse ground-glass opacities, consolidations and air trapping on expiratory examination (10).

Conclusion

This is a case report of a 13-week infant with a confirmed diagnosis of *Mycobacterium abscessus* pneumonia. The diagnostic workup of this case included chest CT scans, gastric aspirate AFB smear and culture, and species-level identification with antimicrobial susceptibility tests. The patient received amikacin, cefoxitin and clarithromycin which was maintained for a total period of 1 year. On follow-up, the patient underwent gastric aspirate AFB smear and cultures every 3 months for a year, and these were negative for NTM. Clinical and radiological improvement were noted gradually over the succeeding months of treatment. Pulmonary NTM may be clinically and radiographically indistinguishable from pulmonary TB.

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