Imaging of pulmonary nontuberculous mycobacterial infection: variations, sequential changes, and differential diagnoses

Poster No.: C-0584
Congress: ECR 2016
Type: Educational Exhibit
Authors: S. Noguchi¹, Y. Nishimoto², S. Noma³; ¹Tenri/JP, ²Kashihara/JP, ³Tenri City, Nara/JP
Keywords: Infection, Diagnostic procedure, CT, Lung
DOI: 10.1594/ecr2016/C-0584

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

This exhibition is aim to show:

1. Typical images of pulmonary nontuberculous mycobacterial infection
2. Sequential change of CT images
3. Unusual clinical and radiological manifestation
4. Differential diagnosis
Background

The nontuberculous mycobacteria (NTM) are a grouping of all Mycobacterium species other than the obligate pathogens *M. tuberculosis* complex and *M. laprae*. They are typically environmental organisms residing in soil and water. Although it is generally of low pathogenicity to humans, NTM can cause a wide array of clinical diseases; pulmonary disease is most frequent. Nowadays in many geographical regions, NTM cause greater burden than tuberculosis (1)(2).

Unlike tuberculosis, single positive culture of NTM does not always mean infection or disease because they are environmental bacteria that humans encounter on a daily basis. In addition patients often have almost no subjective symptoms in its early stage.

Thus imaging tests have important role in diagnosis of pulmonary NTM. In official statement of the American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA), radiologic abnormality and microbiologic cultures are regarded as two major strategy (3). On the other hand, NTM can present variety of pulmonary lesion depend on immunological or structural condition of host's lung, and sometimes hard to distinct from other disease. We radiologist need to know various radiographic patterns and contribute accurate diagnosis.

In this exhibition, we present typical clinical and radiological manifestation of pulmonary NTM. We also show important differential diagnosis of NTM.
Findings and procedure details

1. Clinical and radiologic manifestations of pulmonary NTM

Clinical and radiologic manifestations of pulmonary NTM are usually classified into five categories. Nodular and bronchiectatic form, and fibrocavitary form are well-recognized pattern of infection. Solitary pulmonary nodules, disseminated disease, and Hypersensitivity pneumonitis-like disease is less common.

a. Nodular and bronchiectatic form

Nowadays over 90% of patients who are diagnosed as pulmonary NTM present this pattern (4). It is most commonly seen among elderly women with no predisposing factors. Infection presents in an indolent fashion with a chronic cough; constitutional symptoms are uncommon (5)(6). Although right middle lobe and lingula are most commonly affected, any segment can be involved (7)(8).

In early stage, infected bacilli colonize subpleural area and form granulomatous lesion, followed by transbronchial spread to regional lung parenchyma (9). Reflecting this infection process, typical CT findings are small centrilobular nodules or tree-in-bud opacities, with cylindrical bronchiectasis, usually in the same lobe (Fig.1). Centrilobular nodules histopathologically correspond to NTM granulomas and caseous materials within the terminal or respiratory bronchioles, and bronchiectasis may be formed as a result of chronic inflammation of bronchial wall (10).

Granulomas continuously cluster together and form larger nodules (Fig. 2). After elimination of necrotic tissue from bronchioles, cavitary lesions are formed. Chronic inflammation cause regional lung destruction, and formation of cicatricial atelectasis with bronchiectasis. Although progression of pulmonary NTM infection is generally very slow, in some cases, widespread lung destruction is developed in long term disease course (Fig. 3).

b. Fibrocavitary form

This form of disease is more prevalent among older men with underlying chronic pulmonary disease such as pulmonary emphysema.

Common CT findings are upper lobe cavitary lesions adjacent to the existing lung lesion (Fig. 4). Cavitary lesions can be spreading source of NTM, thus satellite nodules and bronchiectasis in the same lobe are often seen (8)(11). The presence of cavitary lesions is correlate to aural discharge of bacilli, and clinical manifestation of fever or hemoptysis (12).
c. Solitary pulmonary Nodule

Pulmonary NTM infection can manifest as nodules or masses in asymptomatic patients. When it appears as solitary nodule, it may be misdiagnosed as lung cancer (Fig. 5).

CT findings which is helpful for differential diagnosis from malignancy is 1: intralesional calcification or increased attenuation (which is suggestive of granulomatous cause), 2: enhancement of 15 HU or less after administration of contrast material, 3: strong enhancement of just the rim of nodule (so called enhancing rim sign), 4: when multiple, nodules clustered together and have uniform size (8)(13)(14).

d. Disseminated disease

Immunocompromised hosts such as acquired immunodeficiency syndrome (AIDS) patients can develop systemic infection of NTM. Hematogenous spread can occur to many sites, including liver, spleen, bone marrow, skin, and lymph nodes (15). Recently, disseminated NTM infection related to other immune abnormalities, such as autoantibody to interferon gamma are also reported (Fig. 6)(16).

Mediastinal lymphadenopathy is said to be the most common manifestation. Air space opacities, miliary nodules, and pleural effusion are reported but infrequently(17).

e. Hypersensitivity pneumonitis-like disease: so called "Hot tub lung"

Although rare, hypersensitivity pneumonitis associated with inhaled NTM, often from hot tub exposure, has been reported (18).

Characteristic CT findings include ill-defined, ground-glass centrilobular nodules, more diffuse ground glass opacities, and air trapping on expiratory examination (Fig. 7) (19). These findings are quite similar to known feature of subacute hypersensitivity pneumonitis.

Whether this phenomenon represent true hypersensitivity pneumonitis or infection remains controversial.

2. Radiologic pattern of specific species

In developed countries, MAC account for more than 80% of pulmonary NTM. M. kansasii account for 10%; the lest is M. abscessus, M. chelonae, M. fortuitum, and so on. Although it is impossible to identify the bacterial species from CT images, several characteristic findings are reported to each species.
a. *M. kansasii*

Infection of *M. kansasii* is commonly seen in male with history of smoking or occupational exposure to dust. Thus its CT findings has a feature of fibrocavitary form, include cavities located in right posterior or apical segment with a tubular meandering shape and a thin wall (20). Since this organism is susceptible to antibiotics, it is the only NTM which is treatable.

b. *M. abscessus*

The radiologic feature is somewhat similar to MAC, such as bilateral small nodular opacities, bronchiectasis, and cavity formation. However, the lung involvement is said to be more extensive in *M. abscessus* than MAC (21).

3. Differential diagnosis of pulmonary NTM

The main differential diagnoses of pulmonary NTM are (a) Nonspecific bronchiolitis, (b) Tuberculosis, (c) Lung cancer.

a. Nonspecific bronchiolitis

It is not rare that repeated sputum cultures do not detect any specific organism, although centrilobular nodules and mild bronchiectasis are seen in CT images. These cases are clinically diagnosed as nonspecific bronchiolitis. In one study, 50% of patients who present bilateral bronchiectasis were not identified any definite cause(22). However, presence of cavitary lesion is rather specific to NTM infection.

b. Tuberculosis

Tuberculosis is important differential diagnosis for both nodular and bronchiectatic form and fibrocavitary form of NTM infection. Although there is no radiographic finding to reliably differentiate NTM and tuberculosis, in NTM infection, disease progresses more slowly and cavities are more likely to smaller or thinner-walled(11). The presence of bronchiectasis and cavities in sites other than the upper lobes may also suggest possibility of NTM infection as opposed to tuberculosis(23).

c. Lung cancer

The rate of coexisting lung cancer and pulmonary mycobacteriosisis is not very high(1-2%(24)). However when a new nodular lesion appears in the course of NTM infection, we should always consider the possibility of lung cancer. It is important
especially in fibrocavitary form, because patients always have risk factors of lung cancer such as pulmonary emphysema or interstitial pneumonia (Fig. 8).
Fig. 1: 60s Female, MAC infection, Nodular and bronchiectatic form. This case presents typical findings of early stage NTM infection. Regional spread of dense nodules in subpleural area of left S3 is seen. Centrilobular nodules histopathologically correspond to NTM granulomas and caseous materials within the terminal or respiratory bronchioles. Infected bacilli initially colonize subpleural area and form granulomatous lesion, followed by transbronchial spread to regional lung parenchyma.

© Tenri Hospital - Tenri/JP
Fig. 2: 70s female, MAC infection, Nodular and bronchiectatic form. Chest radiograph shows multiple nodules (white arrows), subtle opacities, in both middle and lower lung fields. CT images show centrilobular nodules in right middle lobe, lingula, and right S6. Small foci of consolidation (black arrows) and cicatricial atelectasis with bronchiectasis (circle) are also indicated. Right middle lobe and lingula are most commonly affected in this form of infection.

© Tenri Hospital - Tenri/JP
**Fig. 3:** 60s (in the initial) Female, M. gordonae and M. kansasii infection, Nodular and bronchiectatic form. In this patient, lung destruction has been progressed continuously in long term, though she had received multidrug antibiotic therapy.

© Tenri Hospital - Tenri/JP
**Fig. 4:** 60s Male, MAC infection, Fibrocavitary form. This patient had been observed as CPFE (combined pulmonary fibrosis and emphysema). Follow-up chest radiograph showed occurrence of a consolidation in apex of right lung (circle). In CT images, dense consolidation spread along bulla wall is demonstrated. Sputum culture showed M. avium. The consolidation recessed after antibiotic therapy.

© Tenri Hospital - Tenri/JP
**Fig. 5:** 70s Male, MAC infection, Solitary pulmonary nodule. Initial CT shows small dense nodules clustered together. In three years observation, nodules have been formed a cavity, and then changed to a solid nodule. Partial resection of left upper lobe was proceeded for rule out malignancy, and for treatment of the infection. Histopathologic examination showed necrotizing granulomatous lesion and mycobacteria species.

© Tenri Hospital - Tenri/JP
Fig. 6: 40s female with a history of repetitive pneumonia referred to our hospital because of refractory pneumonia. CT shows dense consolidation with air bronchogram and ground grass opacity in lingula, and small nodules in left lower lobe. After contrast infusion, pulmonary arteries penetrating through consolidation were seen, which were interpreted as CT angiogram sign (black arrows). Lymph nodes swelling were seen in left hilum, mediastinum, and supraclavicular area (white arrows). Diffuse high accumulation of FDG is indicated in bone marrow and spleen. From these radiologic findings, systemic dissemination of malignant lymphoma was suspected. However, no evidence of malignancy was shown in any histopathologic examination. On the other hand, M. avium was detected from each biopsy specimens of bronchus, lymph node, and bone marrow. Immunological examination detected auto-antibodies to IFN-# from her blood plasma.

© Tenri Hospital - Tenri/JP
Fig. 7: 50s Male, MAC infection, Hypersensitivity pneumonitis-like disease : so called "Hot tub lung". He referred to our hospital because of mild fever and cough. He had no underlying disease. Chest radiograph showed bilateral diffuse ground glass opacity. CT images showed diffuse centrilobular ground glass opacities, which is quite similar to known feature of subacute hypersensitivity pneumonitis. Sputum culture detected M. avium, and the same strain was proved from his home bath tub. Histopathological examination with transbronchial lung biopsy found granulomatous lesions.

© Tenri Hospital - Tenri/JP
**Fig. 8:** 60s Male. This patient had been observed for COPD (chronic obstructive pulmonary disease) and pulmonary NTM infection (MAC and M. kansasii infection, fibrocavitary form). Follow-up chest radiograph showed occurrence of a mass in the hilum of left lung (circle). CT image showed thick walled cavitary nodule in left lower lobe. It was difficult to distinguish lung cancer from relapse of NTM lesion. Bronchoscopic examination detected squamous cell carcinoma.

© Tenri Hospital - Tenri/JP
Conclusion

Clinical and radiological manifestations of pulmonary NTM are variable. Nodular and bronchiectatic form, and fibrocavitary form are well-recognized pattern of infection. Solitary pulmonary nodules, disseminated disease, and Hypersensitivity pneumonitis-like disease is less common. To make correct diagnosis and institute appropriate treatment, we radiologist need to familiar with variations, sequential changes, and differential diagnoses.