Original Article

# CLINICAL ANALYSIS OF OSTEOARTICULAR NONTUBERCULOUS MYCOBACTERIAL INFECTION

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**Abstract** [Objective] The incidence rate of nontuberculous mycobacterial (NTM) infection has been increasing globally in recent years. However, reports of osteoarticular NTM infection are relatively rare. We report the characteristic clinical features of patients with osteoarticular NTM infection. [Patients and Methods] We examined 14 patients with osteoarticular NTM infection (mean age, 68 years) were treated in our hospital in the 20 years between 1995 and 2015. [Results] The rate of osteoarticular NTM infection in whole osteoarticular infection during the same period in our hospital was 2.7%. The NTM species isolated from the 14 patients included *Mycobacterium avium* (n=7), *M. intracellulare* (n=5), *M. fortuitum* (n=1), and *M. kansasii* (n=1). Twelve patients had spinal involvements, and their levels were categorized as thoracic (n=3), lumbar (n=4), thoracolumbar (n=1), and cervicothoracic (n=4), with an average number of affected vertebra of 4.4. Nine patients had pulmonary lesions, including fibrocavitary (n=5) and nodular/bronchiectatic types (n=4). Nine patients had lesions in sites other than the spinal and pulmonary regions, including the skin (n=6), rib (n=2), ilium (n=2), humerus (n=2), ulna (n=1), wrist (n=1), knee joint (n=1), femur (n=2), tibia (n=1), toe (n=1), and kidney (n=1). In the initial examination, 11 patients were misdiagnosed, which delayed the final diagnosis in 7 patients. Six patients received chemotherapy with rifampicin, ethambutol, and clarithromycin, and 8 patients received other macrolide-based therapy. Five patients underwent surgical treatments in former hospitals, and 8 patients underwent surgical treatments (including salvage surgeries) in our hospital. With regard to outcome, 9 patients achieved healing, 2 patients with relapse were healed after retreatment, 1 patient was undergoing treatment, 1 patient had interrupted treatment, and 1 patient died during the treatment period. [Discussion] Osteoarticular NTM infection presented widely spread lesions in the spine and other various locations, mostly developed as a part of disseminated infection. Most patients were aged or immunosuppressed, but some patients were healthy individuals with no relevant medical history. Thus, if a patient is diagnosed with disseminated NTM infection, examination for possible lesions in other sites, including the bone and joint, should be performed. Cutaneous lesions, including subcutaneous abscess, were also characteristic. It is worth mentioning that such lesions can develop even under chemotherapy. Given the increasing trend in the overall incidence of NTM infection, awareness that NTM is a causative organism of osteoarticular infection is important.

**Key words** : Nontuberculous mycobacterial infection, Osteomyelitis, Spondylitis, Arthritis, Disseminated infection

Original Article

# ASSOCIATION BETWEEN A pMAH135 PLASMID AND THE PROGRESSION OF PULMONARY DISEASE CAUSED BY *MYCOBACTERIUM AVIUM*

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**Abstract** [Background] Pulmonary disease caused by nontuberculous mycobacteria has a variable clinical course. Although this is possibly the result of not only host factors, but also bacterial factors, many questions remain to be answered regarding these manifestations. [Methods] To assess the relationship between the progression of pulmonary *Mycobacterium avium* disease and bacterial factors, we performed variable number tandem repeats (VNTR) typing analysis of *M.avium* tandem repeats (MATR) in *M.avium* isolates from 46 patients with different clinical courses, and furthermore, examined the association between disease progression and a pMAH135 plasmid derived from *M.avium*. [Results] In patients whose treatment was initiated because of worsened chest radiograph findings and/or clinical symptoms within 18 months after being diagnosed with pulmonary *M.avium* disease, the detection rate of 6 genes located in pMAH135 was 35.3−47.1% for 17 isolates. However, in untreated patients with a stable condition, these rates were 10.3−13.8% in 29 isolates. MATR-VNTR typing analysis showed that isolates from patients with worsened disease and those with stable disease are clustered differently. In cluster III, the number of isolates from patients with worsened disease was higher than that from patients with stable disease ($p=0.019$), and furthermore, the number of isolates carrying pMAH135 genes was higher than that not carrying pMAH135 genes ($p\leqq0.001$). [Conclusion] These results indicate an association between the progression of pulmonary *M.avium* disease and pMAH135. The presence of pMAH135 genes might be a useful prognostic indicator for pulmonary *M.avium* disease and may serve as one criterion for treatment initiation.

**Key words** : *Mycobacterium avium* subsp. *hominissuis*, Disease progression, Variable number tandem repeats, pMAH135 plasmid

Review Article

# TUBERCULOSIS AND LUNG CANCER

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**Abstract** The occurrence of pulmonary tuberculosis (PTB) and lung cancer as comorbidities has been extensively discussed in many studies. In the past, it was well known that lung cancer is a specific epidemiological successor of PTB and that lung cancer often develops in scars caused by PTB. In recent years, the relevance of the two diseases has drawn attention in terms of the close epidemiological connection and chronic inflammation-associated carcinogenesis. In Japanese case series studies, most lung cancer patients with tuberculous sequelae received supportive care alone in the past, but more recently, the use of aggressive lung cancer treatment is increasing. Many studies on PTB and lung cancer as comorbidities have revealed that active PTB is noted in 2–5% of lung cancer cases, whereas lung cancer is noted in 1–2% of active PTB cases. In such instances of comorbidity, many active PTB cases showed Type II (non-extensively cavitary disease) and Spread 2–3 (intermediate–extensive diseases) on chest X-rays, but standard anti-tuberculosis treatment easily eradicates negative conversion of sputum culture for *M.tuberculosis*; lung cancer cases were often stage III–IV and squamous cell carcinoma predominant, and the administration of aggressive treatment for lung cancer is increasing. The major clinical problems associated with PTB and lung cancer as comorbidities include delay in diagnosis (doctor's delay) and therapeutic limitations. The former involves two factors of radiographic interpretation: the principles of parsimony (Occam's razor) and visual search; the latter involves three factors of lung cancer treatment: infectivity of *M.tuberculosis*, anatomical limitation due to lung damage by tuberculosis, and drug-drug interactions between rifampicin and anti-cancer drugs, especially molecularly targeted drugs. The comorbidity of these two diseases is an important health-related issue in Japan. In the treatment of PTB, the possibility of concurrent lung cancer should be kept in mind, while in the treatment of lung cancer, the possibility of concurrent PTB should also be considered.

**Key words**: Tuberculosis, Lung cancer, Comorbidity, Epidemiology, Scar cancer, Doctor's delay, Therapeutic limitation