Respiratory Medicine (2014) **108**, 1706—1712

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/rmed

A shorter treatment duration may be sufficient for patients with *Mycobacterium massiliense* lung disease than with *Mycobacterium abscessus* lung disease☆

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Received 29 March 2014; accepted 4 September 2014
Available online 16 September 2014

KEYWORDS
Nontuberculous mycobacteria (NTM);
Mycobacterium abscessus;
Mycobacterium massiliense;
Treatment outcome

Summary

Background: *Mycobacterium abscessus* complex is the second most common organism isolated from patients with nontuberculous mycobacterial (NTM) lung disease in South Korea. This study aimed to compare clinical features and treatment outcomes of *M. abscessus* and *Mycobacterium massiliense* lung disease.

Methods: We retrospectively identified stored clinical isolates of *M. abscessus* complex as either *M. abscessus* or *M. massiliense* and reviewed medical records to compare clinical characteristics and treatment responses. All patients were treated empirically over several months with multidrug regimens, including a macrolide and one or more parenteral agents.

Results: Of the 249 patient isolates tested, 128 (59 with *M. abscessus* and 69 with *M. massiliense*) met the American Thoracic Society diagnostic criteria for NTM pulmonary disease, and treatment outcomes were analyzed in 48 patients (26 with *M. abscessus* and

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http://dx.doi.org/10.1016/j.rmed.2014.09.002

22 with *M. massiliense*). The clinical and radiologic findings were similar between the two groups. Although the durations of parenteral and total treatment were significantly shorter in patients with *M. massiliense* than in those with *M. abscessus* (4.7 months vs 7.4 months, $P = .006$, and 12.1 months vs 16.3 months, $P = .043$), the treatment success rate was significantly higher in patients with *M. massiliense* (95.5%) than in *M. abscessus* cases (42.3%, $P < .001$).

Conclusion: Patients with *M. massiliense* pulmonary infection responded better to this antibiotic strategy than those with *M. abscessus* infection. A shortened duration of treatment may be sufficient for *M. massiliense* pulmonary infection.

Introduction

Nontuberculous mycobacteria (NTM), which includes rapidly growing mycobacteria (RGM), are ubiquitous organisms increasingly emerging as important human pathogens [1,2]. In Korea, *Mycobacterium abscessus* complex is the most frequent RGM causing chronic lung disease [3]. *M. abscessus* complex is also notable for its resistance to first-line anti-tuberculosis drug and treatment difficulty with poor clinical outcomes [4]. In 2007, the American Thoracic Society (ATS) recommended periodic administration of multidrug therapy for affected cases, including a macrolide and one or more parenteral agents (amikacin, cefoxitin, or imipenem), or a combination of parenteral agents, over several (2—4) months [1]. However, these treatments are quite difficult and there are no established optimal treatment regimens showing good long-term outcomes [5]. *M. abscessus* complex is the second most commonly isolated NTM in Korea. In addition, the prevalence of chronic lung disease due to *M. abscessus* complex is increasing in South Korea [3].

For a long time, *M. abscessus*, *Mycobacterium massiliense*, and *Mycobacterium bolletii* had been thought to represent subgroups of a single species because of an overlap in biochemical and genetic properties. However, in 2006, two of these RGM species, *M. massiliense* and *M. bolletii*, have been separated from *M. abscessus* based on <97% *rpoB* gene sequence homology [6]. Recently, in 2011, *M. massiliense* and *M. bolletii* were united and reclassified as a single subspecies within *M. abscessus*: *M. abscessus* subsp. *bolletii* comb. nov [7]. However, the placement of *M. massiliense* within the boundary of *M. abscessus* subsp. *bolletii* remains highly controversial with regard to clinical aspects. Therefore, we used the old taxonomy instead of new one. In Korea, *M. abscessus* and *M. massiliense* infections present in almost equal numbers, whereas *M. bolletii* is very rare. Two recent studies have reported that patients with *M. massiliense* infections had significantly better treatment responses to combination antibiotic therapy than those with *M. abscessus* infections [8,9]. The aim of the present study was to evaluate the differences in the clinical characteristics and treatment outcomes between *M. massiliense* and *M. abscessus* pulmonary infections in a Korean population.

Materials and methods

Study population

Patients who were diagnosed with *M. abscessus* complex lung disease and who were treated based on 2007 ATS guidelines from January 2006 to June 2012 at the Asan Medical Center (Seoul, South Korea) were retrospectively evaluated. Clinical, radiological, and microbiological characteristics, management, and treatment outcome data were retrospectively collected from medical records. Initial standard posteroanterior and lateral chest radiographs (CXRs) and computed tomography (CT) results were reanalyzed based on seven categories: bronchiectasis, bronchiolitis, cavities, consolidation, bilateral involvement, multilobar involvement ($\geq$3 lobes with abnormalities), and type of disease (nodular bronchiectatic form, upper lobe cavitary form, and unclassifiable form). This study was approved by the Institutional Review Board of the Asan Medical Center. Informed consent was waived because of the retrospective nature of the study.

Microbiological examination

Acid-fast bacilli (AFB) were cultured in both solid Ogawa medium (Korean Institute of Tuberculosis, Osong, Korea) and a liquid MGIT system (Becton Dickinson, Sparks, MD). Cultured isolates were identified as *Mycobacterium tuberculosis* or NTM using the Duplex PCR test (Seegene Inc., Seoul, Korea). NTM species were identified using a polymerase chain reaction-restriction fragment length polymorphism method, based on the *rpoB* gene [10]. Further differentiation among *M. abscessus* complex members was performed at the Department of Microbiology, Seoul National University College of Medicine (Seoul, Korea) using sequence analysis targeting the *rpoB* and *hsp65* genes [8]. The *in vitro* antimicrobial susceptibility of *M. abscess*us was tested using a commercial kit (Sensititre; TREK Diagnostic Systems, Cleveland, OH) and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) document M24-A of 2003 [11].

We defined "persistent culture conversion" as the first negative sputum culture with at least one subsequent negative culture and no subsequent positive results during