Respiratory Medicine (2008) **102**, 437–442

ELSEVIER

respiratoryMEDICINE

Clinical significance of *Mycobacterium fortuitum* isolated from respiratory specimens

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Received 15 April 2007; accepted 5 October 2007
Available online 9 November 2007

KEYWORDS
Atypical mycobacteria;
Mycobacterium fortuitum;
Lung disease

Summary
Background: Although *Mycobacterium fortuitum* is not an uncommon organism among the non-tuberculous mycobacteria isolated from respiratory specimens, its clinical significance had not been well studied.
Methods: We identified all patients whose respiratory specimens were positive for *M. fortuitum* between January 2003 and December 2005. Among 182 patients whose specimens were positive for *M. fortuitum*, 26 were positive at least twice. We retrospectively reviewed their characteristics, and clinical courses.
Results: Of the 26 patients, 15 had two positive culture results for *M. fortuitum*; the other 11 had three or more. Sixteen patients were male and the median age was 61.5 years. Major presenting symptoms were cough (65%) and sputum (58%). Most patients had known underlying lung diseases, including prior tuberculosis (54%), lung cancer (15%), idiopathic pulmonary fibrosis (15%), and other mycobacterial lung disease (15%). The most common CT findings were bronchiectasis (80%). Only one patient received specific prolonged antibiotic therapy against *M. fortuitum* infection; the other 25 did not. No patients showed clinical aggravation during the follow-up period, although in five patients their underlying lung diseases continued to progress. The median follow-up duration was 12.5 months and none of the patients whose sputum specimens were available had persistent positive cultures for *M. fortuitum*.

Abbreviations: AFB, acid-fast bacilli; ATS, American Thoracic Society; CT, computed tomography; IDSA, Infectious Diseases Society of America; MAC, *Mycobacterium avium* complex; NTM, non-tuberculous mycobacteria; RGM, rapidly growing mycobacteria.

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0954-6111/$ - see front matter
doi:10.1016/j.rmed.2007.10.005

Conclusion: *M. fortuitum* usually causes colonization or transient infection in patients with underlying lung disease, such as prior tuberculosis or bronchiectasis. The majority of patients may not need to receive prolonged antibiotic therapy for *M. fortuitum* isolates.

Introduction

Mycobacteria other than *Mycobacterium tuberculosis* complex and *Mycobacterium leprae* are collectively referred to as non-tuberculous mycobacteria (NTM).[1–3] Human disease resulting from NTM infection is classified into four distinct clinical syndromes: pulmonary disease, lymphadenitis, cutaneous disease, and disseminated disease. Among these, chronic pulmonary disease is the most common localized clinical condition.[1–3] Studies have demonstrated that disease attributable to NTM is on the rise. NTM are responsible for an increasing proportion of mycobacterial disease in many developed and developing countries.[4–8]

Non-tuberculous mycobacteria are ubiquitous organisms and are frequently isolated from environmental sources, including surface water, tap water, and soil.[1–3] Accordingly, the isolation of NTM species from a respiratory sample is insufficient evidence for the presence of NTM lung disease. Some patients are infected with NTM without evidence of pulmonary disease. Such infection may indicate colonization or transient infection. Thus, the diagnosis of NTM lung disease must rely on clinical, radiographic, and microbiologic criteria. The American Thoracic Society (ATS) issued diagnostic criteria for NTM lung disease in 1997,[1] and the ATS and the Infectious Diseases Society of America (IDSA) recently revised the criteria in 2007.[2] The guidelines stated that the recommended diagnostic criteria are more appropriate for *Mycobacterium avium* complex (MAC), *Mycobacterium kansasii*, and *Mycobacterium abscessus*, and too little was known about pulmonary disease caused by other NTM to validate the diagnostic criteria for other organisms.[1,2]

Mycobacterium fortuitum is one of the rapidly growing mycobacteria (RGM), which are distinguished from other NTM by their ability to form colonies in less than 1 week and their *in vitro* resistance to antimycobacterials.[9] *M. fortuitum* is a commonly isolated organism from respiratory specimens in clinical laboratories in many countries.[4–7] To date, however, the clinical significance of this organism has not been well studied. Thus, we sought to investigate the clinical significance of *M. fortuitum* recovered from respiratory specimens.

Materials and methods

Study subjects

Permission was obtained from the institutional review board to review and publish information from patients' records. Informed consent was waived due to the retrospective nature of the study.

All patients with positive culture for *M. fortuitum* from a mycobacterial laboratory at the Samsung Medical Center (a 1250-bed tertiary referral hospital in Seoul, Korea) during the 3-year period from January 2003 to December 2005 were identified by a computer-assisted search of medical records. Patients with isolated *M. fortuitum* recovered from non-respiratory specimens were excluded.

Smears, cultures, and species identification

Clinical specimens were stained using the Ziehl–Neelsen method, according to the guidelines of the ATS.[10] The results of smear microscopy were reported semi-quantitatively. A positive smear was defined as one with >1 acid-fast bacilli (AFB) per 100 high-power fields.

Sputum or bronchial washing specimens were decontaminated using the *N*-acetyl-L-cysteine/2% NaOH method, and the processed specimens were plated on Löwenstein–Jensen media. Inoculated tubes were incubated at 37 °C and then inspected weekly for 8 weeks. All AFB isolates were assessed to distinguish between *M. tuberculosis* and NTM, according to growth rates, colony morphology, and pigmentation, and with a commercial DNA probe (Gen-Probe Amplified Mycobacterium Tuberculosis Direct Test; Gen-Probe, San Diego, CA).[10] NTM species identification was performed using a polymerase chain reaction-restriction length polymorphism method based on the *rpoB* gene, as previously described.[6]

Evaluation of clinical and radiographic findings

The medical records of the patients were reviewed, including their age, gender, respiratory symptoms, smoking history, body mass index, underlying illness, AFB smear status, number of positive isolates, and treatment information. Chest radiography and available computed tomography (CT) scan images were reviewed by an experienced chest radiologist (K.S.L.). Chest radiographic findings were evaluated with regard to the presence of reticulonodular opacities, cavitation, consolidation, and volume loss. The CT scans were evaluated with regard to the presence or absence of well-defined nodules, consolidation, cavitation, and bronchiectasis. Clinical course and outcomes following positive sputum culture were assessed by chart review.

Clinical improvement was defined as a decrease or disappearance of the respiratory symptoms (i.e., cough, sputum, hemoptysis, or fever, etc.) and radiographic improvement was defined as a decrease or disappearance of one or more components of the above radiographic findings on the follow-up chest radiography or CT scans.

Results

Characteristics of patients with two or more cultures for *M. fortuitum*

From January 2003 to December 2005, 182 patients were identified with positive cultures for *M. fortuitum* from