Title
Clinical significance of respiratory isolates for Mycobacterium abscessus complex from pediatric patients

Permalink
https://escholarship.org/uc/item/21z8057r

Journal
Pediatric Pulmonology, 48(5)

ISSN
1054-187X

Authors
M., Paul C Nussbaum, Eliezer Moua, John et al.

Publication Date
2013-05-01

DOI
10.1002/ppul.22638

Copyright Information
This work is made available under the terms of a Creative Commons Attribution License, available at https://creativecommons.org/licenses/by/4.0/

Peer reviewed
Clinical Significance of Respiratory Isolates for *Mycobacterium abscessus complex* From Pediatric Patients

Paul C. M. Do, MD,* Eliezer Nussbaum, MD, John Moua, MD, Terry Chin, MD, PhD, and Inderpal Randhawa, MD

Summary. *Mycobacterium abscessus complex* is the most virulent of rapidly growing mycobacteria causing invasive lung disease. To better delineate clinical pediatric experience and outcomes with *M. abscessus complex*, we retrospectively gathered 5-year data on *M. abscessus complex* infection and outcomes in a large, hospital-based pediatric pulmonary center. Patients were selected from the database of the microbiology department at Miller Children’s Hospital in Long Beach, CA. Patients had at least one positive pulmonary isolate for *M. abscessus complex* from February 2006 to May 2011. Treatment modality data were collected and successful therapy of disease was determined as clearance of *M. abscessus complex* infection after antibiotics proven by culture negative respiratory isolate within at least 12 months of therapy initiation. Two cystic fibrosis patients with *M. abscessus complex* were identified, one with failed therapy and the other with stable pulmonary status despite persistent isolation. One primary ciliary dyskinesia patient had successful clearance of *M. abscessus complex*, however is now growing *M. avium intracellulare*. A patient with no prior medical history was successfully treated with antimycobacterial therapy. Eleven patients with neuromuscular disorders had tracheal aspirates positive for *M. abscessus complex*. None were treated due to stable lung status and all but two had spontaneous clearance of the mycobacteria. The two remaining persist with sporadic isolation of *M. abscessus complex* without clinical significance. We concluded that patients with tracheostomy associated *M. abscessus complex* infections do not appear to require treatment and often have spontaneous resolution. Cystic fibrosis or primary ciliary dyskinesia patients may have clinical disease warranting treatment, but current antimycobacterial therapy has not proven to be completely successful. As *M. abscessus complex* gains prevalence, standardized guidelines for diagnosis and therapy are needed in the pediatric population. Multicenter cohort analysis is necessary to achieve such guidelines.

Pediatr Pulmonol. 2013; 48:470–480. © 2012 Wiley Periodicals, Inc.

Key words: nontuberculous; tracheostomy; cystic fibrosis; primary ciliary dyskinesia.

Funding source: none reported.

INTRODUCTION

Nontuberculous mycobacteria (NTM) are a common clinical pathogen.1 *Mycobacterium abscessus complex* is the most virulent and chemotherapy resistant rapidly growing mycobacteria subgroup,2,3 however the true prevalence has not been fully elaborated.4 Pulmonary disease was first described in male smokers with emphysema.5 The majority of NTM infections are pulmonary in origin and rapidly growing mycobacteria such as *M. abscessus complex* are the second most common cause behind *Mycobacterium avium intracellulare* (MAI).6 Manifestations beyond lung disease include skin and soft tissue infections.7 Infected cystic fibrosis patients in particular note a progressive decline in lung function.8

*M. abscessus complex* clinical treatment guidelines are available from the American Thoracic Society and Infectious Disease Society of America (ATS/IDSA) Miller Children’s Hospital, School of Medicine, University of California Irvine, Long Beach, California.

Contributor’s statement: All authors contributed equally to the design, concept, draft, revision, and final approval of this manuscript.

Conflict of interest: None.

*Correspondence to: Paul C. M. Do, MD, Miller Children’s Hospital, 2801 Atlantic Ave. Ground Floor, Long Beach, CA 90806. E-mail: pcdo78.pedspulm@gmail.com

Received 15 December 2011; Accepted 24 April 2012.
DOI 10.1002/ppul.22638
Published online 25 July 2012 in Wiley Online Library (wileyonlinelibrary.com).
with nonclinical trial evidence-based support from adult studies. Recommendations for treatment modalities in children are less specific. To better delineate pediatric experience and outcomes with *M. abscessus complex*, we retrospectively analyzed 5-year data on *M. abscessus complex* infection and outcomes in a large, hospital-based pediatric pulmonary center.

**METHODS**

Approval from the Institutional Review Board was obtained for the medical review of the patients’ history. Patients were selected from the database of the microbiology department at Miller Children’s Hospital in Long Beach, CA. Patients had at least one positive pulmonary isolate for *M. abscessus complex* from February 2006 to May 2011. Pulmonary isolates were defined as a culture from the sputum, tracheal aspirate, or bronchoalveolar lavage (BAL). Decontamination of samples was done with equal volume 4% sodium hydroxide. Acid-fast bacilli (AFB) stains were obtained on each isolate with standard Kinyoun technique (Remel, Lenexa, KS). Positive AFB were cultured in Lowenstein–Jensen medium (Bay Bioanalytical Laboratory, Inc., Hercules, CA) and rapidly growing mycobacteria were identified as appearance of mature, grossly visible colonies in less than 7 days of culture and a positive arylsulfatase test (Remel). Further differentiation of rapidly growing for species identification utilized biochemical techniques. *M. abscessus complex* identification was confirmed by a negative nitrate reduction (Remel), negative iron uptake (Remel), and positive 5% sodium chloride tolerance test (Bay Bioanalytical Laboratory, Inc.). Antimicrobial sensitivities were utilized if requested by the clinician and sent to Associated Regional and University Pathologist laboratory (Salt Lake City, UT). Once identified, patient charts were reviewed for medical history, source of *M. abscessus complex* isolation, body mass index (BMI), preceding chronic macrolide therapy, allergic bronchopulmonary aspergillosis (ABPA), concurrent infections of other NTM, fungi or bacteria, previous computed tomography (CT) scans of the chest, and radiologic evidence of bronchiectasis. Treatment modality data were collected (antibiotic course, respiratory therapy, and duration). Successful clearance of disease was determined as eradication of *M. abscessus complex* infection after therapy proven by culture negative respiratory isolate within at least 12 months of therapy initiation.

**RESULTS**

Miller Children’s Hospital in Long Beach, CA has a pediatric pulmonology service with approximately 3,500 patients that includes 165 cystic fibrosis patients, 5 primary ciliary dyskinesia patients, and 218 patients with tracheostomy tubes of which 57 of them require chronic mechanical ventilation. From February 2006 to May 2011 there were 3,804 negative respiratory AFB cultures and 150 positive respiratory cultures for NTM at the Miller Children’s Hospital microbiology department. A total of 16 patients had a positive sputum, tracheal aspirate, or BAL isolate of *M. abscessus complex* during this time period. One patient was excluded due to lack of readily available clinical data. Fifteen remaining patients were evaluated with primary pulmonary diseases: two cystic fibrosis, one primary ciliary dyskinesia, one with no prior medical history, and eleven tracheostomy dependency (Tables 1 and 2). All patients had BMI between the 25th and 75th percentiles for age without significant change regardless of management course. All the patients, except for the primary ciliary dyskinesia patient, had a diagnosis of gastroesophageal reflux disease by a gastroenterology subspecialist either clinically, by endoscopy, or by pH probe study. None of the patients were found to have a diagnosis of ABPA. Five patients met the ATS/IDSA diagnostic criteria for NTM pulmonary disease, but only three were treated.

**Cystic Fibrosis and Primary Ciliary Dyskinesia**

Two patients had a history of cystic fibrosis, an 8-year-old female and 10-year-old male. Both met the ATS/IDSA diagnostic criteria for NTM clinical pulmonary disease. The 8-year-old female initially isolated both *Mycobacterium avium intracellulare* (MAI) and *M. abscessus complex* from her sputum. Prior to this finding she had previously been treated with chronic azithromycin therapy. Her CT of the chest demonstrated minimal bronchiectasis and mild bibasilar atelectasis. Tiny scattered pulmonary nodules including a 2 mm nodule in right upper lobe were present. A bronchoalveolar lavage (BAL) revealed MAI. Multidrug regimen treatment against MAI with oral (PO) rifampin, PO ethambutol, and PO azithromycin was initiated for 4 months. Her repeat CT scan showed continued ciliary bronchiectasis of the bilateral apices and the right lower lobe. Repeat BAL again resulted in MAI isolation as well as *M. abscessus complex*. Further antimycobacterial drug regimen was recommended for treatment of both MAI and *M. abscessus complex* with PO rifampin, PO ethambutol, IV amikacin, and PO clarithromycin (Table 3). She had also been on IV cefoxitin which was discontinued after 1 month due to an adverse reaction. Bronchoscopy was performed one month later growing only *M. abscessus complex*. She continued to grow *M. abscessus complex* on repeat sputum cultures despite continued use of the described antimicrobial therapy for 12 more months. At the completion therapy, her CT of the chest remained unchanged and repeat BAL again grew *M. abscessus complex*. Prior to her initial mycobacteria culture her forced expiratory volume in one
| Patient number | Age (years) | Pulmonary condition | Tracheostomy/ventilator dependent | ATS/IDSA clinical disease | Date of first +MAB culture and first BAL + MAB<sup>1</sup> (month/year) | Total No. of +/- cultures after initial + MAB<sup>1</sup> | Clinical course | CT chest | Treatment outcome |
|----------------|------------|---------------------|----------------------------------|--------------------------|----------------------------------|-----------------------------------------------|-----------------|----------|------------------|
| 1              | 8          | Cystic fibrosis     | No/no                            | Yes                      | 4/2008 (S)                        | B = 2/1                                      | Declining pulmonary function |                      | Bronchiectasis with centrilobular nodularities, no tree-in-bud | Treatment failure |
|                |            |                     |                                  |                          |                                  | S = 5/23                                    |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          | 5/2008 (B)                       | B = 1/0                                     | Stable pulmonary function            |                      | Micronodular infiltrates with LLL bronchiectasis, no tree-in-bud | Not treated |
|                |            |                     |                                  |                          |                                  | S = 2/8                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 0/0                                     |                              |                      |                                 |                  |
| 2              | 10         | Cystic fibrosis     | No/no                            | Yes                      | 5/2010 (B)                       | S = 2/8                                     | Clearance of MAB                |                      | RLL bronchiectasis with scattered tiny nodular densities, no tree-in-bud | Successful treatment of MAB, however remains on MAI therapy |
|                |            |                     |                                  |                          |                                  | T = 0/0                                     |                              |                      |                                 |                  |
| 3              | 13         | Primary ciliary dyskinesia | No/no                           | Yes                      | 9/2009 (S)                        | B = 2/3                                     | Spontaneous MAB clearance |                      | Spontaneous MAB clearance | Not treated |
|                |            |                     |                                  |                          |                                  | S = 2/1                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          | 8/2010 (B)                       | S = 0/0                                     | Spontaneous MAB clearance |                      | Spontaneous MAB clearance | Not treated |
|                |            |                     |                                  |                          |                                  | T = 0/0                                     |                              |                      |                                 |                  |
| 4              | 15         | Cerebral palsy, mental retardation | Yes/no                           | No                       | 7/2009 (T)                        | B = 0/0                                     | Spontaneous MAB clearance |                      | None | Not treated |
|                |            |                     |                                  |                          |                                  | S = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 4/11                                    |                              |                      |                                 |                  |
| 5              | 18         | Rett syndrome       | Yes/yes                          | No                       | 11/2009 (T)                       | B = 0/4                                     | Spontaneous MAB clearance |                      | Bilateral apical infiltrates, no tree-in-bud or nodules | Not treated |
|                |            |                     |                                  |                          |                                  | S = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 1/4                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | B = 0/1                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | S = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 2/7                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | B = 0/1                                     |                              |                      |                                 |                  |
| 6              | 1          | Myotonic dystrophy  | Yes/yes                          | No                       | 8/2008 (T)                        | B = 0/1                                     | Sporadic MAB culture            |                      | None | Not treated |
|                |            |                     |                                  |                          |                                  | S = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 1/4                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | B = 0/1                                     |                              |                      |                                 |                  |
| 7              | 10         | Cerebral palsy, severe kyphoscoliosis | Yes/no                           | No                       | 10/2008 (T)                       | B = 0/1                                     | Spontaneous MAB clearance |                      | Diffuse bronchial wall thickening with linear atelectasis, no tree-in-bud or nodules | Not treated |
|                |            |                     |                                  |                          |                                  | S = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 4/7                                     |                              |                      |                                 |                  |
| 8              | 16         | Batten Syndrome     | Yes/no                           | No                       | 10/2009 (T)                       | B = 0/0                                     | Spontaneous MAB clearance |                      | Mild LLL bronchiectasis, no tree-in-bud or nodules | Not treated |
|                |            |                     |                                  |                          |                                  | S = 0/0                                     |                              |                      |                                 |                  |
|                |            |                     |                                  |                          |                                  | T = 1/6                                     |                              |                      |                                 |                  |

(Continued)
TABLE 1—(Continued)

| Patient number | Age (years) | Pulmonary condition | Tracheostomy/ventilator dependent | ATS/IDSA clinical disease | Date of first + MAB culture and BAL + MAB<sup>1</sup> (month/year) | Total No. of +/- cultures after initial + MAB<sup>1</sup> | Clinical course | CT chest | Treatment outcome |
|----------------|-------------|---------------------|----------------------------------|--------------------------|---------------------------------------------------------------|------------------------------------------------|----------------|----------|-------------------|
| 9              | 5           | Mitochondrial myopathy, cerebral palsy | Yes/no | No | 5/2008 (T) | B = 0/1 | Spontaneous MAB clearance | None | Not treated |
| 10             | 3           | Cerebral palsy, mental retardation | Yes/yes | No | 9/2008 (T) | B = 0/0 | Spontaneous MAB clearance | None | Not treated |
| 11             | 5           | Chromosome 4q deletion, cerebral palsy | Yes/yes | Yes | 10/2008 (T) | S = 0/0, T = 5/11 | Sporadic MAB culture | Moderate LLL infiltrates with 5 mm nodule, mediastinal adenopathy, no tree-in-bud | Not treated |
|                |             |                     |                                   |                          | 2/2011 (B) | S = 0/0, T = 5/2 | Spontaneous MAB clearance | None | Not treated |
| 12             | 10          | Cerebral palsy, mental retardation | Yes/yes | No | 2/2010 (T) | B = 0/1 | Spontaneous MAB clearance | None | Not treated |
| 13             | 13          | Cerebral palsy, mental retardation | Yes/yes | No | 3/2009 (T) | S = 0, T = 1/6 | Spontaneous MAB clearance | None | Not treated |
| 14             | 6           | Holoprosencephaly, cerebral palsy | Yes/no | No | 7/2010 (T) | S = 0, T = 2/4 | Sporadic MAB culture | Bilateral lower lobe ground glass opacities, no tree-in-bud or nodules | Not treated |
| 15             | 6 (months)  | No prior history, evaluating for IFNγ receptor deficiency | No/no | Yes | 12/2007 (B) | S = 0/2, T = 0/0 | Chronic RLL infiltrate but clearance of MAB | Extensive right lung consolidation with scattered nodular densities, no tree-in-bud | Successful treatment |

MAB, *Mycobacterium abscessus complex*; RLL, right lower lobe; LLL, left lower lobe.  
<sup>1</sup>B = bronchoalveolar lavage, S = sputum, T = tracheal aspirate.
second (FEV₁) was 99% predicted and 6 months after therapy it had decreased to 90% predicted. No further intervention of her mycobacterial infection has been conducted and since then her FEV₁ has declined to 70% predicted 18 months later. Routine sputum cultures every 3–4 months continue to isolate M. abscessus complex.

The 10-year-old male with cystic fibrosis grew M. abscessus complex from a routine surveillance bronchoscopy. He had no prior macrolide therapy. CT of the chest showed nodular bronchiectasis of the left lower lobe and micronodular infiltrates in the bilateral apices and right lower lobe. His FEV₁ was 90% predicted and treatment was not initiated. Fourteen months after his initial culture, repeat BAL was again grew M. abscessus complex. CT scan of the chest showed improved left lower lobe infiltrates, though continued mild bronchiectasis. His FEV₁ increased to 99% predicted and he remains under careful observation. Routine sputum culture every three months continues to grow M. abscessus complex.

A 13-year-old female with primary ciliary dyskinesia had an initial culture of MAI from a BAL. This finding was preceded by chronic azithromycin therapy. She continued to grow MAI from repeated sputum culture and 5 months later her sputum cultures grew M. abscessus complex instead of MAI. Her CT chest had shown extensive right middle lobe bronchiectasis and infiltrates 1 year prior to her initial mycobacteria isolation and the repeat CT afterwards demonstrated continued moderate right middle lobe bronchiectasis. She has since continued to culture M. abscessus complex from her sputum and BAL. Antimicrobial therapy with IV amikacin, IV meropenem, and PO azithromycin was initiated about 18 months after her first isolation and she presently continues on the same treatment regimen. Two bronchoscopies after 3 months of therapy yielded no evidence of NTM after which her FEV₁ was 95% predicted. A bronchoscopy at 8 months into therapy resulted in a negative culture for NTM. Though she has had 12 months negative cultures for M. abscessus complex, she will remain on therapy for approximately 6 more months due to the presence of MAI on her repeat BAL.

Tracheostomy Patients

Of the 11 tracheostomy dependent patients 6 required at least nocturnal mechanical ventilation or full day ventilatory support. All the patients have some form of neuromuscular disorder including cerebral palsy, developmental delay, myotonic dystrophy, Batten syndrome, Rett syndrome, mitochondrial myopathy, chromosomal deletions, and holoprosencephaly. Their ages of initial culture range from 1 to 18 years of age. Tracheal aspirates were obtained for bacterial, fungi, and mycobacteria culture as routine for clinic visits two to three times a year. Positive NTM cultures led to increased testing frequency every 2–3 months. None of the patients had been on chronic macrolide therapy. All but two patients ceased to culture further M. abscessus complex on repeated tracheal aspirate cultures obtained routinely two to three times a year. The two patients continue to have culture positive tracheal aspirates at sporadic intervals. None of the tracheostomy patients were treated with antimycobacterial therapy. All the patients remained clinically stable despite isolation of M. abscessus complex.

**TABLE 2— Characteristics of the 15 Patients**

| Characteristics                      | Patients (n) | n = 15% |
|--------------------------------------|-------------|---------|
| History                              |             |         |
| Cystic fibrosis                      | 2           | 13.3    |
| Primary ciliary dyskinesia           | 1           | 6.6     |
| Neuromuscular disorders              | 11          | 73      |
| No prior disease                     | 1           | 6.6     |
| Other history                        |             |         |
| Tracheostomy dependent               | 11          | 73      |
| Ventilator dependent                 | 6           | 40      |
| Source of MAB                        |             |         |
| Sputum                               | 3           | 20      |
| BAL                                  | 5           | 33      |
| Tracheal aspirate                    | 11          | 73      |
| Other NTM cultured                   |             |         |
| M. avium intracellulare              | 2           | 13.3    |
| M. chelonae complex                  | 9           | 60      |
| M. fortuitum complex                 | 5           | 33      |
| M. fortuitum                         | 1           | 6.6     |
| Fungi cultured                       |             |         |
| Aspergillus fumigates                | 3           | 20      |
| C. albicans                          | 5           | 33      |
| C. parapsilosis                      | 5           | 33      |
| C. glabrata                          | 1           | 6.6     |
| Yeast (unspecified)                  | 3           | 20      |
| Bacteria cultured                    |             |         |
| Pseudomonas aeruginosa               | 8           | 53      |
| Methicillin resistant S. aureus      | 4           | 26.7    |
| Achromobacter xylosoxidans          | 4           | 26.7    |
| Stenotrophomonas maltophilia        | 3           | 20      |
| Serratia marcescens                  | 6           | 40      |
| Acinetobacter baumannii complex      | 1           | 6.6     |
| Klebsiella oxytoca                   | 1           | 6.6     |
| Burkholderia cepacia                 | 1           | 6.6     |
| CT scan                              |             |         |
| Obtained                             | 7           | 46.7    |
| Not obtained                         | 8           | 53      |
| Bronchiectasis                       | 3           | 20      |
| Treatment                            |             |         |
| Treated with success                 | 1           | 6.6     |
| Treated with failure                 | 1           | 6.6     |
| Undergoing treatment                 | 1           | 6.6     |
| Not treated                          | 12          | 80      |

MAB, Mycobacterium abscessus; BAL, bronchoalveolar lavage.
| Patient number | Patient data                              | Antibiotic and dosage | Length of therapy | Antibiotic sensitivities (antibiotic/MIC/resistance) | Positive MAB (months after therapy initiation) | Negative MAB (months after therapy initiation) |
|---------------|-------------------------------------------|-----------------------|-------------------|------------------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| 1             | 8-year old with cystic fibrosis           | Rifampin PO 600 mg TIW| 12 months (Cefoxitin only used for 1 month) | Amikacin 16.00 S                                      | 12, 14, 19                                    | 2, 3, 4, 5, 7, 9, 13                           |
|               |                                           | Ethambutol PO 400 mg TIW | Amikacin IV 240 mg daily | Cefoxitin 32.00 I                                     |                                               |                                               |
|               |                                           | Clarithromycin 250 mg BID | Clarithromycin PO 90 mg daily | Clarithromycin 1.00 S                                 |                                               |                                               |
|               |                                           | Cefoxitin 1 g QID       | Meropenem IV 60 mg TID | Ciprofloxacin ≥8.00 R                                 |                                               |                                               |
|               |                                           |                        | Azithromycin PO 250 mg daily | Doxycycline ≥32.00 R                                 |                                               |                                               |
|               |                                           |                        |                       | Linezolid 32.00 R                                    |                                               |                                               |
|               |                                           |                        |                       | Minocycline ≥16.00                                   |                                               |                                               |
|               |                                           |                        |                       | Moxifloxacin ≥16.00                                  |                                               |                                               |
|               |                                           |                        |                       | TMP/SMX ≥320.00 R                                   |                                               |                                               |
| 3             | 13-year old with primary ciliary dyskinesia | Amikacin IV 350 mg daily | 12 months (continued therapy for MAI) | Amikacin 16.00 S                                      | 0                                             | 5, 6, 8, 12                                   |
|               |                                           | Meropenem IV 2 g TID   | Clarithromycin 300 mg daily | Cefoxitin 32.00 I                                     |                                               |                                               |
|               |                                           | Azithromycin PO 250 mg daily | Clarithromycin PO 90 mg daily | Clarithromycin 1.00 S                                 |                                               |                                               |
|               |                                           |                        |                       | Ciprofloxacin ≥8.00 R                                 |                                               |                                               |
|               |                                           |                        |                       | Doxycycline ≥32.00 R                                 |                                               |                                               |
|               |                                           |                        |                       | Linezolid 32.00 R                                    |                                               |                                               |
|               |                                           |                        |                       | Minocycline ≥16.00                                   |                                               |                                               |
|               |                                           |                        |                       | Moxifloxacin ≥16.00                                  |                                               |                                               |
|               |                                           |                        |                       | TMP/SMX ≥320.00 R                                   |                                               |                                               |
| 15            | 6-month old with no prior medical history | Cefoxitin IV 40 mg QID | 3 months            | Amikacin 32.00 I                                     | 0                                             | 5, 12, 26                                    |
|               |                                           | Meropenem IV 60 mg TID |                        | Cefoxitin 32.00 I                                     |                                               |                                               |
|               |                                           | Amikacin IV 90 mg daily |                        | Clarithromycin 300 mg daily                          |                                               |                                               |
|               |                                           | Clarithromycin PO 45 mg BID |                        | Clarithromycin 0.25 S                               |                                               |                                               |
|               |                                           |                        |                       | Ciprofloxacin ≥32.00 R                               |                                               |                                               |
|               |                                           |                        |                       | Gatifloxacin ≥16.00                                  |                                               |                                               |
|               |                                           |                        |                       | Linezolid 32.00 R                                    |                                               |                                               |
|               |                                           |                        |                       | Moxifloxacin 8.00 I                                  |                                               |                                               |
|               |                                           |                        |                       | TMP/SMX ≥320.00 R                                   |                                               |                                               |

TIW, three times weekly; BID, twice daily; TID, three times daily; QID, four times daily; TMP/SMX, trimethoprim/sulfamethoxazole; S, sensitive; I, intermediate; R, resistant; MIC, minimum inhibitory concentration.

1Positive culture for MAI.
2From initiation of second antibiotic course.
**complex** as defined by no increase in hospitalization, antibiotic use, or ventilatory requirements if they were on a ventilator (Table 4).

CT scans of the chests were obtained on four patients. An 18-year-old female with Rett syndrome had a CT with both apical and lower lobe infiltrates without bronchiectasis. She only grew *M. abscessus complex* once without a positive culture since. A 10-year-old male with severe kyphoscoliosis and cerebral palsy grew *M. abscessus complex* on several tracheal aspirates over the course of 18 months. CT scan showed only bronchial wall thickening with scattered linear atelectasis but no bronchiectasis. He has been culture negative for the past 12 months. A 5-year-old female with chromosome 4q deletion had a CT demonstrating left lower lobe infiltrates without bronchiectasis. She has continued to grow *M. abscessus complex* from tracheal aspirates and BAL over the course of 2 years without clearance. Resolution of her left lower lobe infiltrates on CT scan was seen, though she did develop a 5 mm left lower lobe nodule of unclear clinical significance. A 6-year-old female with holoprosencephaly had a CT scan done 2 years prior to her initial colonization of *M. abscessus complex* showing bilateral lower lobe ground glass opacities without bronchiectasis. Repeat CT was not done and she had three negative cultures of *M. abscessus complex* after 5 months.

**Patient with no Prior Medical History**

A 4-month-old born full term without known prior medical history was found to have pneumonia requiring bronchoscopic evaluation. CT of the chest demonstrated right upper lobe and bilateral lower lobe nodular densities. BAL revealed *M. abscessus complex*. Patient was started on antimicrobial therapy with IV cefoxitin, IV meropenem, IV amikacin, and PO clarithromycin after placement of a Broviac catheter. He was continued on therapy for 3 months and repeat BAL did not culture any mycobacteria. Long-term follow up had residual right upper lobe consolidation without bronchiectasis nearly 2 years later despite continued negative BAL. He had other episodes of bacterial pneumonia diagnosed clinically and radiologically without direct microbial analysis since then. He is in the process of evaluation for possible IFNγ receptor deficiency.

**DISCUSSION**

*M. abscessus complex* is the most virulent of rapidly growing mycobacteria causing invasive lung disease. The name abscessus was first designated due to a report of human knee infection with deep abscess-like lesions. Initially it was grouped under the *Mycobacterium fortuitum complex* but has been differentiated from *Mycobacterium chelonae*. In addition to pulmonary disease, *M. abscessus complex* causes skin, soft tissue, meningitic, and disseminated infections. NTM pulmonary disease in general has been shown to decrease a patient’s quality of life. *M. abscessus complex* has shown to decrease lung function in cystic fibrosis patients.

**Pathogenesis**

*M. abscessus complex* has two main variants, a rough and smooth morphology. The smooth variant is characterized by the ability to form biofilms and sliding motility while the rough variant acquires the ability to replicate in human macrophages and stimulate macrophage toll receptor 2 (TLR-2). The conversion from smooth to rough morphology has been associated with severe and fatal pulmonary infections. The rough

**TABLE 4—Specific Clinical Information for Tracheostomy Patients**

| Patient number | Patient information | Respiratory hospitalizations (before 1st culture/after 1st culture) | Respiratory antibiotic therapies (before 1st culture/after 1st culture) | Ventilator changes (before 1st culture/after 1st culture) |
|----------------|---------------------|---------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------|
| 4              | 15-year old with MRCP | 1/1                                                           | 1/1                                                             | N/A                                                |
| 5              | 18-year old with Rett Syndrome | 2/3                                                           | 3/3                                                             | 0/0                                                |
| 6              | 1-year old with myotonic dystrophy | 5/4                                                           | 5/4                                                             | 1/1                                                |
| 7              | 10-year old with CP, severe kyphoscoliosis | 1/0                                                           | 1/0                                                             | N/A                                                |
| 8              | 16-year old with Batten syndrome | 0/1                                                           | 0/1                                                             | N/A                                                |
| 9              | 5-year old with mitochondrial myopathy and CP | 1/1                                                           | 1/1                                                             | N/A                                                |
| 10             | 3-year old with MRCP  | 0/1                                                           | 1/1                                                             | 2/1                                                |
| 11             | 5-year old with chromosome 4 deletion | 1/0                                                           | 2/1                                                             | 1/1                                                |
| 12             | 10-year old with MRCP | 2/0                                                           | 2/1                                                             | 0/1                                                |
| 13             | 13-year old with MRCP | 1/2                                                           | 1/2                                                             | 0/0                                                |
| 14             | 6-year old with holoprosencephaly and CP | 1/1                                                           | 1/1                                                             | N/A                                                |

MRCP, combined cerebral palsy and mental retardation; CP, cerebral palsy; N/A, not applicable.

B = bronchoalveolar lavage, T = tracheal aspirate, S = sputum culture.

Pediatric Pulmonology
variants are also known to cause rapid death in mice after IV administration and persistent infections with caseous lesions. The transformation has been shown to correlate with the loss of the mycobacterial glycopeptidolipid which helps mask underlying cell wall phosphatidyl-myo-inositol mannosides. Glycopeptidolipids therefore limit the interaction with TLR-2 and decreases the induction of human macrophage interferon gamma (IFN\(\gamma\)).

Deficiencies of the immune system or therapeutic immunosuppression allow NTM infections to present themselves as seen in cases of HIV infection, hyperimmunoglobulin E syndrome, anti-TNF\(\alpha\) therapy, and immune suppression therapy in transplant patients. Indeed NTM infection in lung transplant patients is common. While NTM infection, including *M. abscessus complex* can be treated successfully in lung transplant patients, infections may be a cause for morbidity and mortality. 

Chernenko et al. performed an international multicenter survey showing that in 5,200 patients among 31 centers 0.33% were found to have *M. abscessus complex* infections with two mortalities. *M. abscessus complex* has a variety of manifestations for cystic fibrosis patients. Given *M. abscessus complex* has been shown to affect similar bronchiectatic diseases such as primary ciliary dyskinesia there may exist structural causes for infection. Analysis of the pathogenesis of NTM pulmonary infections in general help to offer data as to the mechanism to which *M. abscessus complex* causes disease. Previous studies have shown that while *Mycobacterium tuberculosis* can attach to healthy mucosa, NTM is only capable of attaching to damaged mucosa. Indeed MAI has a virulence factor called fibronectin attachment protein that can adhere to fibronectin within exposed extracellular matrix on damaged mucosal surfaces. Mucus plugging is a factor for NTM in noncystic fibrosis patients. However it has also been postulated that cystic fibrosis patients have a defect of \(\beta\)-defensins that predispose them to tuberculosis or NTM infections.

Cystic fibrosis transmembrane conductance regulator (CFTR) defects in themselves may allow vulnerability to mycobacteria as evidence by the data showing that a study group reported that 50% of patients with identified NTM infections were either heterozygous or homozygous for pathological CFTR mutations, even though only 20% met the diagnostic criteria for cystic fibrosis.

Huang et al. performed a study involving chronic ventilator dependent patients in hospital long-term respiratory care wards in central Taiwan. Of the 38 patients from which tracheal aspirates were obtained, 23 were found positive isolates for *M. abscessus complex* and 15 were diagnosed with clinical disease based on ATS/IDSA criteria. Five of those patients were placed on antimycobacterial therapy. Studies have not been done on tracheostomy patients without ventilator dependency. Airway mucosal damage may also specify the pathogenesis of *M. abscessus complex* infection in tracheostomy patients. The manner in which these patients develop damage may be secondary primary aspiration, secondary aspiration from gastroesophageal reflux disease or damage from tracheal suctioning. Contaminated water sources also remain a possibility. The chronic airway mucosal damage seen in tracheostomy and bronchiectatic patients may present the manner in which co-infection with other NTM may occur.

### Diagnosis

While clinical isolation of mycobacteria in pulmonary cultures is a necessary step in diagnosing the presence of the organism, it does not delineate the difference between infection and colonization. Common findings on CT scans of the chest are bilateral small nodules, cylindrical bronchiectasis, cavity formation and branching centrilobular nodules. Chung et al. reported a considerable overlap in MAI and *M. abscessus complex* findings, however lobar volume loss, nodules, airspace consolidation, and thin-walled cavities were more common on MAI than *M. abscessus complex*. The difficulty in analyzing radiologic evidence for NTM pulmonary infections stems from differentiation from prior lung disease. Specifically, CF lung disease classically reveals progressive bronchiectasis regardless of NTM disease.

### Treatment

*M. abscessus complex* is characterized as drug resistant requiring multimodal therapy. Clarithromycin is the most useful drug in its treatment. Those patients with macrolide-resistant strains are much more difficult to treat and maintain a poor prognosis. Chopra et al. evaluated 1,040 FDA approved drugs against *M. abscessus complex* in vitro and found that only metronidazole, morfloxacin, resorcinol, praziquantel, doxycycline, natamycin, and puromycin had significant antimicrobial activity. Current recommendations from ATS/IDSA involve the combination treatment with clarithromycin or azithromycin with amikacin plus ceftoxitin or imipenem. *M. abscessus complex*, however is uniformly resistant to all standard antituberculous agents. Chihara et al. showed *M. abscessus complex* is generally resistant to carbapenems though Miyasaka et al. found imipenem had good synergistic effect. Jeon et al. used clarithromycin, ciprofloxacin, and doxycycline with an initial regimen of amikacin and ceftoxitin for the first 4 weeks yielding treatment...
response rate of 83% for symptoms and 74% for high-resolution CT. Rates were much lower for those that were clarithromycin resistant.\textsuperscript{47} Lyu et al.\textsuperscript{48} performed a retrospective study on 41 patients with \textit{M. abscessus complex} treated with a macrolide and amikacin in addition to either cefoxitin or imipenem giving an 80.5% successful treatment rate. Linezolid has shown some activity against several NTM\textsuperscript{49} and evidence suggests it is synergistic with clarithromycin.\textsuperscript{45} Overall, however, treatment of \textit{M. abscessus complex} has yielded limited results.\textsuperscript{50} Greendyke and Byrd\textsuperscript{51} showed even if minimum inhibitory concentrations indicate sensitivity to amikacin, clarithromycin and cefoxitin, the minimal bactericidal concentrations for these drugs were much higher than could be achieved at serum levels.

Given the limitations in antimicrobial therapy, surgical options have been utilized. Jarand et al.\textsuperscript{52} evaluated 107 patients from 2001 to 2008 who were treated with multidrug regimen with surgical resection or antibiotics alone demonstrating similar clinical outcomes. Mitchel et al.\textsuperscript{53} looked at 236 patients who underwent lung resection for NTM yielding a mortality rate of 2.6% and morbidity rate of 11.7%. Much higher mortality of 23% was seen in other studies\textsuperscript{54} and complication rates as high as 35%.\textsuperscript{55}

Alternative therapies include anti-oxidants such as MnTE-2-PyP which has shown to reduce intracellular growth of \textit{M. abscessus complex}.\textsuperscript{56} \textit{N}-acetyl-L-cysteine has also been able to inhibit its growth\textsuperscript{57} and is not an uncommon therapy in patients with chronic airway disease such as cystic fibrosis. IL-24, a novel tumor suppressor and unique member of IL-10 family is demonstrated success.\textsuperscript{58} Inhaled therapy of IFN\textgamma\textsuperscript{59} was used in a refractory case of \textit{M. abscessus complex} cutaneous disease with marked success.\textsuperscript{59} Inhaled therapy of IFN\textgamma\textsuperscript{59} was effective in those with functional IFN\textgamma\textsuperscript{59} deficiency,\textsuperscript{59} however no such therapy has been trialed on patients without IFN\textgamma\textsuperscript{59} defects.

Patients with NTM have increased peripheral mucus plugging.\textsuperscript{60} This would lead to the concept of increased airway clearance as a method of combating pulmonary NTM infections in general.\textsuperscript{57} Limiting the degree of mucosal damage, as seen to be a cause for increased disease due to exposure of fibronectin, may lead to decreased NTM attachment to the epithelial airway walls. Therefore in theory, alleviating mucoid impaction and allowing for an intact mucosa in CF and primary ciliary dyskinesia patients may lead to decreased NTM bacterial colonization and disease. This has yet to be well studied in either basic science or clinical research and further evaluation is warranted.

\textit{Pediatric Pulmonology}

Conclusion

Patients with tracheostomy associated \textit{M. abscessus complex} infections do not appear to require treatment and often clear cultures spontaneously within months. Those who continued to have sporadic isolation, including the one who met the ATS/IDSA diagnostic criteria for clinical disease remain clinically stable without therapy. Alternatively, the disease process in patients with chronic bronchiectatic disease such as cystic fibrosis or primary ciliary dyskinesia may have clinical disease warranting intervention. Current antimicrobial therapy demonstrates limited success when comprehensively treating these patients. Surgical intervention remains an option, though morbidity and mortality remain a concern, especially given questionable clinical improvement. As \textit{M. abscessus complex} gains prevalence, standardized guidelines for diagnosis and therapy are needed in the pediatric population. Multicenter cohort analysis is necessary to achieve such guidelines.

REFERENCES

1. Roux AL, Ray A, Pawlik A, Medjahed H, Etienne G, Rottman M, Catherinot E, Coppee JY, Chauvi K, Monserrat B, Toubert A, Daffe M, Puzo G, Gaillard JL, Brosch R, Dulphy N, Nigou J, Herrmann JL. Overexpression of proinflammatory TLR-2-signalling lipoproteins in hypervirulent mycobacterial variants. Cell Microbiol 2011;13:692–704.
2. Medjahed H, Gaillard JL, Reyat JM. \textit{Mycobacterium abscessus}: a new player in the mycobacterial field. Trends Microbiol 2010;18:117–123.
3. Petriti B. \textit{Mycobacterium abscessus}: an emerging rapid-growing potential pathogen. APMIS 2006;114:319–328.
4. Bicmen C, Coskun M, Gunduz AT, Senol G, Cirak AK, Tibet G. Nontuberculous mycobacteria isolated from pulmonary specimens between 2004 and 2009: causative agent or not? New Microbiol 2010;33:399–403.
5. Saleeb P, Olivier KN. Pulmonary nontuberculous mycobacterial disease: new insights into risk factors for susceptibility, epidemiology, and approaches to management in immunocompetent and immunocompromised patients. Curr Infect Dis Rep 2010;12:198–203.
6. Cassidy PM, Hedberg K, Saulson A, McNelly E, Winthrop KL. Nontuberculous mycobacterial disease prevalence and risk factors: a changing epidemiology. Clin Infect Dis 2009;49:e124–e129.
7. Wallace RJ Jr., Brown BA, Griffith DE. Nosocomial outbreaks/pseudo-outbreaks caused by nontuberculous mycobacteria. Annu Rev Microbiol 1998;52:453–490.
8. Esther CR, Jr., Esserman DA, Gilligan P, Kerr A, Noone PG. Chronic \textit{Mycobacterium abscessus} infection and lung function decline in cystic fibrosis. J Cyst Fibros 2010;9:117–123.
9. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, Holland SM, Horsburgh R, Huitz G, Iademarco MF, Isamian M, Olivier K, Kuoss S, von Reyn CF, Wallace RJ Jr., Winthrop K. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175:367–416.
10. Kubica GP, Buess I, Gordon RE, Jenkins PA, Kwapinski JB, McDermont C, Pattyn SR, Saito H, Silcox V, Stanford JL, Takeya K, Tsukamura M. A co-operative numerical analysis of rapidly growing mycobacteria. J Gen Microbiol 1972;73:55–70.
11. Moore M, Frerichs JB. An unusual acid-fast infection of the knee with subcutaneous, abscess-like lesions of the gluteal region; report of a case with a study of the organism, Mycobacterium abscessus. n. sp. J Invest Dermatol 1953;20:133–169.

12. Kusunoki S, Ezaki T. Proposal of Mycobacterium peregrinum sp. nov., nom. rev., and elevation of Mycobacterium chelonae subsp. abscessus (Kubica et al.) to species status: Mycobacterium abscessus comb. nov. Int J Syst Bacteriol 1992;42:240–245.

13. Sanchez-Chardi A, Olivares F, Byrd TF, Julian E, Brambilla C, Luquin M. Demonstration of cord formation by rough Mycobacterium abscessus variants: implications for the clinical microbiology laboratory. J Clin Microbiol 2011;49:2293–2295.

14. Mehta M, Marras TK. Impaired health-related quality of life in pulmonary nontuberculous mycobacterial disease. Respir Med 2011;105:1718–1725.

15. Nessar R, Reyrat JM, Davidson LB, Byrd TF. Deletion of the mmpL4b gene in the Mycobacterium abscessus glycopeptidolipid biosynthetic pathway results in loss of surface colonization capability, but enhanced ability to replicate in human macrophages and stimulate their innate immune response. Microbiology 2011;157:1187–1195.

16. Sanguinetti M, Ardito F, Fiscarelli E, La Sorda M, D'Argenio P, Ricciotti G, Fadda G. Fatal pulmonary infection due to multidrug-resistant Mycobacterium abscessus in a patient with cystic fibrosis. J Clin Microbiol 2001;39:816–819.

17. Jonsson BE, Gilljam M, Lindblad A, Ridell M, Wold AE, Kusunoki S, Ezaki T. Proposal of Mycobacterium peregrinum sp. nov., nom. rev., and elevation of Mycobacterium chelonae subsp. abscessus (Kubica et al.) to species status: Mycobacterium abscessus comb. nov. Int J Syst Bacteriol 1992;42:240–245.

18. Catherinot E, Clarissou J, Etienne G, Ripoll F, Emile JF, Daffe M, Perronne C, Soudais C, Gaillard JL, Rottman M. Acute respiratory failure involving an R variant of Mycobacterium abscessus. J Clin Microbiol 2009;47:271–274.

19. Catherinot E, Clarissou J, Etienne G, Ripoll F, Emile JF, Daffe M, Perronne C, Soudais C, Gaillard JL, Rottman M. Hypervirulence of a rough variant of the Mycobacterium abscessus type strain. Infect Immun 2007;75:1055–1058.

20. Rottman M, Catherinot E, Hochdeez P, Emile JF, Casanova JL, Gaillard JL, Soudais C. Importance of T cells, gamma interferon, and tumor necrosis factor in immune control of the rapid grower Mycobacterium abscessus in C57BL/6 mice. Infect Immun 2007;75:5898–5907.

21. Rhoades ER, Archambault AS, Greendyke R, Huu FF, Streeter C, Byrd TF. Mycobacterium abscessus Glycopeptidolipid mask underlying cell wall phosphatidyl-myo-inositol mannosides blocking induction of human macrophage TNF-alpha by preventing interaction with TLR2. J Immunol 2009;183:1997–2007.

22. Winthrop KL, Chang E, Yamashita S, Iademarco MF, LoBue PA. Nontuberculous mycobacteria infections and anti-tumor necrosis factor-alpha therapy. Emerg Infect Dis 2009;15:1556–1561.

23. Bemwill J, Babineaux M, Sarria JC. Pulmonary Mycobacterium abscessus in an AIDS patient. Am J Med Sci 2010;339:495–496.

24. van Ingen J, Boeree MJ, Dekhuijzen PN, van Sooilingen D. Mycobacterial disease in patients with rheumatic disease. Nat Clin Pract Rheumatol 2008;4:649–656.

25. Melia E, Freeman AF, Shea YR, Hsu AP, Holland SM, Olivier KN. Pulmonary nontuberculous mycobacterial infections in hyper-IgE syndrome. J Allergy Clin Immunol 2009;124:617–618.

26. Morales P, Gil A, Santos M. Mycobacterium abscessus infection in transplant recipients. Transplant Proc 2010;42:3058–3060.

27. Malouf MA, Glanville AR. The spectrum of mycobacterial infection after lung transplantation. Am J Respir Crit Care Med 1999;160:1611–1616.

28. Gilljam M, Schersten H, Silverborn M, Jonsson B, Ericsson Hollising A. Lung transplantation in patients with cystic fibrosis and Mycobacterium abscessus infection. J Cyst Fibros 2010;9:272–276.

29. Zaidi S, Elidemir O, Heinle JS, McKenzie ED, Schecter MG, Kaplan SL, Dishop MK, Kearney DL, Mallory GB. Mycobacterium abscessus in cystic fibrosis lung transplant recipients: report of 2 cases and risk for recurrence. Transpl Infect Dis 2009;11:243–248.

30. Morales P, Ros JA, Blanes M, Perez-Enguiux D, Saiz V, Santos M. Successful recovery after disseminated infection due to mycobacterium abscessus in a lung transplant patient: subcutaneous nodule as first manifestation—a case report. Transplant Proc 2007;39:2413–2415.

31. Taylor JL, Palmer SM. Mycobacterium abscessus chest wall and pulmonary infection in a cystic fibrosis lung transplant recipient. J Heart Lung Transplant 2006;25:985–988.

32. Fairhurst RM, Kubak BM, Shpiner RB, Levine MS, Pegoas DA, Ardehali A. Mycobacterium abscessus empyema in a lung transplant recipient. J Heart Lung Transplant 2002;21:391–394.

33. Chernenko SM, Humar A, Hutecheon M, Chow CW, Chaparro C, Keshavjee S, Singer LG. Mycobacterium abscessus infections in lung transplant recipients: the international experience. J Heart Lung Transplant 2006;25:1447–1455.

34. Middleton AM, Chadwick MV, Nicholson AG, Dewar A, Groger RK, Brown EJ, Ratliff TL, Wilson R. Inhibition of adhesion of Mycobacterium avium complex and Mycobacterium tuberculosis to fibronectin on the respiratory mucosa. Respir Med 2004;98:1203–1206.

35. Middleton AM, Chadwick MV, Nicholson AG, Dewar A, Groger RK, Brown EJ, Ratliff TL, Wilson R. The role of Mycobacterium avium complex fibronectin attachment protein in adherence to the human respiratory mucosa. Mol Microbiol 2000;38:381–391.

36. Whittaker LA, Teneback C. Atypical mycobacterial and fungal infections in cystic fibrosis. Semin Respir Crit Care Med 2009;30:539–546.

37. Chan ED, Bai X, Kartalija M, Orme IM, Ordway DJ. Host immune response to rapidly growing mycobacteria, an emerging cause of chronic lung disease. Am J Respir Cell Mol Biol 2010;43:387–393.

38. Ziedalski TM, Kao PN, Henig NR, Jacobs SS, Ruoss SJ. Prospective analysis of cystic fibrosis transmembrane regulator mutations in adults with bronchiectasis or pulmonary nontuberculous mycobacterial infection. Chest 2006;130:595–1002.

39. Huang WC, Chiu CS, Chen JH, Shen GH. Molecular epidemiology of Mycobacterium abscessus infections in a subtropical chronic ventilatory setting. J Med Microbiol 2010;59:1203–1211.

40. Jeong YJ, Lee KS, Koh WJ, Han J, Kim TS, Kwon OJ. Nontuberculous mycobacterial pulmonary infection in immune competent patients: comparison of thin-section CT and histopathologic findings. Radiology 2004;231:880–886.

41. Han D, Lee KS, Koh WJ, Yi CA, Kim TS, Kwon OJ. Radiographic and CT findings of nontuberculous mycobacterial pulmonary infection caused by Mycobacterium abscessus. AJR Am J Roentgenol 2003;181:513–517.

42. Chung MJ, Lee KS, Koh WJ, Lee JH, Kim TS, Kwon OJ, Kim S. Thin-section CT findings of nontuberculous mycobacterial pulmonary infections in cystic fibrosis: comparison between Mycobacterium avium-intracellulare complex and Mycobacterium abscessus infection. J Korean Med Sci 2005;20:777–783.
43. Cremades R, Santos A, Rodriguez JC, Garcia-Pachon E, Ruiz M, Escribano I, Royo G. Screening for sterilizing activity of antibiotic combinations in an acid model of rapidly growing mycobacteria during the stationary phase of growth. Chemotherapy 2009;55:114–118.

44. Chopra S, Matsuyama K, Hutson C, Madrid P. Identification of antimicrobial activity among FDA-approved drugs for combating Mycobacterium abscessus and Mycobacterium chelonae. J Antimicrob Chemother 2011;66:1533–1536.

45. Chihara S, Smith G, Petti CA. Carbapenem susceptibility patterns for clinical isolates of Mycobacterium abscessus determined by the Etest method. J Clin Microbiol 2010;48:579–580.

46. Miyasaka T, Kunishima H, Komatsu M, Tamai K, Mitsutake K, Kanemitsu K, Ohisa Y, Yanagisawa H, Kaku M. In vitro efficacy of imipenem in combination with six antimicrobial agents against Mycobacterium abscessus. Int J Antimicrob Agents 2007;30:255–258.

47. Jeon K, Kwon OJ, Lee NY, Kim BJ, Kook YH, Lee SH, Park YK, Kim CK, Koh WJ. Antibiotic treatment of Mycobacterium abscessus lung disease: a retrospective analysis of 65 patients. Am J Respir Crit Care Med 2009;180:896–902.

48. Lyu J, Jang HJ, Song JW, Choi CM, Oh YM, Lee SD, Kim WS, Kim DS, Shim TS. Outcomes in patients with Mycobacterium abscessus pulmonary disease treated with long-term injectable drugs. Respir Med 2011;105:781–787.

49. Brown-Elliott BA, Crist CJ, Mann LB, Wilson RW, Wallace RJ, Jr. In vitro activity of linezolid against slowly growing nontuberculous Mycobacteria. Antimicrob Agents Chemother 2003;47:1736–1738.

50. van Ingen J, de Zwaan R, Dukal Stewart N, van Sooijin AF. van Sooijin D. Clinical relevance of Mycobacterium chelonae–abscessus group isolation in 95 patients. J Infect 2009;59:324–331.

51. Greendyke R, Byrd TF. Differential antibiotic susceptibility of Mycobacterium abscessus variants in biofilms and macrophages compared to that of planktonic bacteria. Antimicrob Agents Chemother 2008;52:2019–2026.

52. Jarand J, Levin A, Zhang L, Huitt G, Mitchell JD, Daley CL. Clinical and microbiologic outcomes in patients receiving treatment for Mycobacterium abscessus pulmonary disease. Clin Infect Dis 2011;52:565–571.

53. Mitchell JD, Bishop A, Cafaro A, Weyant MJ, Pomerantz M. Anatomic lung resection for nontuberculous mycobacterial disease. Ann Thorac Surg 2008;85:1887–1892; discussion 1883–1892.

54. Sherwood JT, Mitchell JD, Pomerantz M. Completion pneumonectomy for chronic mycobacterial disease. J Thorac Cardiovasc Surg 2005;129:1258–1265.

55. Koh WJ, Kim YH, Kwon OJ, Choi YS, Kim K, Shim YM, Kim J. Surgical treatment of pulmonary diseases due to nontuberculous mycobacteria. J Korean Med Sci 2008;23:397–401.

56. Oberley-Deegan RE, Lee YM, Morey GE, Cook DM, Chan ED, Crapo JD. The antioxidant mimetic, MnTE-2-PyP, reduces intracellular growth of Mycobacterium abscessus. Am J Respir Cell Mol Biol 2009;41:170–178.

57. Oberley-Deegan RE, Rehmel JW, Tollefson AK, Bai X, McGibney M, Ovrutsky AR, Chan ED, Crapo JD. An oxidative environment promotes growth of Mycobacterium abscessus. Free Radic Biol Med 2010;49:1666–1673.

58. Colsky AS, Hanly A, Elgart G, Kerdel FA. Treatment of refractory disseminated Mycobacterium abscessus infection with interferon gamma therapy. Arch Dermatol 1999;135:125–127.

59. Hallstrand TS, Ochs HD, Zhu Q, Liles WC. Inhaled IFN-gamma for persistent nontuberculous mycobacterial pulmonary disease due to functional IFN-gamma deficiency. Eur Respir J 2004;24:367–370.

60. Fowler SJ, French J, Screaton NJ, Foweraker J, Condliffe A, Haworth CS, Exley AR, Bilton D. Nontuberculous mycobacteria in bronchiectasis: prevalence and patient characteristics. Eur Respir J 2006;28:1204–1210.

Pediatric Pulmonology