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ORIGINAL ARTICLE

Risk factors for microbiologic failure among Taiwanese adults with *Mycobacterium abscessus* complex pulmonary disease

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Background: The *Mycobacterium abscessus* complex is a common cause of pulmonary nontuberculous mycobacteria infections in Taiwan. We examined the risk factors associated with treatment outcome in Taiwanese adults with pulmonary disease caused by the *M. abscessus* complex.
Methods: We retrospectively reviewed the records of all patients from a southern Taiwan medical center from 2006 to 2012 who had respiratory specimens identified as *M. abscessus* complex and met the American Thoracic Society criteria for pulmonary disease.
Results: Of the 106 included patients, females (58.5%) and nonsmokers (79.2%) predominated. The mean age of patients was 64.8 years. Sixty-three patients (59.4%) had pre-existing lung

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disease. Previous mycobacterial pulmonary disease (34.9%) was the most common underlying disorder. Chest radiography indicated that bronchiectasis was common (47.2%) and that cavitations were less common (14.2%). Fifty-six patients received antibiotic treatment. Clinicians were more likely to prescribe antibiotics if the initial sputum acid-fast staining was positive ($p < 0.001$). Treatment outcome was analyzed in 26 patients who were treated for more than 3 months; three of these patients (11.5%) had clinical failure and 18 (69.2%) experienced sputum conversion. Patients with cavitary lesions were more likely to experience microbiologic failure ($p = 0.02$). Nine patients had positive cultures after antibiotic treatment for > 1 year. Previous mycobacterial pulmonary disease ($p = 0.011$) and cavitary lesion ($p = 0.034$) are risk factors for persistence of *M. abscessus* complex.

Conclusion: With antimicrobial therapy, previous mycobacterial disease, and cavitary lesion are associated with microbiologic failure in Taiwanese adults with *M. abscessus* complex pulmonary disease.

Introduction

Nontuberculous mycobacteria (NTM) are environmental pathogens that are a focus of recent concern because of the increasing trend of NTM pulmonary infections.[1–5] In Taiwan, the proportion of NTM isolations among all mycobacterial isolations increased from 32.3% in 2000 to 49.8% in 2008.[3] Although the reasons for this increase are not entirely clear, it is probably related to the increased number of patients who are immunocompromised, increased prevalence of chronic lung diseases, increased numbers of the elderly patients, and improved methods of detection.[3,5–9]

The *Mycobacterium abscessus* complex belongs to the group of rapidly growing NTM (RGM).[2,10] This species causes a wide range of clinical infectious diseases that range from localized cutaneous infection to disseminated disease.[10–12] A previous study reported a nosocomial outbreak of pseudoinfection by this species from an infected endoscope washer,[13] and another study reported a cluster of endophthalmitis caused by *M. abscessus* after cataract surgery.[14] The pulmonary system is the most common site of infection, although empyema resulting from NTM is rare compared with that from tuberculosis.[15] The *M. abscessus* complex accounts for over 80% of RGM chronic respiratory diseases[16] and is the second most common pulmonary NTM infections in South Korea.[17] The *M. abscessus* complex is the most common cause of pulmonary NTM infections in southern Taiwan,[18] and the second most common cause in northern Taiwan.[3]

Earlier studies divided the *M. abscessus* complex (*M. abscessus sensu lato*) into three closely related species, namely, *M. abscessus* subsp. *abscessus* (*sensu stricto*), *Mycobacterium massiliense*, and *Mycobacterium bolletii*.[19,20] However, recent research proposed that *M. massiliense* and *M. bolletii* should be reclassified as *M. abscessus* subsp. *bolletii*.[21]

Treatment of NTM infections is difficult because of their resistance to most antibiotics. In particular, few drugs have *in vitro* activity against the *M. abscessus* complex, and the reported susceptibilities were 83–99% for clarithromycin, 95–97% for amikacin, 11–99% for cefoxitin, 8–55% for imipenem, 10–57% for ciprofloxacin, and 22.5–73% for moxifloxacin.[22–24] A recent study reported that the *in vitro* susceptibility of NTM to tigecycline was 86–100%.[25] The American Thoracic Society (ATS) recommends treatment with a combination of intravenous antibiotics (amikacin, cefoxitin, or imipenem) and oral antibiotics (macrolide) and/or surgery.[2] Recent studies of patients with NTM infections reported that those who received surgery in combination with multiple medications[26] and those infected by *M. massiliense* had more favorable outcomes.[27]

Studies in Western countries indicated that most patients with RGM lung diseases were white, female, nonsmokers, older than 60 years, and had no predisposing conditions or previously recognized lung diseases.[2] To date, there have been only a few reports on diseases caused by the *M. abscessus* complex in Taiwan and risk factors related to treatment outcome.[25,28] In this study, we analyzed the demographic characteristics and treatment outcomes of patients with *M. abscessus* complex pulmonary diseases in a Taiwan medical center.

Methods

Patients

We retrospectively reviewed the medical charts of all patients who had positive cultures of respiratory specimens (sputum or bronchial washing) for *M. abscessus* complex and who visited or were admitted to the Kaohsiung Medical University Hospital, a 1600-bed medical center in southern Taiwan, from 2006 to 2012. Diagnosis of *M. abscessus* pulmonary disease was based on the 2007 ATS criteria.[2] Patients were followed up until December 2013. We recorded all clinical symptoms, underlying diseases, laboratory data, chest radiography results, and use of medications. Previous mycobacterial disease was defined by the diagnosis of a mycobacterial pulmonary infection (including tuberculosis and NTM) 1 year before the isolation of the first positive culture of *M. abscessus*. The other isolated NTMs were defined by the presence of at least one NTM-positive

culture, with isolation of a species other than *Mycobacterium avium* complex (MAC) or *M. abscessus* complex. This study was approved by the hospital's Ethical Review Board (KMUH-IRB-20110287).

Identification of *M. abscessus* complex

Sputum or bronchial washing specimens were sent to a regional mycobacteriology reference laboratory for acid-fast bacilli (AFB) smears and culturing. AFB smears were performed initially with the fluorochrome method, and the results were confirmed by the Ziehl–Neelsen method. Prior to 2008, specimens were inoculated into the Löwenstein–Jensen (L–J) medium; since 2009, specimens were inoculated into L–J medium and grown in the BACTEC MGIT 960 liquid culture system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). Colonies were identified using polymerase chain reaction-restriction length polymorphism analysis.[29] Molecular identification of species within the *M. abscessus* complex was not performed.

Radiologic findings

Chest radiographs [including initial and follow-up chest X-rays, and chest high-resolution computed tomography (CT) data] were reviewed by an experienced chest medicine specialist (J.-R.T.). The radiography patterns were categorized according to the presence of bronchiectasis, consolidations, cavities, and nodules. The high-resolution CT findings were classified according to the presence of bronchiectasis with nodules, cavities, and consolidations.

Treatment and outcome

A macrolide-based regimen was defined as a regimen that included a macrolide. When treatment duration was $<$ 3 months or when clinicians stopped treatment after a positive culture for *M. abscessus* complex, the clinical and microbiologic outcomes were not analyzed. Outcome measurements were recorded at the end of the 12th month after treatment onset or at the end of the study. Sputum conversion was defined by the presence of three consecutive negative cultures within 6 months. The time of conversion was defined as the date of the first negative culture. If the patient could not expectorate sputum during treatment, the sputum was classified as converted. Microbiologic failure of sputum conversion was defined by the presence of positive cultures throughout the whole course of follow up. Sputum relapse was defined by the presence of two consecutive positive cultures after sputum conversion.[30] We also determined the rates of initial sputum conversion (rate of sputum conversion from positivity to negativity during treatment) and final sputum conversion (rate of sputum conversion at the end of the study).

Clinical outcome was classified as success, improvement, failure, or default.[31] Clinical success was defined by the presence of all of the following: (1) disappearance or amelioration of clinical symptoms; (2) improvement or no change in radiographic findings; (3) sputum conversion; and (4) completion of treatment according to the physician's judgment. Clinical improvement was defined by the presence of amelioration of symptoms and/or signs, no evidence of deterioration based on radiology results, and no sputum conversion. Clinical failure was defined by the presence of persistent symptoms and/or signs, deterioration based on radiology results, and positive sputum cultures. The default was defined by the presence of any of the following before the completion of treatment: (1) lost to follow up, (2) death, or (3) self-stopping of medication or missing medication two consecutive times.

Statistical analysis

All statistical calculations were performed with SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Continuous data were reported as means $\pm$ standard deviations. Pearson's χ^2 test, Fisher's exact test, the *t* test, and multivariate logistic regression were used to analyze statistical correlations. A p value < 0.05 was considered significant.

Results

Patient characteristics

During the study period, 390 patients had at least one positive respiratory culture for *M. abscessus* complex, and 106 of these patients met the ATS criteria for NTM pulmonary infection (Fig. 1). One hundred and sixty-three patients were excluded because of the presence of only one positive culture, and the other 121 patients were excluded for various other reasons.

Table 1 shows the demographic and clinical characteristics of the 106 patients. The average age of the patients was 64.56 $\pm$ 14.11 years; 58.5% of the patients were female and 79.2% of the patients were nonsmokers. Ninety-seven patients (91.5%) had at least one underlying disorder and 63 patients (59.4%) had pre-existing lung diseases. Previous mycobacterial infection was the most common underlying disorder (34.9%), and 28 patients (26.4%) had histories of pulmonary tuberculosis. None of the patients had cystic fibrosis. Cough was the most common symptom (96.2%).

Fig. 2 shows the number of isolates, colonizations, and infections caused by respiratory *M. abscessus* complex from 2006 to 2012. There was no obvious change in the annual incidence of infection, but the colonization rates increased significantly from 0.38/100,000 inpatients and outpatients in 2006 to 4.24/100,000 inpatients and outpatients in 2012. The timing of this increase corresponds to the introduction of the BACTEC MGIT 960 liquid culture system in our institution.

Radiographic findings

Table 2 summarizes the abnormalities observed in the radiographic chest examinations. Most lesions were bilateral (54.7%) and the right upper lung field was the most frequently affected region (55.7%). The most frequent pattern was bronchiectasis (50/106, 47.2%). The presence of a cavitary lesion was significantly associated with a history of tuberculosis (8/28 vs. 7/78, $p = 0.023$) and previous mycobacterial pulmonary disease (10/37 vs. 5/69, $p = 0.008$).

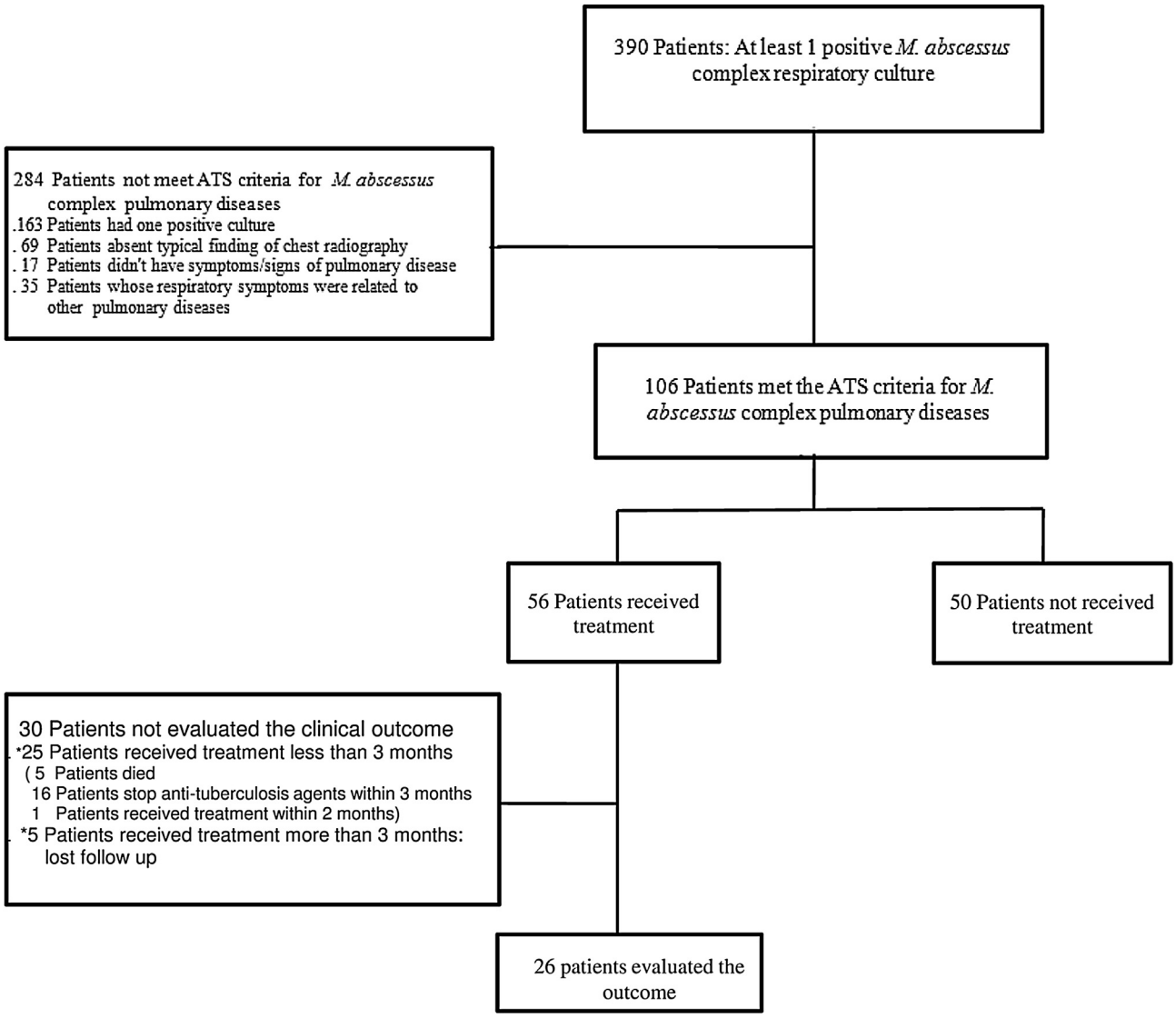

Figure 1. Patient identification flow diagram. *Mycobacterium abscessus* complex. ATS = American Thoracic Society.

Most cavitary lesions were identified before the diagnosis of infection by *M. abscessus* complex. Forty-seven patients (44.3%) received CT examinations, and the most common finding was bronchiectasis with nodules (45/47, 95.7%).

Treatment and outcome

Fifty-six patients received antibiotic treatment and 50 patients did not receive treatment (Fig. 1 and Table 1). Significantly more patients with initial sputum AFB positivity were given antibiotics than those with initial sputum AFB negativity (39/56, 69.6% vs. 8/50, 16%; $p < 0.001$). In addition, there were trends for antibiotic treatment to be given to patients with previous mycobacterial disease (24/56 vs. 13/50, $p = 0.102$), previously isolated other NTM in a pulmonary specimen (12/56 vs. 4/50, $p = 0.062$), fever at initial diagnosis (17/56 vs. 8/50, $p = 0.109$), and cavitary lesion (11/56 vs. 4/50, $p = 0.101$), although these differences were not statistically significant. A higher acid-fast smear (AFS) staining (from 3 + to 4+) result was also associated with prescription of antibiotics (16/56, 28.6% vs. 4/50, 8.0%; $p = 0.012$). Multivariate analysis with adjustment for age and sex indicated that only initial AFS positivity was independently and significantly associated with prescription of antibiotics (odds ratio, 10.75; 95% confidence interval, 4.1–28.17; $p < 0.001$).

Forty-seven of 50 patients who did not receive treatment had follow-up clinical symptoms, and 20 of these 47 patients (42.5%) experienced an amelioration of symptoms. Thirty-six of the 47 patients had chest radiography follow ups; the results indicated deterioration in 15 patients (41.7%), improvement in five patients (13.9%), and no change in 16 patients (44.4%).

Only 31 of the 56 treated patients (55.4%) received treatment for > 3 months, and five of these 31 patients were lost to follow up (Fig. 1). Thus, we analyzed the clinical and microbiologic outcomes of 26 cases (Table 3). Fifteen cases (57.7%) were clinical successes, three cases (11.5%) had clinical improvements, three cases (11.5%) were clinical failures, and five cases (19.2%) achieved default. The initial

Table 1 Baseline characteristics of the 106 patients who met the criteria of the American Thoracic Society for pulmonary infection caused by *Mycobacterium abscessus* complex

Characteristic	All patients ($N = 106$)	Treated patients ($N = 56$)	Untreated patients ($N = 50$)	p (treated vs. untreated)
Age at the time of diagnosis, y	64.76 ± 14.05 (27–95)	64.3 ± 13.38 (27–95)	65.26 ± 14.88 (27–92)	0.729
Female	62 (58.5)	34 (60.7)	28 (56)	0.695
BMI	21.29 ± 4.35 (13.85–39.35)	21.19 ± 4.22 (15.48–39.35)	21.41 ± 4.56 (13.85–34.43)	0.795
Cigarette smoking				
Never smoked	84 (79.2)	45 (80.4)	39 (78)	0.814
Immunosuppressive therapy within 1 mo[a]	8 (7.5)	6 (10.7)	2 (16)	0.277
Underlying disorders	97 (91.5)	53 (94.6)	44 (88)	0.301
Pre-existing pulmonary diseases	63 (59.4)	32 (57.1)	31 (62)	0.693
Previous mycobacterial pulmonary disease[b]	37 (34.9)	24 (42.9)	13 (26)	0.102
Previous history of pulmonary tuberculosis	28 (26.4)	17 (30.4)	11 (22)	0.382
Previous history of MAC	2 (1.9)	2 (3.6)	0 (0)	0.497
Other NTMs isolated[c]	16 (15.1)	12 (21.4)	4 (8)	0.062
Bronchiectasis	29 (27.4)	13 (23.2)	16 (32)	0.384
GERD	22 (20.8)	12 (21.4)	10 (20)	0.999
Diabetes mellitus	10 (9.4)	4 (7.1)	6 (12)	0.511
Cirrhosis	5 (4.7)	2 (3.6)	3 (6)	0.665
Malignancies	14 (13.2)	8 (14.3)	6 (12)	0.781
HIV infection	2 (1.9)	2 (3.6)	0 (0)	0.497
Initial AFS positive	47 (44.3)	39 (69.6)	8 (16)	<0.001
AFS 3 + to 4+	20 (18.9)	16 (28.6)	4 (8.0)	0.012
Cough	102 (96.2)	55 (98.2)	47 (94)	0.341
Hemoptysis	41 (38.7)	24 (42.9)	17 (34)	0.425
Fever[d]	25 (23.6)	17 (30.4)	8 (16)	0.109
Dyspnea	63 (59.4)	32 (57.1)	31 (62)	0.693
Death	15 (14.2)	7 (12.5)	8 (16)	0.781

[a] Steroid or chemotherapy or target therapy.
[b] Diagnosed mycobacterial infection (including tuberculosis and NTM) 1 year prior to the first positive cultures of *Mycobacterium abscessus* being isolated.
[c] At least one NTM culture was isolated except for the *Mycobacterium avium* complex and *M. abscessus* complex.
[d] Body temperature above 38°C at initial diagnosis.
Data are presented as *n* (%), mean ± SD, or mean + SD (range).
AFS = acid-fast smear; BMI = body mass index; GERD = gastroesophageal reflux disease; HIV = human immunodeficiency virus; MAC = *Mycobacterium avium* complex, NTM = nontuberculous mycobacteria.

sputum conversion rate was 73.1%. Three patients had sputum relapse, but two of these patients ultimately had sputum conversion. Thus, the final sputum conversion rate was 69.2%. There were no differences in the rate of clinical failure in patients who received a macrolide-based regimen, a macrolide–quinolone regimen, and an intravenous drug regimen (Table 3). There were trends for an association of history of tuberculosis with failure of sputum conversion (4/8 vs. 3/18, $p = 0.149$) and clinical failure (2/3 vs. 5/23, $p = 0.167$), but the differences were not statistically significant. The presence of cavitary lesions was significantly associated with microbiologic failure (sputum conversion: 4/8; no sputum conversion: 1/18, $p = 0.02$).

Analysis of microbiologic outcome at 1 year after treatment for these 26 patients indicated that nine patients had positive cultures and 17 patients had negative cultures for *M. abscessus* complex (Table 4). Pre-existing mycobacterial infection (8/9 vs. 5/17, $p = 0.03$) and cavitary lesion (4/9 vs. 1/17, $p = 0.02$) were associated with microbiologic failure. In addition, previous mycobacterial disease was associated with cavitary lesions (10/37 vs. 5/69, $p = 0.008$), bilateral pulmonary lesions (26/37 vs. 32/69, $p = 0.024$), and multiple-lobe lesions (13/37 vs. 9/69, $p = 0.011$).

Mortality

Among the 106 patients who met the ATS criteria for pulmonary *M. abscessus* complex infection, 15 patients died (14.1%). This included nine of the 50 patients (18%) in the

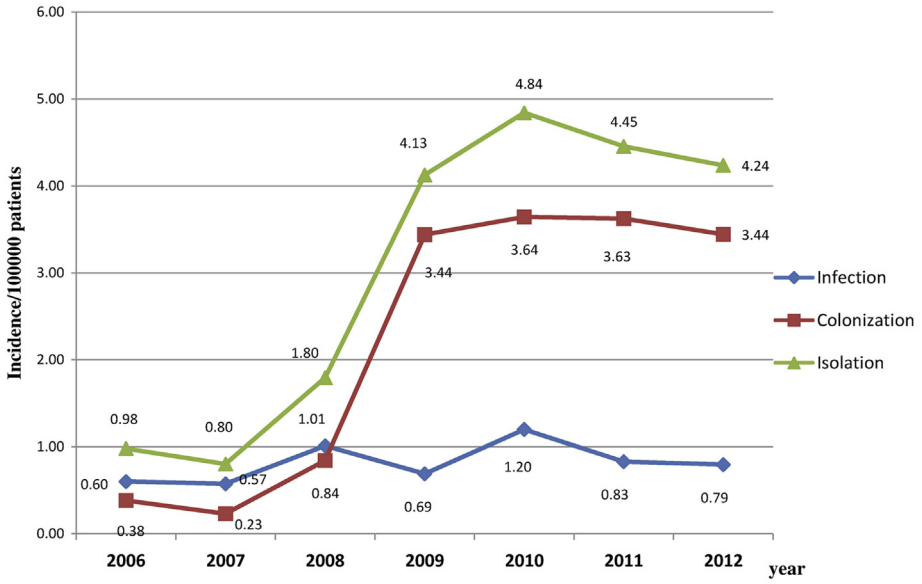

Figure 2. Annual incidence of the number of isolates, colonizations, and infections by respiratory *Mycobacterium abscessus* complex.

no-treatment group and six of the 56 patients (10.7%) in the treatment group. None of the deaths was attributable to the *M. abscessus* complex pulmonary disease.

Discussion

In our study population, only 27.1% (106/390) of patients with one or more pulmonary isolates of *M. abscessus* complex met the ATS criteria for diagnosis of NTM lung disease. This result is comparable with that of a previous study in North Taiwan, where the infection rate was 23.6%.[32] By contrast, Huang et al[25] reported that 45% (18/40) of *M. abscessus* complex isolates from patients at Taichung Veterans General Hospital (from January 2006 to December 2008) were colonization isolates. The number of *M. abscessus* isolates increased at our hospital from 2006 to 2012, but this increase was most likely due to the introduction of the additional use of the BACTEC MGIT 960 liquid culture system in 2009. The isolation of NTM has increased worldwide, but the clinical significance of this increase needs careful evaluation.

The patients in our study were mainly elderly females and nonsmokers, as in the populations of patients with NTM infections in Western countries.[26] Most of our cases (91.5%) had at least one underlying disorder. A 1993 study of a Western population showed that a specific underlying disease was rare in patients with RGM infections,[16] but it is increasingly reported that NTM disease occurs in patients with underlying disorders, especially lung disease.[1,4,7,26,33] The rate of previous mycobacterial diseases was high among *M. abscessus* complex cases in the current study (34.6%), as in Korea (53.1–61%).[27,31] A study in the United States reported that the rate of previous or coexisting MAC in *M. abscessus* complex pulmonary disease was 55.1%.[26] There appears to be differences among countries in the occurrence of previous tuberculosis in patients with *M. abscessus* complex pulmonary disease. In particular, the occurrence of previous pulmonary tuberculosis in patients with *M. abscessus* complex pulmonary disease was only 8.5–10% in the United States,[16,26] 11% in The Netherlands,[33] and 18% in France.[7] However, the rate is higher in southern Taiwan (26.9% in the current study and 56.7% in a previous study[18]), central Taiwan (31.8%),[25] and Korea (53.1%).[27] In addition, none of our patients had cystic fibrosis, although 6% of patients from the United States[16] and 44% of patients from The Netherlands[33] had this disease. The higher prevalence of tuberculosis and the lower prevalence of cystic fibrosis in Taiwan may contribute to the differences in susceptibility to *M. abscessus* complex pulmonary infection in Taiwan and Western countries.

Table 2 Results of chest radiography of 106 patients with pulmonary *Mycobacterium abscessus* complex infections

	n (%)		*n* (%)
Location		Pattern	
Right upper lobe	59 (55.7)	Bronchiectasis	50 (47.2)
Left upper lobe	37 (34.9)	Cavity	15 (14.2)
Right lower lobe	54 (51.9)	Consolidation	21 (19.8)
Left lower lobe	49 (46.2)	Nodular	19 (17.9)
Bilateral lesions	58 (54.7)		
Multiple lobes ($\geq$ 3)	22 (20.8)		

The radiographic characteristics of our patients were variable. Cavitations were present in 13.5% of patients, but were present in 15–44%, 17%, 6.2%, and 16–29.3% of patients in the United States,[2,26] The Netherlands,[33] France,[7] and Korea,[27,30,31] respectively. The relatively low rate of lung cavitations and the association of this condition with previous mycobacterial disease make this radiographic finding a limited utility for the diagnosis of *M. abscessus* complex lung diseases.

According to the ATS guidelines, a diagnosis of NTM lung disease does not necessarily require therapy, and initiation of therapy is based on potential risks and benefits.[2] A

Table 3 Clinical outcome of 26 treated patients for whom clinical and microbiologic outcomes were available

Characteristic	Total ($N = 26$)	Success ($N = 15$)	Improvement ($N = 3$)	Failure ($N = 3$)	Default ($N = 5$)
Age, y	59.23 ± 14.25	60.21 ± 17.04	60.42 ± 10.38	59.11 ± 1.24	55.66 ± 13.37
Female	20 (76.95)	11 (73.33)	3 (100)	3 (100)	3 (60)
Duration (mo)	13.2 ± 13.19	15.1 ± 12.27	9.83 ± 4.75	10.5 ± 5.41	11.1 ± 4.9
Medication					
Macrolide[a]	19 (73.07)	10 (52.6)	2 (10.5)	2 (10.5)	5 (26.3)
Macrolide + quinolone[b]	14 (53.8)	7 (50)	2 (14.2)	2 (14.2)	3 (21.4)
Intravenous medicine[c]	3 (11.5)	1 (33.3)	0 (0)	1 (33.3)	1 (33.3)
HERZ[d]	7 (26.9)	5 (71.4)	1 (14.3)	1 (14.3)	0 (0)

[a] All 19 cases received clarithromycin; two cases also have been receiving azithromycin.
[b] Nine cases received clarithromycin with moxifloxacin; five cases received clarithromycin with ciprofloxacin.
[c] All three cases received amikacin; one case also received meropenem and another received imipenem/cilastatin.
[d] Isoniazid, ethambutol, rifampin, and pyrazinamide.
Data are presented as *n* (%) or mean ± SD.

Korean retrospective study reported that female patients who were younger had more respiratory symptoms and positive sputum AFB smears, and cavitations on chest radiography were more likely to be treated, with an initial strategy of observation for 6–12 months after *M. abscessus* complex pulmonary disease diagnosis.[30] By contrast, our multivariate analysis indicated that only initial sputum AFS positivity was significantly associated with the decision to prescribe an antibiotic.

For our 56 patients who received treatment, clinical symptoms were ameliorated in 76.9% of patients and the final sputum conversion rate was 69.2%. This conversion rate is higher than reported in previous studies in Korea (58%)[26] and the United States (48%).[30] As in previous studies of *M. abscessus* complex pulmonary disease, we found that microbiological clearance was more difficult than amelioration of clinical symptoms.

Table 4 Microbiologic outcome at 1 year after treatment in the 26 treated patients for whom clinical and microbiologic outcomes were available

Characteristic	No sputum conversion ($N = 9$)	Sputum conversion ($N = 17$)	*p*
Age, y	56.2 ± 9.9	60.8 ± 16.15	0.449
Female	7 (77.8)	13 (76.5)	>0.999
Pre-existing lung disease	8 (88.9)	9 (52.9)	0.098
Previous mycobacterial disease	8 (88.9)	5 (29.4)	0.011
Previous tuberculosis	3 (33.3)	4 (23.5)	0.661
Cavitary lesion	4 (44.4)	1 (5.9)	0.034
Medication			
Macrolide[a]	7 (77.8)	12 (70.6)	>0.999
Intravenous medication[b]	2 (22.2)	1 (5.9)	0.268
Macrolide + quinolone[c]	7 (77.8)	7 (41.2)	0.11
HERZ[d]	2 (22.2)	5 (29.4)	>0.999

[a] All 19 cases received clarithromycin; two cases also have been receiving azithromycin.
[b] Nine cases received clarithromycin with moxifloxacin; five cases received clarithromycin with ciprofloxacin.
[c] All three cases received amikacin; one case also received meropenem and another received imipenem/cilastatin.
[d] Isoniazid, ethambutol, rifampin, and pyrazinamide.
Data are presented as *n* (%) or mean ± SD.

There is no specific regimen of choice for treatment of *M. abscessus* complex pulmonary disease. Multidrug regimens that include a macrolide may cause symptomatic improvement and disease regression.[2,30] We found no significant difference in clinical outcome of those treated with a macrolide-based regimen and those treated with a nonmacrolide regimen. The nonmacrolide regimens in our study were first-line medications for pulmonary tuberculosis, and had no *in vitro* effects on *M. abscessus* complex. However, only one patient (14.3%) experienced clinical failure. van Ingen et al[33] also reported that five patients with *M. abscessus* complex pulmonary disease received ineffective regimens, although all were cured. Thus, they questioned the current ATS guidelines regarding the overdiagnosis of NTM pulmonary diseases. In our group of untreated patients, 42.6% experienced amelioration of symptoms, and only 44.4% had radiographic evidence of deterioration. Thus, it is uncertain whether the observed clinical success of treated patients can be explained by the use of antibiotics or the natural course of NTM pulmonary disease.

A study in northern Taiwan showed that *Mycobacterium chelonae-abscessus* pulmonary disease initially has underlying comorbidity, structural lung disease, and sputum AFS positivity as risk factors for persistent *M. chelonae-abscessus* pulmonary disease and is associated with radiographic deterioration.[28] Our study showed that the presence of a cavitary lesion and the occurrence of previous mycobacterial pulmonary disease were associated with poor microbiologic outcome. The presence of previous mycobacterial disease was associated with the presence of bilateral lesions, multiple-lobe lesions, and cavitary lesions, and resulted in structural lung disease. Thus, patients with previous or underlying mycobacterial infection and cavitary lesion may require prolonged or more aggressive treatment to achieve sputum conversion.

Recent studies have also focused on expression of the *erm* gene and inducible resistance to clarithromycin in *M. abscessus* and *M. massiliense*.[34] Previous studies on *M. massiliense* infections in Korea and Japan reported better

clinical outcome and lower resistance to clarithromycin in patients without the *erm* gene or with an inactive form of this gene.[27,35] A study in The Netherlands reported that *M. abscessus* subsp. *abscessus* was more likely to cause true NTM disease than *M. abscessus* subsp. *bolletii* and to have high resistance to clarithromycin.[33] Currently, there is a tendency to identify species of *M. abscessus* complex in clinically significant isolates in the world.

There are limitations in this study. First, as a retrospective study, the treatment regimens were diverse and this made it difficult to compare the efficacy of different regimens. The follow-up protocol also varied, and therefore, the precise time of sputum conversion was not available. Second, we did not differentiate *M. massiliense* from *M. abscessus* and perform antimicrobial susceptibility testing, and therefore, we were not able to examine the correlation of clinical response and *in vitro* results.

In conclusion, patients with *M. abscessus* complex pulmonary disease were mainly elderly, female, nonsmokers, and had pre-existing pulmonary diseases. Initial AFS positivity was associated with the administration of antibiotics by clinicians. With antimicrobial therapy, previous mycobacterial disease and cavitary lesion were associated with microbiologic failure in Taiwanese adults with *M. abscessus* complex pulmonary disease.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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