Nontuberculous Mycobacterial Lung Disease in Southern Taiwan

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Background: The aim of this study was to assess the prevalence of the major nontuberculous mycobacterium (NTM) species and the outcome of their treatment in southern Taiwan (a high-prevalence area for *mycobacterium tuberculosis* [MTB]).

Methods: The study was a retrospective review of patients with NTM pulmonary disease at the Kaohsiung Chang Gung Memorial Hospital from 2004 to 2005. The variables recorded and analyzed included demographics, particularly age and gender; primary clinical presentations; chest radiographic findings; risk factors; medication and outcome of treatment.

Results: The study included 67 patients with NTM pulmonary disease. The average age was 66.6 ± 14.5 years and they were predominantly male (70.1%). Of these patients, 88.1% had pre-existing lung disease, with chronic obstructive pulmonary disease (61.2%) and TB (58.2%) as the main underlying lung diseases. Rapid-growth species (*M. abscessus,* 44.8% and *M. fortuitum,* 23.9%) were the most commonly isolated species. Of the forty patients that were treated and followed up for at least one year, 31 had a favorable outcome (mean duration of therapy, 8.46 ± 2.96 months).

Conclusions: The predominant species in southern Taiwan differ from those in other countries as well as in northern Taiwan, with rapid-growth species predominating in southern Taiwan.
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Key words: lung disease, nontuberculous mycobacterium (NTM), *Mycobacterium tuberculosis* (MTB), *Mycobacterium abscessus,* southern Taiwan

Nontuberculous mycobacterium (NTM) are generally free-living organisms that are ubiquitous in our environment and can also inhabit body surfaces or secretions without causing disease.[1,2] Therefore, occasional isolates of NTM species are largely regarded as contaminants or colonizers.[3] However, their importance in human disease has increasingly become evident due to the development of modern microbiological methods.[4]

Many large-series studies have been performed in recent decades that demonstrate the following findings: (1) NTM organisms are acquired from the environment. Unlike *M. tuberculosis* (MTB), no solid data has been found demonstrating human to human or animal to human transmission of NTM. (2) NTM diseases have significant geographic variation.

Slow-growth species, such as the *Mycobacterium avium* complex (MAC) in America and *M. kansasii* in Europe are the most commonly isolated species. (3) NTM causes four distinct clinical diseases, namely progressive pulmonary disease, superficial lymphadenitis, disseminated disease, and skin and soft tissue infection. (4) NTM diseases are also associated with various immunodeficiency diseases, including acquired immune-deficiency syndrome (AIDS) and leukemia. As a result, AIDS has led to a rise in NTM infections in developed countries. (5) NTM diseases are particularly prevalent in patients with underlying pulmonary diseases, including chronic obstructive pulmonary disease (COPD), tuberculosis (TB), cystic fibrosis, pneumoconiosis, bronchiectasis, and lung cancer.[5-13] Because of the increasing disease burden associated with NTM, the American Thoracic Society (ATS) and the British Thoracic Society (BTS) have issued guidelines on the diagnosis and management of NTM infections.[14,15]

However, only a few reports on NTM disease are available in Taiwan and these focus on NTM diseases in the northern Taiwan area.[16,17] According to the Center for Disease Control of Taiwan, about 15,000 new patients per year (incidence rate: 64.8 per 10^5 people in 2001 and 74.6 in 2002) have confirmed TB in Taiwan.[18] Taiwan is thus an area with a high TB prevalence rate, especially in southern Taiwan. This study addresses the differences in TB prevalence rates between southern and northern Taiwan, and whether high TB prevalence is an important risk factor for NTM diseases.

The study aims: (1) to assess the NTM species involved and describe their geographic variation; (2) to describe the treatment outcome of patients; and (3) to compare these data with those of other countries.

METHODS

The study was reviewed and approved by the Institutional Review Board of Kaohsiung Chang Gung Memorial Hospital [No. 97-1209B].

Hospital setting and subjects

A total of 473 adult patients (≥ 18 years old, both in-patients and out-patients) with NTM-positive cultures at the Kaohsiung Chang Gung Memorial Hospital (KS-CGMH), the largest tertiary medical center in southern Taiwan with a 2500-bed capacity,

were enrolled in this study from January 2004 to December 2005. All 473 patients were initially suspected of having TB but were then recognized to be infected with NTM.

All of the NTM isolates were examined and confirmed by cultures and polymerase chain reaction using restriction fragment length polymorphism (PCR-RFLP) analysis. Specimens were inoculated onto both Lowenstein-Jensen slants and BACTEC medium for fluorometric assay. The proportion method was used for antibiotic susceptibility testing on the Lowenstein-Jensen medium. Diagnosis was based on the 2007 ATS criteria for the diagnosis of NTM lung disease.[14] Patients who fulfilled the ATS criteria (clinical, radiographic, and bacteriologic) were included, while those who were co-infected with TB and NTM were excluded from this study.

Study design

A retrospective study was conducted by using the patient's medical records. The following variables were recorded: (1) demographics, particularly age and gender; (2) main clinical symptoms and signs; (3) chest radiographic findings; (4) related risk factors, such as smoking, hypertension, diabetes mellitus, stroke, liver cirrhosis, underlying pulmonary disease (COPD, TB, bronchiectasis, lung cancer), HIV serology condition; and (5) medication and outcome of treatment.

Chest radiography

Analysis of all chest radiographies and computed tomography (CT) was conducted by three experienced chest clinicians based on infiltration, nodules, cavity formation, pleural effusion, and lung mass.

Risk factors

Risk factors were recorded if they fit the following definitions: (A) smoking, if exposure was greater than 10 pack-years (defined as one pack of cigarettes smoked each day for more than 10 years); (B) hypertension and diabetes mellitus (DM), if controlled with regular medication; (C) stroke, if confirmed by a neurologist; (D) liver cirrhosis, if confirmed by abdominal sonography; (E) COPD, if clinical and radiological findings were consistent, or confirmatory findings of a pulmonary function test were available; (F) HIV, if confirmed by a serological report; (G) lung cancer, if confirmed by a pathology report;

(H) bronchiectasis, if confirmed by high resolution computed tomography (HRCT); and (I) a previous history of TB completely treated with anti-tuberculosis medication prior to getting NTM pulmonary disease.

Outcome measures

A favorable outcome was defined as all of the following findings: clinical improvement, radiological improvement, and clearance of the mycobacterial isolate from 3 consecutive sputum specimens (sustained for at least 6 months). A failure outcome was defined as continuing deterioration of clinical or radiological findings and non-clearance of NTM after 6 months of treatment. A default condition occurred when a patient withdrew from therapy before the prescribed treatment end point, when the outcome at 6 months after treatment was not evaluated, or when a patient was lost to follow-up or transferred out.[6]

Statistics analysis

Data were gathered and analyzed using SPSS for Windows version 10.0 (SPSS Inc., Chicago, IL, U.S.A.). Much of the data provided is presented as summary statistics. Quantitative variables were characterized using means $\pm$ standard deviations (SD).

RESULTS

Of the 473 adult patients with NTM-positive cultures submitted from January 2004 to December 2005 at the KS-CGMH, 67 patients fulfilled the ATS criteria and were included in this study.

Distributions and characteristics of the study patients

Table 1 shows the distributions and characteristics of the study patients. The most frequent species present was *M. abscessus* (30/67, 44.8%). The mean age was 66.6 $\pm$ 14.5 years (range: 23-86 years) with

Table 1. Distribution and Characteristics of Patients with Nontuberculous Mycobacterial Pulmonary Diseases

Characteristics	Total N = 67 (100%)	*M. abscessus* N = 30 (44.8%)	*M. fortuitum* N = 16 (23.9%)	MAC N = 10 (14.9%)	*M. kansasii* N = 9 (13.4%)	Others[‡] N = 2 (1.5%)
Age in years (mean $\pm$ SD)	66.6 $\pm$ 14.5	65.7 $\pm$ 12.5	70.1 $\pm$ 14.2	68.8 $\pm$ 16.3	61.8 $\pm$ 20.1	66.5 $\pm$ 2.1
Max (years)	86	83	86	82	84	68
Min (years)	23	23	38	26	26	65
Gender, N (%)						
Male	47 (70.1%)	15 (50%)	13 (81.3%)	9 (90%)	8 (88.9%)	1 (50%)
Female	20 (29.9%)	15 (50%)	3 (18.7%)	1 (10%)	1 (11.1%)	1 (50%)
HIV serology, N (%)						
Positive	3 (4.5%)	1 (3.3%)	1 (6.3%)	0 (0%)	1 (11.1%)	0 (0%)
Negative	64 (95.5%)	29 (96.3%)	15 (93.7%)	10 (100%)	8 (88.9%)	2 (100%)
Tobacco use, N (%)	28 (41.8%)	8 (26.7%)	8 (50%)	6 (60%)	4 (44.4%)	2 (100%)
Hypertension, N (%)	17 (25.4%)	6 (20%)	5 (31.3%)	2 (20%)	3 (33.3%)	1 (50%)
DM, N (%)	13 (19.4%)	7 (23.3%)	3 (18.8%)	0 (0%)	2 (22.2%)	1 (50%)
Stroke, N (%)	6 (9.0%)	3 (10%)	2 (12.5%)	1 (10%)	0 (0%)	0 (0%)
Liver cirrhosis, N (%)	4 (6.0%)	2 (6.7%)	1 (6.3%)	0 (0%)	1 (11.1%)	0 (0%)
Pre-existing lung disease, N (%)	59 (88.1%)	27 (90%)	13 (81.3%)	10 (100%)	7 (77.8%)	2 (100%)
COPD	41 (61.2%)	16 (53.3%)	8 (50%)	8 (80%)	5 (55.6%)	2 (100%)
Tuberculosis	39 (58.2%)	17 (56.7%)	11 (68.8%)	6 (60%)	4 (44.4%)	1 (50%)
Bronchiectasis	13 (19.4%)	8 (26.7%)	1 (6.3%)	2 (20%)	2 (22.2%)	0 (0%)
Lung cancer*	4 (6.0%)	2 (6.7%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)
Pneumoconiosis	1 (1.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other cancer[†], N (%)	7 (10.4%)	1 (3.3%)	3 (18.8%)	1 (5%)	2 (22.2%)	0 (0%)

Abbreviations: DM: Diabetes Mellitus; COPD: chronic obstructive pulmonary disease; *: 2 squamous cell, 1 alveolar cell, 1 small cell; †: 1 gastric, 1 prostate, 2 tongue, 3 urinary bladder cancer; ‡: Others include *M. gordonae* and *M. malmoense*.

a male predominance of 70.1%. Only three patients (4.5%) were HIV seropositive. Fifty-nine patients (88.1%) had associated pre-existing lung disease: COPD (61.2%) and TB (58.2%) were the two major diseases. Furthermore, 11 (16.4%) patients had associated malignancies: 4 had lung cancer and 7 had malignancies other than lung cancer. No hypersensitivity pneumonitis was found in these patients.

In terms of the associated underlying diseases among different NTM species, the frequency of COPD was greater than 50% for all species. The frequency of TB associated with *M. kansasii* was 44.4%, which was lower than that for other NTM species. The prevalence of TB among NTM pulmonary disease species was not distinctly different.

Male predominance was observed for almost all species except for *M. abscessus*. Most patients were aged 71 to 80 years (*M. abscessus, M. fortuitum,* and MAC) or > 80 years (*M. kansasii*).

Clinical presentation and radiographic findings

Table 2 shows the chest radiographic presentations of the patients. The most frequent symptom was chronic cough (53/67, 79.1%). Although most of the radiographic findings were non-specific, infiltration with or without nodules was the main radiographic finding for all patients infected with various NTM species. Seventeen of these presented with cavity formation (25.4%). The percentage of *M. Kansasii*-infected patients who presented with cavity formation was higher than that of patients infected with other species.

Treatment outcomes

Forty (59.7%) of the 67 study patients were treated for more than 1 month and had follow-up information for at least one year. Thirty-one (77.5%) of them had a favorable outcome following treatment, while 9 (22.5%) had a failure outcome (Table 3). Thirty-three (82.5%) of these 40 patients were initially treated with first-line anti-tuberculosis drugs: pyrazinamide, isoniazid, rifampin, and ethambutol. Three patients were not treated until a proven NTM culture was obtained.

After NTM culture specimens were isolated, the medications for 21 patients (52.5%) were modified. Nineteen of these patients (19/31, 61.3%) had a favorable outcome and only two (2/9, 22.2%) had a failure outcome. Clarithromycin, co-trimoxazole, rifabutin, azithromycin, ciprofloxacin, levofloxacin, and moxifloxacin were the primary medications used after adjustment. The mean duration of therapy for patients with favorable outcomes was 8.46 ± 2.96 months (range: 2.5-15 months), while for patients with a failure outcome, it was 6.67 ± 2.92 months (range: 2-11 months).

Underlying disease and pre-existing diseases were compared between those that were treated successfully and those that were treated but had a failure outcome; no significant differences were found.

Twenty-seven patients (27/67, 40.3%) met one of the default conditions: 9 patients died during the treatment process, 5 were transferred out, and 13 were lost to follow-up.

DISCUSSION

All patients were initially suspected of having TB due to their clinical and radiographic presentations, but were then recognized to be infected with

Table 2. Chest Radiographic Findings of Patients by Nontuberculous Mycobacterial Species

Species (Patient numbers)	*M. abscessus* (30)	*M. fortuitum* (16)	MAC (10)	*M. kansasii* (9)	Others (2)	Total (67)*
Infiltration with or without nodules, N (%)	26 (86.7%)	12 (75%)	8 (80%)	8 (88.9%)	2 (100%)	56 (83.6%)
Cavity formation, N (%)	6 (20%)	4 (25%)	3 (30%)	4 (44.4%)	0 (0%)	17 (25.4%)
Nodule only, N (%)	2 (6.7%)	1 (6.3%)	0 (0%)	1 (11.1%)	0 (0%)	4 (6.0%)
Pleural effusion, N (%)	1 (3.3%)	1 (6.3%)	2 (20%)	0 (0%)	2 (100%)	6 (9.0%)
Lung mass, N (%)	1 (3.3%)	0 (0%)	1 (10%)	0 (0%)	0 (0%)	2 (3.0%)

Abbreviations: MAC: *Mycobacterium avium*-complex; *: Totals include *M. gordonae*, *M. malmoense*.

An individual patient might have more than one chest radiographic pattern.

Table 3. Treatment Regimens for Study Patients with Favorable and Failed Outcomes

Patient #	Sex	Age	Species	Treatment (number of months)		Total months of treatment
				Initial	Against NTM	
				Favorite outcome (N = 31)		
5	M	67	*M. abscessus*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (4)	9
7	F	51	*M. abscessus*	INH, RIF, PZA, EMB (2)	RIB, EMB, Clm (10)	12
8	M	64	*M. abscessus*	INH, RIF, PZA, EMB (3)	Clm (6)	9
10	F	74	*M. abscessus*	None	EMB, SM, Levo (4) then SM, Levo (5) then Clm, Doxycycline (6)	15
16	F	61	*M. abscessus*	INH, RIF, PZA, EMB (2)	Clm (6)	8
17	F	59	*M. abscessus*	None	Clm, Amikin (1), then Clm (6)	7
18	M	23	*M. abscessus*	INH, PZA, EMB, Cipro (3)	INH, EMB, Cipro, Clm (9)	12
21	M	63	*M. abscessus*	INH, RIF, PZA, EMB (1)	Cipro, INH, EMB (1.5)	2.5
34	F	61	*M. abscessus*	None	Amikin, Clm (1) then Clm (5)	6
39	F	55	*M. abscessus*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (4) then Amikin, Clm (6)	12
46	M	57	*M. abscessus*	INH, RIF, PZA, EMB (2)	Clm (4)	6
53	F	76	*M. abscessus*	INH, PZA, SM, Cipro (2)	Amikin (1) then Moxi, Azm (3)	6
56	M	55	*M. abscessus*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB, Cipro (4)	6
4	M	74	*M. fortuitum*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (3) then Levo (3)	8
15	M	70	*M. fortuitum*	INH, RIF, PZA, EMB (1.5)	Cipro, RIF, CMZ (10.5)	12
29	M	70	*M. fortuitum*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (7)	9
35	M	38	*M. fortuitum*	INH, RIF, PZA, EMB (3)	Cipro, CMZ, Clm (4)	7
42	F	74	*M. fortuitum*	INH, RIF, PZA, EMB (2)	Clm (2)	4
55	M	77	*M. fortuitum*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (4)	6
22	M	75	MAC	INH, RIF, PZA, EMB (2)	INH, RIF, PZA, EMB (7)	9
44	M	76	MAC	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (10)	12
52	M	76	MAC	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (7)	9
63	M	26	MAC	INH, RIF, PZA, EMB (2)	INH, EMB, Moxi (5)	7
6	M	39	*M. kansasii*	INH, RIF, PZA, EMB, Clm (3)	INH, EMB, Clm (12)	15
27	F	26	*M. kansasii*	INH, RIF, PZA, EMB (3)	INH, RIF, EMB (3)	6
38	M	65	*M. kansasii*	INH, EMB, Levo (2)	INH, EMB, Levo (7)	9
57	M	68	*M. kansasii*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (4)	6
60	M	59	*M. kansasii*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (4)	6
61	M	84	*M. kansasii*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (7)	9
20	M	68	*M. gordonae*	INH, RIF, PZA, EMB (3)	INH, RIF, EMB (5)	8
24	M	65	*M. malmonse*	INH, RIF, PZA, EMB (3)	INH, RIF, PZA, EMB (6), then Cipro, CMZ (1)	10
				Failure outcome (N = 9)		
3	M	73	*M. abscessus*	INH, RIF, PZA, EMB (3)	INH, RIF, EMB (6)	9
14	F	53	*M. abscessus*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (6)	8
23	M	74	*M. abscessus*	INH, RIF, PZA, EMB (1.5)	Cipro, CMZ (0.5)	2
58	M	78	*M. abscessus*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (2)	4
25	M	45	*M. fortuitum*	INH, RIF, PZA, EMB (3)	INH, RIF, EMB (3)	6
41	F	66	*M. fortuitum*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (7)	9
43	M	69	*M. fortuitum*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (5)	7
67	F	86	*M. fortuitum*	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (4.5) then INH, RIF, EMB, Cipro (4.5)	11
65	M	75	MAC	INH, RIF, PZA, EMB (2)	INH, RIF, EMB (2)	4

Abbreviations: INH: isoniazid; RIF: rifampin; PZA: pyrazinamide; EMB: ethambutol; Clm: clarithromycin; CMZ: cotrimoxazole; Cipro: ciprofloxacin; Levo: levofloxacin; Moxi: moxifloxacin; RIB: rifabutin; SM: streptomycin; Azm: azithromycin.

NTM based on bacteriological reports. Three patients were co-infected with TB and NTM, according to their culture reports, and were excluded. Among the 67 patients with NTM lung disease, 57 (85.1%) met the inclusion criterion of at least two positive cultures and one positive acid-fast bacillus smear (AFB) from at least three sputum samples; 10 (14.9%) met the criterion of one positive culture with at least 2+ growth or AFB smear from a single bronchial washing under bronchofiberscopy examination; and none were confirmed by tissue biopsy.

In the present study, most (46/67, 68.7%) of the NTM species were rapid-growth species (*M. abscessus* 44.8% and. *M. fortuitum* 23.9%). *M. abscessus* was found to be the predominant species in southern Taiwan, in contrast to previously published studies in other areas (MAC in the U.S.A., the U.K., Northern Australia, and Switzerland; *M. chelonae/abscessus* in Brazil; *M. kansasii* in Western Australia, the Netherlands, Wales, and the Czech Republic; *M. scrofulaceum* in South Africa; *M. chelonae* in Hong Kong; and *M. malmoense* in Scotland).[5-7,19-29]

Ding et al reported that the predominant species of NTM lung disease was MAC (44.1%) in Taipei (northern Taiwan),[16] which indicates that geographical variation might occur even within the same country. Moreover, Ding et al also reported that the fre-

quency (41.4%) of total rapid-growth species isolated was greater than that of MAC (39%). Table 4 shows a comparison of patients with NTM lung disease between southern Taiwan and northern Taiwan and a different distribution of underlying disease between these two areas. Table 5 shows a comparison of the NTM species distribution of patients with NTM lung disease between southern Taiwan and northern Taiwan. Comparing these two studies, rapid-growth species appear to be the major NTM species in Taiwan. Additional evaluation would be required to further validate this.

In the United States, although *M. abscessus* disease has been reported from all geographic areas, the southeastern areas from Florida to Texas appear to be the major endemic area for *M. abscessus* lung disease.[14] In the present study, the most frequent species of NTM lung diseases was *M. abscessus* in southern Taiwan. Southern areas apparently tend to be the major endemic area for *M. abscessus* lung disease. Whether *M. abscessus* is the major NTM species in the southern environment and prefers to grow in sub-tropical climates requires further evaluation.

This study found that the majority of NTM lung disease cases occurred in patients with pre-existing lung disease (59/67, 88.1%), and this situation was

Table 4. Comparison of Characteristics of Patients with Nontuberculous Mycobacterial Lung Disease between Southern Taiwan and Northern Taiwan

Area	Southern Taiwan	Northern Taiwan	
Year	2004-2005	1997-2003	*p* value
	N = 67	N = 245	
Age in years (mean ± SD)	66.6 ± 14.5	64 ± 19	0.147*
Gender, N (%)			
Male / Female	47 (70.1%) / 20 (29.9%)	142 (58%) / 103 (42%)	0.070†
HIV serology, N (%)	3 (4.5%)	12 (4.9%)	1.000†
DM, N (%)	13 (19.4%)	16 (6.5%)	0.001†
Liver cirrhosis, N (%)	4 (6.0%)	21 (8.6%)	0.487†
Pre-existing lung disease, N (%)	59 (88.1%)	135 (55.1%)	< 0.001†
COPD	41 (61.2%)	38 (15.5%)	< 0.001†
Previous tuberculosis	39 (58.2%)	59 (24.1%)	< 0.001†
Bronchiectasis	13 (19.4%)	38 (15.5%)	0.445†
Malignancy, N (%)	11 (16.4%)	54 (22.0%)	0.315†

Abbreviations: DM: Diabetes mellitus; COPD: chronic obstructive pulmonary disease; *: by 1-sample t-test; †: by chi-square test.

Table 5. Comparison of Distribution of Patients with Nontuberculous Mycobacterial Lung Disease between Southern Taiwan and Northern Taiwan

Southern Taiwan 2004-2005 (N = 67)	Northern Taiwan 1997-2003 (N = 245)	p value
M. abscessus (30, 44.8%)	*M. abscessus* (47, 19.2%)	< 0.001*
M. fortuitum (16, 23.9%)	*M. fortuitum* (26, 10.6%)	0.005*
MAC (10, 14.9%)	MAC (108, 44.19%)	< 0.001*
M. kansasii (9, 13.4%)	*M. kansasii* (20, 8.2%)	0.188*
Others (2, 3.0%)	*M. chelonae* (23, 9.4%)	
	M. gordonae (11, 4.5%)	
	Others (10, 4.1%)	

Abbreviations: MAC: *Mycobacterium avium*-complex; *: by chi-square test.

confirmed in other countries.[5,6,19,20] This study also showed that COPD and TB were the two most common pre-existing lung diseases, which was also similar to other countries. However, the relative frequency of COPD (41/67, 61.2%) and TB (39/67, 58.2%) in the present study was higher than in other countries. The relative frequency of bronchiectasis (13/67, 19.4%) in this study was higher than that of the United States (6.9%) and Brazil (5%).[5,19] Bronchiectasis contributes to a relatively high prevalence of *M. abscessus* in our study (Table 1). In contrast, as AIDS and cystic fibrosis are relatively rare diseases in Taiwan, their relative frequencies in NTM infection were very low. MAC has been shown to be the predominant species for most NTM patients with AIDS and cystic fibrosis.[10,14] The different distributions of the primary risk factors in this study from those applicable to other countries might also explain the comparatively high prevalence of rapidly growing mycobacterium.

In the present study, cavitation occurred in 44.4 percent of patients with *M. kansasii* lung disease and most closely paralleled the clinical course of *M. tuberculosis* with symptoms generally identical to those associated with pulmonary TB. The chest radiographic abnormalities are also very similar to reactivation pulmonary TB, including cavitary infiltrates with an upper lobe predilection.[30-32] Previous studies have reported that cavitation occurs in 85 to 95 percent of patients with *M. kansasii* lung disease.[30,33] The cavities tend to have thinner walls and less sur-

rounding parenchymal infiltration than in TB.[30,33]

In the United States, *M. abscessus* is the third most frequently recovered NTM respiratory pathogen and accounts for approximately 80% of rapidly growing mycobacterial respiratory disease isolates.[34] Underlying disorders that are associated with the disease include bronchiectasis and prior mycobacterial infection. High-resolution computed tomography of the lung frequently shows associated cylindrical bronchiectasis and multiple small (< 5 mm) nodules.[4]

Sex and age distributions of patients in this study were similar to those of previous studies, with a male predominance and with most patients over 60 years of age. However, a distinct difference between the sex distributions for individual NTM species was observed among patients infected with *M. abscessus*. The clinical and radiographic presentations were not specific. However, the percentage frequencies of hemoptysis and infiltration with or without nodules in radiographic findings were higher than those in previous studies, possibly owing to the high prevalence of TB.

According to the recommendations for therapeutic regimen in the ATS guidelines, no drug regimen (including first-line anti-TB drugs) has been proven to be efficient for rapid-growth NTM pulmonary disease.[14] Among patients infected with *M. abscessus* that had a failure outcome, only one patient's medication was adjusted based on culture results and for only 2 weeks of treatment (patient #23, Table 3); conversely, the medication regimen of 12 of the 13 patients with favorable outcomes was modified. Among the patients infected with *M. fortuitum,* the medication of three of the four patients with failure outcomes were not adjusted based on culture results, while four of the six patients with favorable outcomes were adjusted. Thus, it can be concluded that medication regimens should be adjusted with an appropriate adjustment in treatment duration.

The major medications prescribed for the MAC-infected and *M. kansasii*-infected pulmonary diseases with both favorable and failure outcomes were the first-line anti-tuberculosis medications, but the treatment durations of patients with failure outcomes were shorter than those of patients with favorable outcomes. The treatment regimens for NTM pulmonary disease in this study were similar to the ATS therapeutic recommendation, but the average dura-

tion of treatment of patients with a favorable outcome was shorter than the ATS therapeutic recommendation (at least 12 months). Whether the minimum 12-month course of treatment recommended by ATS is necessary should be reviewed.

This retrospective study has several limitations. First, it was conducted at a single medical center and the patient population may be biased by a patient selection and referral pattern; however, the potential for bias was minimized by the use of very strict selection criteria. Secondly, because NTM species are environmental mycobacterium, only a few patients of clinical significance were noted and only certain NTM species were isolated; therefore, there was a relatively small sample size. Thirdly, this was a retrospective survey, which not only resulted in incomplete data, but also did not allow control of the treatment of the patients. Nonetheless, despite these limitations, the study provides useful information about NTM infection in southern Taiwan.

In summary, this study provides a descriptive epidemiology of a class of conditions that continues to be a significant problem in Taiwan. Older patients with pre-existing lung disease are the highest-risk group for NTM lung disease. Since rapid-growth species are predominant in this area, appropriate treatment regimens must be considered that may be different from those in other countries.

REFERENCES

1. Wolinsky E, Rynearson TK. Mycobacteria in soil and their relation to disease-associated strains. Am Rev Respi Dis 1968;97:1032-7.
2. Hanak V, Kalra S, Aksamit TR, Hartman TE, Tazelaar HD, Ryu JH. Hot tub lung: presenting features and clinical course of 21 patients. Respir Med 2006;100:610-5.
3. Gruft H, Falkinham JO III, Parker BC. Recent experience in the epidemiology of disease caused by atypical mycobacteria. Rev Infect Dis 1981;3:990-6.
4. Joos L, Chhajed PN, Wallner J, Battegay M, Steiger J, Gratwohl A, Tamm M. Pulmonary infections diagnosed by BAL: a 12-year experience in 1066 immunocompromised patients. Respir Med 2007;101:93-7.
5. O'brien RJ, Geiter LJ, Snider DE Jr. The epidemiology of nontuberculous mycobacterial diseases in the United States. Results from a national survey. Am Rev Respir Dis 1987;135:1007-14.
6. Henry MT, Inamdar L, O'Riordain D, Schweiger M, Watson JP. Nontuberculous mycobacteria in non-HIV patients: epidemiology, treatment and response. Eur Respir J 2004;23:741-6.
7. O'Brien DP, Currie BJ, Krause VL. Nontuberculous mycobacterial disease in northern Australia: a case series and review of the literature. Clin Infect Dis 2000;31:958-67.
8. Henriques B, Hoffner SE, Petrini B, Juhlin I, Wåhlén P, Källenius G. Infection with *Mycobacterium malmoense* in Sweden: report of 221 Cases. Clin Infect Dis 1994;18:596-600.
9. British Thoracic Society. Pulmonary disease caused by *M. malmoense* in HIV negative patients: 5-yr follow-up of patients receiving standardised treatment. Eur Respir J 2003;21:478-82.
10. Olivier KN, Weber DJ, Wallace RJ Jr, Faiz AR, Lee JH, Zhang Y, Brown-Elliot BA, Handler A, Wilson RW, Schechter MS, Edwards LJ, Chakraborti S, Knowles MR; Nontuberculous Mycobacteria in Cystic Fibrosis Study Group. Nontuberculous mycobacteria in cystic fibrosis study group: Nontuberculous mycobacteria. I: multicenter prevalence study in cystic fibrosis. Am J Respir Crit Care Med 2003;167:828-34.
11. Doucette K, Fishman JA. Non-tuberculous mycobacterial infection in hematopoietic stem cell and solid organ transplant recipients. Clin Infect Dis 2004;38:1428-39.
12. Watanabe K, Fujimura M, Kasahara K, Yasui M, Myou S, Watanabe A, Nakao S. Characteristics of pulmonary *Mycobacterium avium*-intracellulare complex (MAC) infection in comparison with those of tuberculosis. Respir Med 2003;97:654-9.
13. Marras TK, Daley CL. Epidemiology of human pulmonary infection with non-tuberculous mycobacteria. Clin Chest Med 2002;23:553-67.
14. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, Holland SM, Horsburgh R, Huitt G, Iademarco MF, Iseman M, Olivier K, Ruoss S, von Reyn CF, Wallace RJ Jr, Winthrop K; ATS Mycobacterial Diseases Subcommittee; American Thoracic Society; Infectious Disease Society of America. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175:367-416.
15. The Subcommittee of the Joint Tuberculosis Committee of the British Thoracic Society. Management of opportunist mycobacterial infections: Joint Tuberculosis Committee guidelines 1999. Thorax 2000;55:210-8.
16. Ding LW, Lai CC, Lee LN, Hsueh PR. Disease caused by non-tuberculous mycobacteria in a university hospital in Taiwan, 1997-2003. Epidemiol Infect 2006;22:1-8.
17. Shih JY, Hsueh PR, Lee LN, Wang HC, Yang PC, Kuo SH, Luh KT. Nontubeculous mycobacteria isolates: clinical significance and disease spectrum. J Formos Med Assoc 1997;96:621-7.
18. Centers for Disease Control, Republic of China (Taiwan). 2004. Department of health, The Executive Tuan, Taiwan. (Available at http://www.cdc.gov.tw)
19. Matos ED, Santana MA, de Santana MC, Mamede P, de

Lira Bezerra B, Panão ED, Filho CS, Lemos AC. Nontuberculosis mycobacteria at a multiresistant Tuberculosis reference center in Bahia: clinical epidemiological aspects. Braz J Infect Dis 2004;8:296-304.

20. Good RC, Snider DE Jr. Isolation of nontuberculous mycobacteria in the United States, 1980. J Infect Dis 1982;146:128-33.

21. Debrunner M, Salfinger M, Brandli O, von Graevenitz A. Epidemiology and clinical significance of nontuberculous mycobacteria in patients negative for human immunodeficiency virus in Switzerland. Clin Infect Dis 1992;15:330-45.

22. Engel HW, Berwald LG, Lindeboom BW, Havelaar AH. *Mycobacterium kansasii* infections in the Netherlands: a brief summary. Rev Infect Dis 1981;3:1024.

23. Kaustová J, Chmelík M, Ettlová D, Hudec V, Lazarová H, Richtrová S. Disease due to *Mycobacterium kansasii* in the Czech Republic: 1984-89. Tuber Lung Dis 1995;76:205-9.

24. Pang SC. *Mycobacterium kansasii* infections in Western Australia (1962-1987). Respir Med 1991;85:213-8.

25. Bollert FG, Watt B, Greening AP, Crompton GK. Nontubetculous pulmonary infections in Scotland: a cluster in Lothian? Thorax 1995;50:188-90.

26. Jenkins PA. The epidemiology of opportunist mycobacterial infections in Wales, 1952-1978. Rev Infect Dis 1981;3:1021-3.

27. Corbett EL, Hay M, Churchyard GJ, Herselman P, Clayton T, Williams BG, Hayes R, Mulder D, De Cock KM. *Mycobacterium kansasii* and *M. scrofulaceum* isolates from HIV-negative South African gold miners: incidence, clinical significance and radiology. Int J Tuberc Lung Dis 1999;3:501-7.

28. Corbett EL, Blumberg L, Churchyard GJ, Moloi N, Mallory K, Clayton T, Williams BG, Chaisson RE, Hayes RJ, De Cock KM. Non-tuberculous mycobacteria: defining disease in a prospective cohort of South African miners. Am J Respir Crit Care Med 1999;160:15-21.

29. Hosker HS, Lam CW, Ng TK, Ma HK, Chan SL. The prevalence and clinical significance of pulmonary infection due to non-tuberculous mycobacteria in Hong Kong. Respir Med 1995;89:3-8.

30. Ahn CH, McLarty JW, Ahn SS, Ahn SI, Hurst GA. Diagnostic criteria for pulmonary disease caused by *Mycobacterium kansasii* and *Mycobacterium intracellulare*. Am Rev Respir Dis 1982;125:388-91.

31. Shitrit D, Baum GL, Priess R, Lavy A, Shitrit AB, Raz M, Shlomi D, Daniele B, Kramer MR. Pulmonary *Mycobacterium kansasii* infection in Israel, 1999-2004: clinical features, drug susceptibility, and outcome. Chest 2006;129:771-6.

32. Johanson WG Jr, Nicholson DP. Pulmonary disease due to *Mycobacterium Kansasii*. An analysis of some factors affecting prognosis. Am Rev Respir Dis 1969;99:73-85.

33. Christensen EE, Dietz GW, Ahn CH, Chapman JS, Murry RC, Hurst GA. Radiographic manifestations of pulmonary *Mycobacterium kansasii* infections. AJR Am J Roentgenol 1978;131:985-93.

34. Griffith DE, Girard WM, Wallace RJ Jr. Clinical features of pulmonary disease caused by rapidly growing mycobacteria. An analysis of 154 patients. Am Rev Respir Dis 1993;147:1271-8.

南台灣之非結核分支桿菌之肺部感染

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背 景： 探討南台灣之非結核分支桿菌之肺部感染之主要菌種。

方 法： 回朔性之研究方法。回顧 2004 至 2005 年高雄長庚紀念醫院所有非結核分支桿菌之肺部感染之病例。收集病例相關基本資料、臨床表現、X 光片變化、相關危險因子之資料，加以分析比較。

結 果： 總共 67 個病人有非結核分支桿菌之肺部感染，平均年齡 66.6 ±14.5 歲，男性佔大多數 (70.1%)。88.1% 合併有其他之肺部疾病，其中慢性阻塞性肺疾 (61.2%) 與陳舊性肺結核 (58.2%) 為主要之肺部疾病。快速生長菌種 (*M. abscessus,* 44.8% 和 *M. fortuitum,* 23.9%) 為最主要之菌種。共 40 個病人有給與藥物治療且追蹤至少一年以上，其中 31 個病人臨床症狀有明顯改善 (平均治療期間為 8.46 ±2.96 月)。

結 論： 南台灣之非結核分支桿菌之肺部感染之主要菌種不同於其他國家，亦不同於北台灣。快速生長菌種 (*M. abscessus* 和 *M. fortuitum*) 為南台灣最主要之菌種。
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關鍵詞： 肺部感染，非結核分支桿菌，肺結核，*M. abscessus*，南台灣