Rapidly Growing Mycobacteria in King Chulalongkorn Memorial Hospital and Review of the Literature in Thailand

Prasit Phowthongkum, MD*, Vichit Prasanthai, MD*,
Nibhondh Udomsantisook, BSc**, Chusana Suankratay, MD, PhD*

** Department of Medicine, Faculty of Medicine, Chulalongkorn University*
*** Department of Microbiology, Faculty of Medicine, Chulalongkorn University*

Rapidly growing mycobacteria (RGM) have emerged as important human pathogens that can cause a variety of diseases. Thirty isolates of the pathogenic RGM were recovered from patients who attended King Chulalongkorn Memorial Hospital during 1997 and 2003. There were 16 isolates of Mycobacterium chelonae, ten isolates of M. fortuitum and four isolates of M. abscessus. Clinical data was available in only nine patients (five males and four females) including six M. chelonae, two M. abscessus, and one M. fortuitum. The mean age was 37 years (range: 13-62 years). The associated conditions were present in five patients including two diabetes, one HIV infection, one pregnancy, one SLE and one chronic renal failure. A wide spectrum of clinical features was observed. These included two chronic pulmonary infections, two post-traumatic wound infections, two disseminated infections, one lymphadenitis, one keratitis and respiratory colonization. AFB staining was positive in six patients (66.67 %). The MIC of one M. chelonae and one M. abscessus were determined by Epsilon test. For M. chelonae, the MIC of clarithromycin, amikacin, ciprofloxacin, sulfamethoxazole and imipenem were 0.25, 2.0, 1.00, > 64, and 0.54 μg/ml, respectively. For M. abscessus, the MIC of clarithromycin, amikacin, ciprofloxacin, tetracycline and sulfamethoxazole were 0.016, 0.016, 0.038, > 16 and 0.002 μg/ml, respectively. Six of eight patients (75%) were initially treated with four first-line antituberculous drugs (isoniazid, rifampicin, pyrazinamide and ethambutol) before obtaining the culture result. Of these, three patients with pulmonary and disseminated infections improved after a prolonged course of these combinations. The patients improved after switching to specific anti-RGM antibiotics. One patient died after 10 months of therapy of four anti-tuberculous drugs. One patient with post-traumatic wound infection was cured with surgical debridement and dicloxacillin. One patient improved after treatment as acute bronchitis with oral amoxicillin. An extensive review of the literature of RGM infections in Thailand is also presented.

Keywords: *Rapidly growing mycobacteria, Nontuberculous mycobacteria, Mycobacterium fortuitum, M. chelonae/abscessus, M. smegmatis*

J Med Assoc Thai 2005; 88(8): 1153-62
Full text. e-Journal: *http://www.medassocthai.org/journal*

Rapidly growing mycobacteria (RGM), capable of producing diseases in humans, comprise primarily three groups including the *Mycobacterium fortuitum* group, the *M. chelonae/abscessus* group and the *M. smegmatis* group. They can cause a wide spectrum of diseases ranging from localized to disseminated infections. Furthermore, community- and hospital-acquired infections were both reported[1,2].

In Thailand, there were a handful of reports of RGM infections. The first case, a pulmonary infection due to *M. fortuitum*, was reported in 1968 from the Central Chest Hospital. To date, a total of 112 patients were reported[3-19].

Correspondence to : Suankratay C, Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. Phone: 0-2256-4249, Fax: 0-2256-4578, E-mail: schusana @hotmail.com

RGM in King Chulalongkorn Memorial Hospital (KCMH)

The authors retrospectively reviewed the clinical manifestations and in vitro susceptibility test of RGM in KCMH during 1997 and 2003.

There were thirty isolates of RGM obtained from various clinical specimens. These included 16 *M. chelonae*, ten *M. fortuitum* and four *M. abscessus*. The clinical data was available in only nine patients.

Patient demographic data

There were five males and four females. The mean age was 37 years (range: 13-62 years) (Table 1). The underlying diseases or associated conditions were present in five patients including two diabetes, one human immunodeficiency virus (HIV) infection, one pregnancy, one systemic lupus erythematosus and one chronic renal failure.

Clinical manifestations

There were two categories of RGM infections including two disseminated and six localized infections. One patient was categorized as colonization (Table 1). Of disseminated infections, one had chronic pulmonary and peritoneal infections as well as another who had chronic pulmonary and colonic infections. Of localized infections, two had chronic pulmonary infections, two had chronic skin infections, one had chronic lymphadenitis and one had chronic keratitis. One sputum specimen from the ninth patient grew *M. fortuitum* which was thought to be colonization.

Species and susceptibility testing

Of nine patients, there were six *M. chelonae*, two *M. abscessus* and one *M. fortuitum*. The acid-fast bacilli (AFB) staining was performed in eight cases, and yielded a positive result in six cases (75%). The minimal inhibitory concentration (MIC) was determined by standard E-test in only two isolates including one *M. chelonae* and one *M. abscessus* (Table 2). *M. chelonae* was sensitive to clarithromycin (MIC 0.25 μg/ml), amikacin (MIC 2.0 μg/ml), ciprofloxacin (MIC 1.0 μg/ml), imipenem (MIC 0.054 μg/ml), and was resistant to sulfamethoxazole (MIC > 64 μg/ml). *M. abscessus* was sensitive to clarithromycin (MIC 0.016 μg/ml), amikacin (MIC 0.016 μg/ml), ciprofloxacin (MIC 0.038 μg/ml), sulfamethoxazole (MIC 0.002 μg/ml) and was resistant to tetracycline (MIC > 16 μg/ml).

Case 1

A 13-year-old girl was admitted due to

Table 1. A summary of RGM infections in King Chulalongkorn Memorial Hospital.

No.	Sex	Age (yrs)	Species	Infection	Duration of illness	Associated conditions	AFB staining	Specimen	Treatment regimens*	Outcome	Duration of Rx/FU
1	F	13	*M. chelonae*	Post-traumatic wound	1 week	None	Not done	Wound	None	Cure	7 days
2	M	19	*M. chelonae*	Keratitis	3 months	None	Positive	Corneal scrape	LoAmFlEd/ AmiAmFlEd	Improved	2 months
3	F	27	*M. chelonae*	Disseminated (L, P)	2 months	Pregnancy	Negative	Peritoneum, sputum	2IRZE/4IR	Improved	6 months
4	M	37	*M. chelonae*	Lymphadenitis	9 months	HIV infection	Positive	Lymph node	9IRZE/IRZECl	Improved	10 months
5	M	48	*M. chelonae*	Chronic lung infection	3 months	DM	Positive	Sputum	IRZE	Dead	10 months
6	M	62	*M. chelonae*	Chronic lung infection	2 months	DM	Positive	Sputum	IRZE	Improve	9 months
7	M	33	*M. abscessus*	Chronic skin infection	1 months	None	Positive	Skin	CiCoClAmi	Improved	10 months
8	F	54	*M. abscessus*	Disseminated (L, C)	3 months	None	Positive	Skin	IRZE	Not improved	2 months, loss of FU
9	F	50	*M. fortuitum*	Sputum colonization	None	SLE, CRF	Negative	Sputum	Amoxycillin	Improved	1 week

M: male, F: female, DM: diabetes mellitus, L: lung, P: peritoneum, C: colon, HIV: human immunodeficiency virus, SLE: systemic lupus erythematosus, CRF: chronic renal failure, AFB: acid-fast bacilli, Rx: treatment, FU: follow-up, Ed: eye drop, Lo: lomefloxacin, Am: amphotericin B, Fl: Fluconazole, Ami: amikacin, I: isoniazid, R: rifampicin, E: ethambutol, P: pyrazinamide, Cl: clarithromycin, Ci: ciprofloxacin, Co: cotrimoxazole.

* The number before the name of drug means duration of treatment (months) and the slash (/) means the initial treatment regimen was switched to the second regimen.

Table 2. Susceptibility testing of RGM in King Chulalongkorn Memorial Hospital.

Patient number	Species	MIC (μg/ml)*					
		Clarithromycin	Amikacin	Ciprofloxacin	Tetracycline	Sulfamethoxazole	Imipenem
4	*M. chelonae*	0.25 (S)	2.0 (S)	1.0 (S)	-	>64 (R)	0.054 (S)
7	*M. abscessus*	0.016 (S)	0.016 (S)	0.038	>16 (R)	0.002 (S)	-

* S and R in parenthesis represent sensitive and resistant, respectively

multiple injuries from a car accident. The exploratory laparotomy was performed and mild liver injury was noted. The wound at her left leg became infected and was debrided every day for a week with concomitant oral dicloxacillin. She gradually improved and was discharged after a week of hospitalization without specific anti-RGM antibiotics.

Case 2

A 19-year-old man had left chronic ulcerative keratitis for three months. He received lomefloxacin and amphotericin B eye drops for six weeks, and subsequent anterior-chamber injection of amphotericin B without any clinical improvement. Fluconazole eye drop was then also added. His visual acuity was still only hand movement. After obtaining the result of positive AFB staining from the anterior-chamber aspirate, amikacin eye drop was added to the topical amphotericin B and fluconazole regimens, and lomefloxacin eye drop was discarded. Minimal improvement was observed after 8 weeks of treatment when he was lost from a follow-up.

Case 3

A 27-year-old woman with 28-weeks pregnancy was admitted due to chronic productive cough for two months. Her chest radiography revealed diffuse reticulonodular infiltrates. Sputum was positive for AFB staining. During hospitalization, emergency Caesarian section was performed due to acute fetal distress, and a healthy male baby was delivered. During operation, the caseous inflammation throughout the lower part of greater omentum was noted and excised. The histopathological examination showed caseous granulomatous inflammation without any demonstrated organisms. She was treated as disseminated tuberculous infection with four first-line antituberculous drugs (isoniazid, rifampicin, pyrazinamide and ethambutol). Clinical improvement was observed after two months of treatment before obtaining the sputum culture result of *M. chelonae*. The patient was doing well, and was seen for the last time six months after treatment.

Case 4

A 37-year-old man with HIV infection was treated as tuberculous lymphadenitis with four first-line antituberculous drugs for nine months without any clinical improvement. The pus from a cervical lymph node aspiration was positive AFB staining, and subsequently grew *M. chelonae.* The MIC was determined, and the result was described above. His condition was slightly improved after one month of addition of clarithromycin when he decided to continue treatment at a private hospital.

Case 5

A 48-year-old man had chronic productive cough for three months. His chest radiography revealed infiltrates with calcification of both upper lobes more than lower lobes. It also showed multiple bullae at the right lung. He was treated with four first-line antituberculous drugs due to positive AFB staining of his sputum without improvement. He died due to progressive respiratory failure after ten months of treatment when the sputum was still positive by AFB staining.

Case 6

A 62-year-old man had chronic productive cough for two months. His chest radiography showed diffuse reticulonodular infiltrates of both upper lobes more than lower lobes with pleural thickening and some fibrotic streaks in both lower lungs. He was treated with four first-line antituberculous drugs for eight months when his sputum was still positive AFB staining. However, his clinical condition and radiographic findings were markedly improved. He was seen for the last time after nine months of treatment.

Case 7

A 33-year-old woman suffered from chronic wound infection with multiple sinus drainages at the right foot and associated painful groin lymphadenopathy. She had a previous history of mild abrasion at the right foot during her daily work one month prior to

infection. After one month of her illness, the debridement was performed and multiple courses of antibiotics including cloxacillin and amoxicillin/clavulanate were given without any improvement. After obtaining the culture result of *M. abscessus* from the discharge, a combination of oral ciprofloxacin 500 mg twice daily, clarithromycin 500 mg twice daily, cotrimoxazole (80 mg of trimethroprim/400 mg of sulfamethoxazole) six tablets daily and intramuscular amikacin 15 mg/kg daily were given to the patient. Marked improvement was observed after two months of treatment when amikacin was discontinued. The wound was completely healed after three months of treatment. Cotrimoxazole was discontinued after eight months of treatment because of marked pancytopenia. She was seen for the last time after ten months of treatment.

Case 8

A 54-year-old man without preexisting diseases, was incorrectly diagnosed with pulmonary tuberculosis from a history of chronic productive cough for three months, positive AFB staining of sputum and bilateral upper lung infiltrates on chest radiography. He also had chronic watery diarrhea. Colonoscopy was performed and revealed a large cecal ulcer with a diameter of 2 cm, multiple colonic ulcers and nodular lesions with varying diameters from 0.5-1 cm throughout the colon. The histopathological examination showed caseous granulomatous inflammation and positive AFB staining. The disseminated tuberculous infection was diagnosed, and he was empirically treated with four first-line antituberculous drugs before obtaining the culture result of *M. abscessus*. His condition did not improve after two months of treatment when he was lost from follow-up.

Case 9

A 50-year-old woman with SLE and chronic renal failure had productive cough for one week without any lung infiltrates on chest radiography. The sputum yielded negative AFB staining. She was treated as acute bacterial bronchitis with oral amoxicillin. She gradually improved after three days of treatment before obtaining the culture result of *M. fortuitum* from one sputum specimen.

RGM in Thailand

It is difficult to compare RGM in KCMH with those published by others because of variations in the study periods, selection criteria, case ascertainment and patient populations. The incidence of RGM infections in KCMH is very low[3-19]. The true incidence of RGM infections in Thailand is probably underestimated. From all previous reports of RGM infections in Thailand, there were 112 cases (36 females, 42 males, and data not available in 34 cases) (Table 3). The mean age was 38.5 years (range: 2-68 years). 37, 31, 26, 6 and one cases were from Ramathibodi, Siriraj, Srinagarind, Central Chest and Pramongkutklao Hospitals. There was no previous report from King Chulalongkorn Memorial Hospital.

Although RGM can easily grow on bacterial culture media, the insidiously cultivated pattern leaves them no report on routine culture laboratory without special request. In addition, clinical specimens, which are positive AFB staining, are not routinely sent for mycobacterial culture. Most patients are empirically treated as tuberculous infections[1,2].

There is a wide spectrum of diseases caused by RGM. *M. chelonae* and *M. abscessus* comprises eight of nine isolates in KCMH, compared to all previous reports in Thailand which described 56 cases (50%) of *M. chelonae/abscessus*, 37 cases (33%) of *M. fortuitum*, one case (0.89%) of *M. smegmatis* and 18 cases (16.1%) of unidentified species (Table 3). *M. chelonae* and *M. abscessus* were previously categorized within the same species but different subspecies of *chelonae* and *abscessus*, respectively[2].

Localized infections were observed in three-fourths of the patients in KCMH including three pulmonary, two cutaneous, one corneal, and one lymph-node infections. Corneal and cutaneous infections are well recognized among localized infections caused by RGM. Localized infections were observed in 70 of 112 patients (62.5%) from all previous reports in Thailand. Of these, the involved organs included the lung (30 cases, 42.8%), skin (24 cases, 34.3%), eye and ear (nine cases, 12.8%) and lymph nodes (seven cases, 10%). There were two cases of prosthetic hip joint infection, two cases of peritonitis, one case of septic arthritis and one case of subphrenic abscess. There were four cases (3.5%) who were believed to be colonized with RGM[3-19]. RGM wound infection which is associated with an augmentation mammoplasty or cardiac surgery was not observed in Thailand. This absence may be due to no special request for RGM culture from those infected wounds.

Only one patient in KCMH had HIV infection, consistent with the result of the previous study of Srinagarind Hospital which showed no HIV infection in all patients[14-16]. Of 112 cases with RGM infections, there were 12 cases in the pre-AIDS era (the first

Table 3. A summary of RGM infections in Thailand

Years	Number	Age (y), sex	Hospital	Species	Sites of infection	Duration of illness (months)	Associated conditions	AFB staining	Specimen	Treatment	Outcome	Duration of Rx/FU (months)
1968	1[3]	NA	NA	*M. fortuitum*	Lung	NA	NA	NA	NA	NA	NA	NA
1969-78	2[4]	NA	Chest	*M. fortuitum*	Lung	NA	NA	NA	NA	NA	NA	NA
1969-78	3[4]	NA	Chest	*M. fortuitum*	Lung	NA	NA	NA	NA	NA	NA	NA
1979-80	4, 5[3]	NA	NA	*M. chelonae*	Lung	NA	NA	NA	NA	NA	NA	NA
1979-86	6, 7[5]	NA	Siriraj	*M. fortuitum*	Lung	NA	NA	NA	NA	NA	NA	NA
1979-86	8[5]	NA	Siriraj	*M. fortuitum*	Skin	NA	NA	NA	NA	NA	NA	NA
1979-86	9[5]	NA	Siriraj	*M. chelonae*	Lung	NA	NA	NA	NA	NA	NA	NA
1979-86	10[5]	NA	Siriraj	*M. chelonae*	Skin	NA	NA	NA	NA	NA	NA	NA
1979-86	11[5]	NA	Siriraj	*M. chelonae*	Skin	NA	NA	NA	NA	NA	NA	NA
1980	12[6]	44, F	Siriraj	*M. fortuitum*	Skin, LN	3	CML in remission	Pos	LN, skin	Er/EHRZ	P	4
1986	13-16[7]	NA	Siriraj	NA	Skin	NA	NA	NA	Skin	NA	NA	NA
1989	17-21[8]	NA	NA	*M. fortuitum*	NA	NA	NA	NA	NA	NA	NA	NA
1989	22-23[8]	NA	NA	*M. chelonae*	NA	NA	NA	NA	NA	NA	NA	NA
1990	24[9]	NA	Chest	*M. fortuitum*	Colonization	NA	NA	Neg	Sputum	None	NA	NA
1992	25[11]	50, F	Siriraj	*M. smegmatis*	Eye	3	None	Pos	Eyelid mass	AEO/AED/ED	P	9
1992	26[11]	NA	Chest	*M. chelonae/ abscessus*	Lung	NA	NA	NA	Sputum	NA	NA	NA
1993	27[11]	NA	Chest	*M. chelonae/ abscessus*	Lung	NA	NA	NA	Sputum	NA	NA	NA
1994	28[12]	45, F	Pramongkutklao	*M. chelonae*	Li, BM, LN, skin	20	None	Pos	Li, BM, Pl	CACi	Co	NA
1997	29[13]	25, F	NA	*M. chelonae*	Skin	6	TB LN, penicilliosis	Neg	Skin	CA	P	1
1994-98	30-31[14]	NA	Srinagarind	NA	Prosthetic hip joint	NA	NA	NA	NA	NA	NA	NA
1994-98	32-33[14-16]	NA	Srinagarind	NA	Peritoneum	NA	ESRD	NA	NA	NA	NA	NA
1994-98	34-35[14-16]	NA	Srinagarind	NA	Lung	NA	NA	NA	NA	NA	NA	NA
1994-98	36[14-16]	NA	Srinagarind	NA	Cornea	NA	NA	NA	NA	NA	NA	NA
1994-98	37[14-16]	NA	Srinagarind	NA	Skin	NA	NA	NA	NA	NA	NA	NA
1994-98	38[14-16]	NA	Srinagarind	NA	Joint	NA	NA	NA	NA	NA	NA	NA
1994-98	39[14-16]	38, F	Srinagarind	*M. chelonae/ abscessus*	LN, Si, TT, Br, S, B, J	60	None	NA	LN, Si, TT, Br, S	IAC	P, 2R	32
1994-98	40[14-16]	35, M	Srinagarind	*M. chelonae/ abscessus*	LN, Lu	8	None	NA	LN	KC	P, D	5
1994-98	41[14-16]	25, M	Srinagarind	*M. chelonae/ abscessus*	LN, Li, Sp, B, Na	12	Meliodosis	NA	LN, Na	JAC	P	18
1994-98	42[14-16]	42, F	Srinagarind	*M. chelonae/ abscessus*	LN, Li, Sp	3	Penicilliosis	NA	LN	CfAK /CAz	P	24

Table 3. (Continue)

Years	Number	Age (y), sex	Hospital	Species	Sites of infection	Duration of illness (months)	Associated conditions	AFB staining	Specimen	Treatment	Outcome	Duration of Rx/FU (months)
1994-98	43[14-16]	46, M	Srinagarind	*M. abscessus*	LN, Lu	36	None	NA	LN	IAC	Co, R	12
1994-98	44[14-16]	51, M	Srinagarind	*M. chelonae/ abscessus*	LN, TL, Si	24	Salmonellosis	NA	LN	IAC	Co, R	18
1994-98	45[14-16]	41, F	Srinagarind	*M. chelonae/ abscessus*	LN, Si	48	None	NA	LN	AC	Co	24
1994-98	46[14-16]	31, F	Srinagarind	*M. abscessus*	LN, Si, S, Li	7	Salmonellosis, TB, Penicilliosis	NA	LN	IACAz	P	18
1994-98	47[14-16]	41, F	Srinagarind	*M. abscessus*	LN, Si, S, Li, Sp	3	Salmonellosis	NA	LN, S	ACCf	P	14
1994-98	48[14-16]	36, M	Srinagarind	*M. abscessus*	LN, Lu	6	Penicilliosis	NA	LN	AC	P	13
1994-98	49[14-16]	55, M	Srinagarind	*M. abscessus*	LN, Lu	6	None	NA	LN	AC	P	12
1994-98	50[14-16]	72, F	Srinagarind	*M. abscessus*	LN	24	None	NA	LN	AC	Co	11
1994-98	51[14-16]	54, M	Srinagarind	*M. abscessus*	LN	5	Salmonellosis, TB	NA	LN, blood	I/CfAC	P, D	3
1994-98	52[14-16]	47, M	Srinagarind	*M. abscessus*	LN, Si	5	None	NA	LN	AC	P, loss	3
1994-98	53[14-16]	50, F	Srinagarind	*M. abscessus*	LN	5	None	NA	LN	AC	P, loss	2
1994-98	54[14-16]	51, M	Srinagarind	*M. abscessus*	LN	1	Cryptococcosis	NA	LN	KAzC	Co	5
1999	55[14-16]	51, M	Srinagarind	*M. chelonae*	LN	NA	Salmonellosis	NA	LN	IAC	Co, R	24
1999	56[17]	50, M	Chest	*M. abscessus*	Lung	13	TB	Pos	Sputum	IEHRZ/2AD/ 2D/4Ci/9E/2C	P	70
1990-97	57-62[18v	NA	Ramathibodi	NA	Skin	NA	None	NA	NA	a	P	Mean: 76
1990-97	63-68[18]	NA	Ramathibodi	NA	Skin	NA	None	NA	NA	b	P	NA
1990-97	69-71[18]	NA	Ramathibodi	NA	Skin	NA	None	NA	NA	c	P	NA
1990-97	72[18]	NA	Ramathibodi	NA	Skin	NA	None	NA	NA	d	N	NA
1990-97	73[18]	NA	Ramathibodi	NA	Eye and ear	NA	None	NA	NA	a	P	11.3
1990-97	74-75[18]	NA	Ramathibodi	NA	Eye and ear	NA	None	NA	NA	b	P	NA
1990-97	76-79[18]	NA	Ramathibodi	NA	Eye and ear	NA	None	NA	NA	c	P	NA
1990-97	80[18]	NA	Ramathibodi	NA	Eye and ear	NA	None	NA	NA	c	N	NA
1990-97	81[18]	NA	Ramathibodi	NA	Lung	NA	HIV	NA	NA	None	L	L
1990-97	82[18]	NA	Ramathibodi	NA	LN	NA	HIV	NA	NA	a	P	4.8
1990-97	83[18]	NA	Ramathibodi	NA	LN	NA	None	NA	NA	a	N	NA
1990-97	84[18]	NA	Ramathibodi	NA	Subphrenic abscess	NA	Cancer	NA	NA	a	P	0.5
1990-97	85-87[18]	NA	Ramathibodi	NA	Dissemination	NA	HIV	NA	NA	a	P	3.1
1990-97	88[18]	NA	Ramathibodi	NA	Dissemination	NA	DM, CRF	NA	NA	a	P	NA
1990-97	89[18]	NA	Ramathibodi	NA	Dissemination	NA	Malnutrition	NA	NA	a	N	NA
1990-97	90[18]	NA	Ramathibodi	NA	Dissemination	NA	Sweet's syndrome	NA	NA	a	N	NA
1990-97	91[18]	NA	Ramathibodi	NA	Dissemination	NA	DM, CRF	NA	NA	a	D	NA
1990-97	92-93[18]	NA	Ramathibodi	NA	Dissemination	NA	None	NA	NA	a	D	NA

Table 3. (Continue)

Years	Number	Age (y), sex	Hospital	Species	Sites of infection	Duration of illness (months)	Associated conditions	AFB staining	Specimen	Treatment	Outcome	Duration of Rx/FU (months)
1998-00	94[19]	29, F	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ/AEO	P	NA
1998-00	95[19]	34, M	Siriraj	*M. fortuitum*	Lung	NA	HIV	NA	Sputum	EHRZ	D	NA
1998-00	96[19]	27, M	Siriraj	*M. fortuitum*	Lung	NA	HIV	NA	Sputum	EHRZ	L	NA
1998-00	97[19]	37, M	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ	L	NA
1998-00	98[19]	39, M	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ	P	NA
1998-00	99[19]	39, M	Siriraj	*M. fortuitum*	Lung	NA	HIV	NA	Sputum	EHRZ/CiE	P	NA
1998-00	100[19]	46, M	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ	D	NA
1998-00	101[19]	31, F	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ	D	NA
1998-00	102[19]	36, M	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ	D	NA
1998-00	103[19]	30, M	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	EHRZ	L	NA
1998-00	104[19]	33, M	Siriraj	*M. fortuitum*	Lung	NA	HIV	NA	Sputum	EHRZ/DTr	P	NA
1998-00	105[19]	32, F	Siriraj	*M. fortuitum*	Lung	NA	HIV	NA	Sputum	EHRZ/ACCf	P	NA
1998-00	106[19]	45, F	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	None	D	NA
1998-00	107[19]	29, F	Siriraj	*M. fortuitum*	Lung	NA	HIV	NA	Sputum	None	L	NA
1998-00	108[19]	22, F	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	None	L	NA
1998-00	109[19]	25, M	Siriraj	*M. chelonae*	Lung	NA	HIV	NA	Sputum	None	L	NA
1998-00	110[19]	52, F	Siriraj	*M. chelonae*	Colonization	NA	HIV	NA	Sputum	None	P	NA
1998-00	111[19]	36, M	Siriraj	*M. fortuitum*	Colonization	NA	HIV	NA	Sputum	None	P	NA
1998-00	112[19]	20, F	Siriraj	*M. chelonae*	Colonization	NA	HIV	NA	Sputum	None	P	NA

A: amikacin, Az: azithromycin, C: clarithromycin, Ci: ciprofloxacin, Cf: cefoxitin, D: doxycycline, Er: erythromycin, E: ethambutol, H: isoniazid, I: imipenem, K: kanamycin, O: ofloxacin, Tr: trimethoprim/sulfamethoxazole, R: rifampicin, Z: pyrazinamide, CML: chronic myeloid leukemia, ESRD: end stage renal disease, HIV: human immunodeficiency virus, TB: tuberculosis, F: female, M: male, BM: bone marrow, Br: breast, J: joint, LN: lymph node, Lu: lung, Li: liver, Pl: pleural fluid, S: skin, NA: not available, Na: nasopharynx, Si: sinus, Sp: spleen, T: tonsil, Co: complete response, P: partial response, D: death, L: loss of follow-up, N: no response, R: relapse, FU: follow-up, Rx: treatment, Neg: negative, Pos: positive

Treatment regimens: a = medical treatment with specific anti-RGM antibiotics, b = surgical treatment alone or with inappropriate drugs, c = medical and surgical treatment and d = medical treatment with inappropriate drugs

AIDS patients was reported in Thailand in 1984) and 100 cases in the AIDS-era. 24 cases (24%) had HIV coinfection.

From previous studies of other countries, more than 90% of patients with disseminated cutaneous disease had identified risk factors such as chronic renal failure, renal transplantation and chronic corticosteroid therapy. However, they rarely had HIV coinfection[21-23]. In Thailand, nine of 14 patients (64.7%) with disseminated infections and 25 of 70 patients (35.7%) with localized infections had associated conditions causing cell-mediated immunity defect. They had previous episodes of infections or coinfections caused by opportunistic organisms including five salmonellosis, four penicilliosis, four pulmonary tuberculosis, one melioidosis and one cryptococcosis[3-19].

In KCMH, in vitro susceptibility testing was performed in only two isolates. RGM are generally resistant to antituberculous drugs including isoniazid, streptomycin, rifampicin, ethambutol and pyrazinamide. According to the recommendation of the American Thoracic Society (ATS), the in vitro susceptibility testing of RGM should be performed against these antibiotics including amikacin, doxycycline, imipenem, fluoroquinolones, sulfonamide, cefoxitin, clarithromycin and tobramycin. The suggested broth microdilution breakpoints of susceptibility testing of RGM were recently reported from the National Committee of Clinical Laboratory Standards[25]. Amikacin, tetracycline, imipenem, ciprofloxacin, sulfonamide, and clarithromycin were tested in KCMH. The ATS recommended that therapy of RGM infections should be based on in vitro susceptibility testing[1,2].

In Thailand, all ten tested isolates of *M. fortuitum* were sensitive to amikacin, nine of ten isolates (90%) were sensitive to ciprofloxacin, five of seven isolates (71.4%) were sensitive to clarithromycin, three of seven isolates (42.9%) were sensitive to imipenem, and only four of ten isolates (40%) were sensitive to sulfamethoxazole. For *M. chelonae*, 13 of 16 tested isolates (81.3%), three of 16 isolates (18.8%), 12 of 13 isolates (92.3%), two of 12 isolates (16.7%) and four of 13 isolates (30.7%) were sensitive to amikacin, ciprofloxacin, clarithromycin, imipenem and sulfamethoxazole, respectively[5,18]. The susceptibility testing of one isolate of *M. abscessus* was performed in the patient of KCMH.

Minor RGM wound infections may resolve with surgical debridement without specific anti-RGM antibiotics like the first case in the study of KCMH. Six of eight patients (75%) in KCMH were initially treated with four first-line antituberculous drugs. Two patients with *M. chelonae* disseminated and pulmonary infections improved without specific anti-RGM antibiotics. The possible explanation may be due to mixed infections of *M. tuberculosis* and RGM, partial activity of antituberculous drugs against RGM or accompanying improvement of host immunity after delivery in case 3 with pregnancy state and after good control of plasma glucose in case 6 with diabetes.

M. chelonae pulmonary infection was rarely observed. In the series of 154 patients with chronic pulmonary infections due to RGM, only one of 146 isolates was *M. chelonae*[24]. In the study of KCMH, there were two chronic pulmonary infections caused by *M. chelonae* and two disseminated infections involving the lung and peritoneum caused by *M. chelonae* and *M. abscessus*. One patient with *M. chelonae* chronic pulmonary infection died with persistently positive AFB staining of sputum. One patient with *M. abscessus* disseminated infection was continuously given antituberculous drugs for two months without clinical improvement before a loss of follow-up. Generally, *M. abscessus* disseminated infection has not been possibly cured even after a prolonged course of specific treatment[2]. The other three patients were switched to specific anti-RGM antibiotics either monotherapy or combined therapy after obtaining the culture result. A clinical improvement was observed in all patients with a follow-up period of two months, one month and ten months, respectively.

From all available data in Thailand, the mortality rate from RGM infections was 12.98% (ten of 77 patients). Of these, there were six of 22 patients (27.7%) and one of ten patients (10%) who died during empirical treatment with antituberculous drugs and without any specific antibiotics, respectively[3-19]. Only three of 45 patients (6.7%) died during treatment with specific anti-RGM antibiotics.

In conclusion, RGM infection should be included in the list of differential diagnosis in a patient presented with chronic suppurative infection of any organs, either positive or negative AFB staining of clinical specimens and refractory to treatment with antibiotics or antituberculous drugs.

References

1. Barbara A, Brown-Elliot, Wallace JR. Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. Clin Microbiol Rev 2002; 15: 716-46.

2. American Thoracic Society. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. Am J Respir Crit Care Med 1997; 156: S1-25.
3. Bovornkitti S, Pushpakom R, Nana A, Charoenratanakul S. Siriraj Hosp Gaz 1991; 43: 392-6.
4. Sriyabhaya N, Wongwatana S. Pulmonary infection caused by atypical mycobacteria: a report of 24 cases in Thailand. Rev Infect Dis 1981; 3: 1085-9.
5. Vanittanakom N, Thasnakorn P. Bacteriological study of *Mycobacterium fortuitum* and *M. chelonei* strains isolated from six patients at Siriraj Hospital. J Infect Dis Antimicrob Agents 1987; 4: 1-5.
6. Youngchaiyud U, Prijyanonda B, Visudhiphan S, Nuchprayoon C, Chantarakul N. Disseminated cutaneous abscess caused by atypical mycobacterium report of 2 cases. J Med Assoc Thai 1983; 66: 551-7.
7. Suthipinittharm P, Nuchprayoon C, Thianprasit M. Cutaneous atypical mycobacterial infection in Siriraj hospital. Thai J Dermatol 1989; 5: 53-4 (abstract).
8. Rienthong S, Rienthong D, Saitanu K. Numerical classification study of the rapidly growing mycobacteria isolated from patients and environments. Thai J Tuberc Chest Dis 1991; 12: 127-39.
9. Wongwatana S, Sriyabhaya N. Nontuberculous mycobacterial infection of the lung in a chest hospital in Thailand. J Med Assoc Thai 1992; 75: 1-10.
10. Chierakul N, Mekanant P, Nana A. *Mycobacterium smegmatis* infection in a Thai woman. J Infect Dis Antimicrob Agents 1993; 10: 25-8.
11. Chuchottaworn C, Sudsamart C, Kanpai M. Prevalence of nontuberculous mycobacterial infection in Central Chest Hospital. Thai J Tuberc Chest Dis 1998; 19: 25-31.
12. Sareebutra W, Vassanasiri E. Case No. 4. Society proceeding: Pramongkutklao Hospital. Thai J Dermatol 1994; 10: 36-7.
13. Sukonthapirom P, Kullavanijaya P. Case No. 2. Extensive cutaneous infection of *Mycobacterium chalonae*. Society proceeding: interhospital conference. Thai J Dermatol 1997; 13: 71-3.
14. Chetchotisakd P, Jirarattanapochai K, Chuchottaworn C. Clinical pictures of 11 cases with atypical mycobacterial infection in non-HIV patients: Srinagarind Hospital experience. Srinagarind Med J 1996; 11: 346.
15. Chetchotisakd P, Mootsikapun P, Annunatsiri S. Disseminated infection due to rapidly growing mycobacteria in immunocompetent hosts presenting with chronic lymphadenopathy: a previously unrecognized clinical entity. Clin Infect Dis 2000; 30: 29-34.
16. Choonhakarn C, Chetchotisakd P, Jirarattanapochai K, Mootsikapun P. Sweet's syndrome associated with non-tuberculous mycobacterial infection: a report of five cases. Br J Dermatol 1998; 139: 107-10.
17. Chuchottaworn C, Sudsamart C, Pornchaipoonthavee S. Pulmonary infection caused by *Mycobacterium abscessus*: the first case report in Thailand. Thai J Tuberc Chest Dis 1999; 20: 119-29.
18. Chittasobhaktra T, Vibhagool A, Prachaktam R. Clinical manifestation and drug susceptibility of rapidly growing mycobacteria. J Infect Dis Antimicrob Agents 1999; 16: 109-14.
19. Ratanasuwan W, Anekthananont T, Techasathit W. Infection due to nontuberculous mycobacterium other than MAC in AIDS patients at Siriraj Hospital during 1998-2000: saprophyte vs pathogen. J Med Assoc Thai 2002; 85: 886-93.
20. Ingram CW, Tanner DC, Durack DT. Disseminated infection with rapidly growing mycobacteria. Clin Infect Dis 1993; 16: 463-71.
21. Wallace RJ Jr. The clinical presentation, diagnosis, and therapy of cutaneus and pulmonary infections due to the rapidly growing mycobacteria, *M. fortuitum* and *M. chelonei*. Clin Chest Med 1989; 10: 419-29.
22. Wallace RJ Jr, Brown BA, Onyi G. Skin, soft tissue, and bone infections due to *Mycobacterium chelonei* subspecies chelonei-importance of prior corticosteroid therapy, frequency of disseminated infection and resistance to oral antimicrobials other than clarithromycin. J Infect Dis 1992; 166: 405-12.
23. Wallace RJ Jr, Tanner D, Brennan PJ, Brown BA. Clinical trial of clarithromycin for cutaneous (disseminated) infection due to *Mycobacterium chelonae*. Ann Intern Med 1993; 119: 482-6.
24. 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.
25. Woods GL, Brown-Elliott BA, Desmond EP, Hall GS, Heifets L, Pfyffer GE, et al. Susceptibility testing of mycobacteria, *Nocardia*, and other aerobic Actinomycetes: tentative standard-second edition. NCCLS, M24-T2, 2000.

มัยโคแบคทีเรียซนิดเจริญเร็วในโรงพยาบาลจุฬาลงกรณ์และทบทวนวรรณกรรมในประเทศไทย

ประสิทธิ์ เผ่าทองคำ, วิชิต ประสานไทย, นิพนธ์ อุดมสันติสุข, ชุษณา สวนกระต่าย

มัยโคแบคทีเรียซนิดเจริญเร็วเป็นเชื้อก่อโรคหลายชนิดในมนุษย์ สามารถแยกเชื้อมัยโคแบคทีเรียซนิดเจริญเร็วที่ก่อโรคจากผู้ป่วยของโรงพยาบาลจุฬาลงกรณ์ 30 ราย ระหว่างปี พ.ศ. 2540-2546 โดยใน 16 ราย เป็นมัยโค-แบคทีเรียเซโลนี 10 ราย เป็นมัยโคแบคทีเรียม ฟอร์ทูอิทุม และ 4 ราย เป็นมัยโคเบคทีเรียม แอบเซสซุส ข้อมูลทางคลินิกได้จากผู้ป่วย 9 ราย (ชาย 5 ราย และหญิง 4 ราย) เป็นมัยโคแบคทีเรียม เซโลนี 6 ราย มัยโคแบคทีเรียม แอบเซสซุส 2 ราย และมัยโคแบคทีเรียม ฟอร์ทูอิทุม 1 ราย อายุเฉลี่ย 37 ปี (ระหว่าง 13-62 ปี) โรคและภาวะร่วมพบในผู้ป่วย 5 ราย ได้แก่ เบาหวาน 2 ราย โรคติดเชื้อภูมิคุ้มกันบกพร่อง 1 ราย ตั้งครรภ์ 1 ราย โรคเอสแอลอี 1 ราย และไตวายเรื้อรัง 1 ราย โรคที่พบประกอบด้วย โรคปอดเรื้อรัง 2 ราย แผลได้รับบาดเจ็บติดเชื้อ 2 ราย โรคติดเชื้อแพร่กระจาย 2 ราย ต่อมน้ำเหลืองอักเสบ 1 ราย แก้วตาอักเสบ 1 ราย และอาณานิคมเชื้อ 1 ราย การย้อมสีทนกรดติดในสิ่งส่งตรวจจากผู้ป่วย 6 ราย (ร้อยละ 66.67) ค่าความเข้มข้นของยาในการยับยั้งเชื้อ ได้รับการตรวจด้วยวิธีเอปไซลอนจากเชื้อมัยโคแบคทีเรียม เซโลนี และมัยโคแบคทีเรียม แอบเซสซุส อย่างละ 1 ราย ผู้ป่วย 6 ราย (ร้อยละ 75) ได้รับการรักษาแบบวัณโรคด้วยยาไอโสไนอะสิด ไรแฟมปิซิน พัยราซินาไมด์ และอีแธมบูธอล ก่อนทราบผลเพาะเชื้อ ในผู้ป่วยปอดเรื้อรัง 1 ราย และผู้ป่วยติดเชื้อแพร่กระจาย 1 ราย มีลักษณะทางคลินิกดีขึ้น ผู้ป่วย 3 ราย เปลี่ยนการรักษาด้วยยาเฉพาะโรคมัยโคแบคทีเรียซนิดเจริญเร็ว ผู้ป่วย 1 ราย เสียชีวิตขณะรักษาด้วยยารักษาวัณโรคมา 10 เดือน ผู้ป่วยที่มีแผลได้รับบาดเจ็บติดเชื้อหายจากการรักษาด้วยการตัดเนื้อเยื่อที่ติดเชื้อออกและยาไดคลอกซาซิลิน ผู้ป่วย 1 ราย ดีขึ้นหลังการรักษาแบบหลอดลมอักเสบติดเชื้อเฉียบพลันด้วยยารับประทานอะม็อกซิซิลิน