Original Report

Infections with rapidly growing mycobacteria: report of 20 cases

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Objectives: A series of cases infected with rapidly growing mycobacteria was studied to determine the spectrum of disease, antimicrobial susceptibility, treatment, and outcome.

Methods: The cases identified as infections with rapidly growing mycobacteria in Ramathibodi Hospital from January 1993 to December 1999 were retrospectively studied.

Results: Most of the cases had no underlying disease. Only two cases were HIV-infected patients. The presenting clinical features were lymphadenitis (seven cases), skin and/or subcutaneous abscess (seven cases), localized eye infection (four cases), pulmonary infection (one case), and chronic otitis media (one case). Four of seven cases with lymphadenitis had Sweet's syndrome, and one had psoriasis as an associated skin manifestation. Anemia was present in five cases, and improved with treatment of the primary disease. The organisms were *Mycobacterium chelonae/abscessus* group (17 cases) and *Mycobacterium fortuitum* group (three cases). Susceptibility patterns of the organisms showed susceptibility to amikacin, netilmicin, and imipenem. *M. fortuitum* group was susceptible to more antibiotics than *M. chelonae/abscessus* group. The clinical responses corresponded to the antimicrobial susceptibility. Combinations of two or more drugs were used for the medical treatment. Surgical resection was performed where possible, to reduce the load of the organism, especially in cases with very resistant organisms.

Conclusions: Infections with rapidly growing mycobacteria can occur in apparently normal hosts. The clinical syndrome is variable. The pathology is nonspecific. Clinical responses varied, but seemed to correlate with the in vitro susceptibility result. More studies are needed to enable us to deal with this infection effectively.

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INTRODUCTION

Mycobacterium chelonae, *Mycobacterium abscessus* and *Mycobacterium fortuitum* group are the major pathogens among the rapidly growing mycobacteria. Infections caused by these organisms are not uncommon, and the incidence is increasing. The clinical syndrome is variable.[1] The diseases can involve many tissues and organ systems, and include skin and soft tissue infections,[2–4] lymphadenitis,[5] pulmonary infections,[6–8] arthritis,[9] keratitis,[10–12] endophthalmitis,[13] otitis media and mastoiditis,[14,15] catheter-related infection,[16,17] peri-prosthetic infection,[18] and disseminated infection.[19,20] Most of the patients are immunosuppressed or have antecedent chronic illness.[20] The course of disease is highly variable.[1,20] Treatment is difficult, because the organisms do not respond to traditional antituberculous agents and most antibiotics, and relapse is common. A controlled trial defining the optimal treatment regimen is not available, due to limited numbers of patients, and variations in the clinical syndrome and clinical course. Our report of 20 cases may offer data that will be of use in both treatment and research in the future.

MATERIALS AND METHODS

Clinical aspects

Records of the cases infected with *M. chelonae/abscessus* group and *M. fortuitum* group in our Division of Infectious Diseases and Microbiology Laboratory from January 1993 to December 1999 were retrospectively reviewed. Only the cases that fulfilled the diagnostic criteria for nontuberculous mycobacterial infection as described by the American Thoracic Society[21] were included. The medical records of the cases were reviewed for demographic data and information regarding underlying diseases, clinical features, antimicrobial susceptibility, pathology of the tissues, treatment, and outcome.

The definition of organ involvement required positive culture from the tissue or sterile specimen, or suggestive histologic findings of second organ involvement. The outcome of treatment was defined as good,

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fair, or poor, depending on general condition, body weight, resolution of presenting symptoms and physical findings, negative culture, and absence of clinical relapse.

Microbiological aspects

Acid-fast stain of the clinical specimens was done by the carbol fuschin method (Kinyoun stain). Clinical specimens from various sites were cultured on routine aerobic and mycobacterial media. The colonies were small, rough and creamy white or slightly yellow on blood agar, and appeared smooth, dull and creamy white on Lowenstein–Jensen media after incubation at 37°C for 3–7 days. They are gram-variable and positive for acid-fast stain. The identification of rapidly growing mycobacteria was based on growth on MacConkey agar (crystal violet free) and a positive arylsulfatase reaction within 3 days. *M. fortuitum* group was differentiated from *M. chelonae/abscessus* group on the basis of positive iron uptake and nitrate reduction.[22] With our set of biochemical tests, *M. chelonae* was not distinguished from *M. abscessus*, and *M. fortuitum* group was not differentiated from the biovar. Susceptibility testing was done by the disk diffusion method. A Mueller–Hinton agar plate was swabbed with OADC (oleic acid albumin dextrose catalase) on its surface. The organisms in Mueller–Hinton broth with a turbidity equivalent to 0.5 McFarland were swabbed onto the surface. Commercial bacterial antibiotic disks were used and incubated at 37°C for 3–4 days until there were signs of growth. The zones of inhibition were measured. Susceptibility or resistance to individual agents was recorded according to the suggested susceptibility-zone diameter.[23]

RESULTS

There were 22 cases infected by *M. chelonae/abscessus* group or *M. fortuitum* group from January 1993 to June 1999 in Ramathibodi Hospital. Two cases were excluded because the files were not available. The details of 20 cases are given in Table 1. The pathologic diagnosis of the tissues or pus from infected organs is shown in Table 2. Table 3 shows the patterns of susceptibility of various antimicrobial agents to the organisms. Three of 20 cases with different presentations and different problems are presented as case reports.

Case reports

Case 7

A 40-year-old man was admitted due to prolonged fever for 6 weeks. He had been well until 6 weeks prior to admission, when he developed persistent low-grade fever. Four weeks prior to admission, he had developed migratory joint pain from the right big toe, to both ankles, both knees, both wrists, and the right index finger. The joint pain spontaneously disappeared 1 week prior to admission, but a rash on the right hand appeared instead. He noticed a 7-kg weight loss in these 6 weeks.

On admission, he had a temperature of 38.5°C. There was lymphadenopathy in the right submandibular and left anterior cervical areas. The liver was enlarged. Erythematous maculopapular rashes were found on the upper chest, both hands, and both feet. Other physical findings were unremarkable. The results of laboratory investigations, including complete blood count, liver function test, blood urea nitrogen and creatinine, antinuclear antibody, rheumatoid factor, venereal disease research laboratory (VDRL), chest radiograph, and ultrasound of abdomen, were within normal ranges. Anti-HIV antibody was negative, and three hemoculture specimens were negative.

Cervical lymph node biopsy was performed, and the imprint stain showed rare acid-fast bacilli. The pathologic diagnosis of the node was chronic and acute lymphadenitis with poorly formed granuloma. Skin lesion biopsy was done, and the pathologic diagnosis was Sweet's syndrome. The patient was primarily treated as for tuberculosis, with isoniazid, rifampicin, ethambutol, and pyrazinamide. After 1 week of treatment, the patient still had fever and no improvement.

Table 1. Cases infected with rapidly growing mycobacteria

Case	*Age, gender*	*Diagnosis*	*Organism*	*Underlying diseases*	*Treatment*	*Outcome*
1	57, M	Intraabdominal lymphadenitis, anemia	*M. fortuitum* group	None	Clarithromycin + doxycycline + gentamicin	Good, but lost to follow-up after 7 weeks' treatment
2	39, F	Bilateral cervical lymphadenitis, left parotitis, anemia, Sweet's syndrome	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin + imipenem (doxycycline)[a]	Good, but relapse 6 months after stopping treatment
3	32, F	Right supraclavicular lymphadenitis,	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin (doxycycline)[a]	Good, but relapsed after stopping treatment

Table 1. (Continued)

Case	*Age, gender*	*Diagnosis*	*Organism*	*Underlying diseases*	*Treatment*	*Outcome*
4	59, F	Right cervical lymphadenitis, anemia	*M. chelonae/ abscessus* group	Rheumatoid arthritis	Clarithromycin + netilmicin (fusidic acid)[a]	Good, no relapse 4 months after stopping treatment
5	47, F	Bilateral cervical lymphadenitis, multiple bone infection, right parotitis, anemia, Sweet's syndrome	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin (netilmicin)[a]	Poor, needed surgery, relapse 3 weeks after stopping treatment
6	52, F	Cervical lymphadenitis, anemia, Sweet's syndrome	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin + ciprofloxacin + (cotrimoxazole)[a]	Good, no relapse 7 months after stopping treatment
7	40, M	Cervical and inguinal lymphadenitis, Sweet's syndrome, psoriasis	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin	Poor, needed surgery, breakthrough on medication
8	24, F	Neck abscess	*M. chelonae/ abscessus* group	None	Drainage	Lost to follow-up before treatment
9	27, F	Breast abscess	*M. chelonae/ abscessus* group	None	Drainage	Lost to follow-up before treatment
10	40, F	Chronic subcutaneous nodule	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin	Good, needed surgery
11	18, F	Nodule on tattoo	*M. chelonae/ abscessus* group	None	Excision Cotrimoxazole	Good, no relapse 15 months after stopping treatment
12	27, F	Chronic skin ulcers & subcutaneous abscess	*M. chelonae/ abscessus* group	SLE	Clarithromycin + amikacin + cotrimoxazole + doxycycline	Good, breakthrough on medication, needed surgery
13	52, F	Skin plaque	*M. chelonae/ abscessus* group	None	Clarithromycin Ciprofloxacin	Good, no relapse 2 years after stopping treatment
14	34, M	Genital inguinal abscess	*M. fortuitum* group	HIV positive	Clarithromycin + amikacin + cotrimoxazole + ofloxacin	Good, no relapse 6 months after stopping treatment
15	38, M	Pulmonary infection	*M. chelonae/ abscessus* group	HIV positive Previous pulmonary TB	–	Died before treatment
16	41, F	Right COM, right mastoiditis, sigmoid sinus thrombosis	*M. chelonae/ abscessus* group	None	Clarithromycin + amikacin + imipenem	Poor, breakthrough on medication, needed multiple operations
17	44, M	Right corneal ulcer	*M. fortuitum* group	None	Cotrimoxazole Rifampicin Cefazolin ED Gentamicin ED	Good
18	39, M	Left corneal ulcer	*M. chelonae/ abscessus* group	None	Clarithromycin Fusidic acid Amikacin ED	Good
19	66, F	Left corneal ulcer, endophthalmitis	*M. chelonae/ abscessus* group	Hypertension	Tetracycline Cefazolin ED Gentamicin ED	Good
20	24, F	Endophthalmitis	*M. chelonae/ abscessus* group	None	Enucleation Choramphenicol ED	Good

ED, eyedrop; SLE, systemic lupus erythematosus; COM, chronic otitis media.
[a]Short course of treatment.

Table 2. Pathologic findings of the tissue from infected organs

Infected organ and pathological diagnosis	*AFB*	*Number (specimens)*
1. Lymph node		
Nonspecific lymphadenitis	−	1
Acute / chronic inflammation	−	2
Acute and chronic lymphadenitis with focal fibrosis	+	2
Acute suppurative lymphadenitis	+	1
Suppurative granuloma with eosinophilia	+	1
Suppurative granuloma with caseous necrosis	−	1
Caseous granuloma	−	1
Granulomatous lymphadenitis	−	2
Non-caseating granulomatous lymphadenitis	−	1
Mixed lymphoid cells with vascular proliferation	−	1
2. Tonsils		
Pleomorphic reticulosis	+	1
3. Bone		
Necrotic tissue with acute inflammation	−	1
Acute inflammation with multinucleated giant cells	−	1
4. Skin and soft tissue		
Chronic inflammation	−	1
Chronic eczema with excoriation	+	1
Suppurative granulomatous inflammation	−	2
Suppurative and focal granulomatous inflammation	+	1
Necrotizing granulomatous inflammation	−	1
5. Mastoid and middle ear		
Chronic inflammation with epitheloid granuloma	−	2
Granulomatous inflammation with caseous necrosis	−	1
Cholesteatoma	−	1
6. Pus from abscess	+	3/4
7. Sputum	+	2/2

Mycobacterial culture of the node on the seventh day revealed growth of colonies with positive acid-fast bacilli, and rapidly growing mycobacteria were considered. Treatment was then switched to oral clarithromycin 500 mg twice daily and intravenous amikacin 500 mg once daily. The organism was identified on the 14th day as *M. chelonae/abscessus*, and was susceptible to gentamicin, netilmicin, amikacin, tobramycin, and erythromycin, and resistant to cefoxitin, imipenem, meropenem, ofloxacin, ciprofloxacin, cotrimoxazole, and tetracycline. The right submandibular and left anterior cervical lymph nodes were not palpable after 2 months of treatment. The patient was discharged on clarithromycin, and continued to be given intravenous amikacin in the outpatient clinic.

Although the patient showed good adherence to the medication, he had two episodes of breakthrough lymphadenitis and two individual episodes of dermatologic disease in a period of 6 months. The first episodes of breakthrough lymphadenitis occurred when he had been receiving clarithromycin and amikacin for 4 months. The manifestations were acute fever, matted nodes at the right groin, and a right upper thigh abscess. Culture of the pus from the right thigh abscess grew *M. chelonae/abscessus* group, and the the results of susceptibility testing were similar to those of the first strain. The abscess was drained, and the right inguinal lymph nodes were excised. The pathologic diagnosis was necrotizing granulomatous inflammation. Treatment was switched to oral azithromycin 750 mg, oral sparfloxacin 200 mg, and intravenous netilmicin 300 mg once daily.

The second episode of breakthrough lymphadenitis occurred when the patient had taken azithromycin, sparfloxacin and netilmicin for 4 weeks and presented with acute fever and bilateral cervical lymphadenopathy. Right radical neck dissection with left-modified radical neck dissection was performed. The node culture grew the same organism, with the same susceptibility. Susceptibility testing for trovafloxacin was done, and showed the organism to be resistant to this agent. Azithromycin, imipenem and amikacin were given. In both episodes, the patient improved with combined medical and surgical treatment. The intention was for him to take long-term, unlimited medication. However, a new relapse is possible, and he might need further surgical resection.

The two individual episodes of dermatologic disease in this patient were psoriasis and Sweet's syndrome. Both episodes occurred few weeks before the episodes of breakthrough lymphadenitis, and were confirmed by biopsy. The organism was not found in cultures of the blood and skin lesions. Psoriasis was improved with etretinate and topical mineral oil, and Sweet's syndrome subsided after a short course of prednisolone.

Case 12

A 27-year-old woman presented with a history of chronic ulcers on the right leg for 3 months. She had no underlying disease. Three months prior to admission, she had developed an ulcer with pus on the pretibial area of the right leg. The ulcer then enlarged, and became surrounded by multiple small ulcers. The patient had no fever or other symptoms. She went to see a doctor, and a skin biopsy was done. Acid-fast bacilli were found in acid-fast stain of the pus, and skin biopsy showed mixed acute suppurative inflammation and focal granulomatous inflammation within the deep dermis and subcutaneous fat. Tuberculosis of the skin was diagnosed, and antituberculous drugs were given. The skin lesions did not improve after 2 months of medication, and the patient was transferred to Ramathibodi Hospital.

The patient had underlying disease, diagnosed as systemic lupus erythematosus with renal involvement, and was on oral prednisolone 15 mg daily. She could not recall any previous injury to the right leg.

Table 3. Susceptibility patterns of rapidly growing mycobacteria to antibiotics

Antibiotics	M. chelonae/abscessus *group*				M. fortuitum *group*			
	All tested (strains)	*Resistant (strains)*	*Susceptible (strains)*	*(%)*	*All tested (strains)*	*Resistant (strains)*	*Susceptible (strains)*	*(%)*
Penicillin	13	13	0	0	2	2	0	0
Cefoxitin	13	13	0	0	1	0	1	100
Imipenem	10	3	7	70.0	1	0	1	100
Gentamicin	13	6	7	53.8	3	0	3	100
Amikacin	13	0	13	100	3	0	3	100
Netilmicin	13	0	13	100	3	0	3	100
Tobramycin	13	0	13	100	3	0	3	100
Ofloxacin	13	13	0	0	2	0	2	100
Ciprofloxacin	11	10	1	9.1	1	0	1	100
Lincomycin	11	10	1	9.1	3	3	0	0
Erythromycin	13	8	5	38.5	3	3	0	0
Chloramphenicol	4	4	0	0	2	1	1	50
Cotrimoxazole	13	11	2	15.4	3	0	3	100
Tetracycline	10	10	0	0	2	0	2	100
Fosfomycin	7	7	0	0	2	2	0	0
Vancomycin	12	11	1	8.3	1	0	1	100
Teicoplanin	6	5	1	16.7	1	1	0	0
Fusidic acid	9	7	2	22.2	2	1	1	50

On admission, the patient had a cushingoid appearance. There was a dirty wound with exudate, 2 × 2 cm in diameter, surrounded by multiple small ulcers, crust, and erythematous papules, on the right leg. Acid-fast stain of the pus from the large ulcer showed numerous acid-fast bacilli. Culture revealed *M. chelonae/abscessus* group, which was susceptible to gentamicin, netilmicin, tobramycin, and amikacin, and resistant to cefoxitin, imipenem, meropenem, ofloxacin, ciprofloxacin, erythromycin, cotrimoxazole, and tetracycline. Clarithromycin 500 mg twice daily and amikacin 750 mg once daily were given. The skin lesions improved within 3 weeks, and treatment was discontinued.

Four weeks after discontinuation of treatment, the patient had relapse of an ulcer on the pretibial area of the right leg, and pustular eruptions on the right thigh. The organism was not found with acid-fast stain and culture. Clarithromycin and amikacin were given. An operation for wide excision of the ulcer and subsequent skin graft was performed. The pathologic diagnosis of the ulcer was necrotizing granulomatous inflammation. The pustular eruptions subsided after 3 weeks of medication, and the surgical wound healed. The medication was continued for 8 weeks. The patient was discharged, and was followed up for 8 months at the outpatient clinic without any relapse.

Case 16

A 41-year-old woman presented with progressive headache, a painful right eye, and a painful right ear. She had a 3-year history of chronic otitis media of the right ear and multiple operations for tympanoplasty. She was admitted with the diagnosis of right chronic otitis media and sclerosing mastoiditis. A right radical mastoidectomy was performed. The pathologic diagnosis was chronic inflammation with focal tissue necrosis. After the operation, the patient's headache persisted, and she developed tinnitus in the right ear. Examination of the right ear showed whitish granulation tissue in the middle ear and mastoid cavity. The results of neurologic examination were normal. MRI of the brain and temporal bone showed a mixed enhancing soft tissue mass at the right petrous ridge, cerebropontine angle cisterns, tentorium, right sigmoid sinus, right middle ear cavity, and mastoid air cells, compatible with a chronic infectious process. Biopsy of the granulation tissue in the right middle ear and mastoid cavity was performed. The pathologic diagnosis of the granulation tissue was granulomatous inflammation with caseous necrosis. Acid-fast stain was negative. Tissue culture grew *M. chelonae/abscessus* group, which was susceptible to imipenem, netilmicin, amikacin, and erythromycin, and resistant to cefoxitin, ofloxacin, ciprofloxacin, cotrimoxazole, and tetracycline. Oral clarithromycin 500 mg twice daily, intravenous imipenem 500 mg every 6 h and amikacin 750 mg once daily were given.

After 8 weeks of treatment, the patient's symptoms had slightly improved, but follow-up MRI of the temporal bone gave the same results as the first MRI. A right radical mastoidectomy was performed. The pathologic diagnosis of the right mastoid mucosa was cholesteatoma, and no organism was found with the special stain. Treatment was continued throughout the 4-month hospitalization period. The third MRI of the temporal bone showed moderate reduction of the enhancing lesion in the rest of the right mastoid air cell and middle ear cavity. The patient was discharged on clarithromycin and alternate-day amikacin. Her clinical status was stable.

The patient was admitted on two more occasions, with acute attacks of headache and right ear pain.

Multiple operations for the revision of the right mastoidectomy were performed before improvement was seen. There was no growth of organisms in tissue culture for mycobactera in three individual episodes. The patient had sigmoid sinus thrombosis as a complication of disease on one admission. Oral clarithromycin and cotrimoxazole, and amikacin eardrops, were given concurrently and continued for 18 months without clinical relapse.

DISCUSSION

Rapidly growing infections with mycobacteria in humans are primarily caused by *M. chelonae/abscessus* group and *M. fortuitum* group. Both groups grow on routine bacteriologic media, as well as on mycobacterial media, in 7 days or less.[24] The organisms are increasingly recognized as pathogens, and the clinical syndrome is variable. According to the organ infected, the cases in our study could be divided into five groups. The first group had lymphadenitis, and consisted of the first seven cases. The second group had skin and soft tissue infections, and consisted of cases 8–14. The 15th case was in the third group, pulmonary infection, and the 16th case was in the fourth group, ear infection. The fifth group, eye infection, consisted of the last four cases. The fifth and seventh cases were considered to have disseminated infection, because of simultaneous multiple bone infections and multiple areas of lymphadenitis, respectively.

Among 20 cases, only four were considered to be immunocompromised hosts, consisting of two cases with HIV infection, one case with systemic lupus erythematosus on steroid therapy, and one case with rheumatoid arthritis on steroid therapy. The higher proportion of immunocompetent patients in our study than in the previous study[20] suggests that infections with rapidly growing mycobacteria could occur in apparently normal hosts. The incidence of *M. chelonae/abscessus* group infection was higher than that of *M. fortuitum* group infection in our study, consistent with the results of previous studies.[10,11,20]

Seven of the 20 patients in our study presented with lymphadenitis. The number was higher than that in a recent review, which identified 54 cases of infections with rapidly growing mycobacteria since 1960, only three of which resulted in lymphadenitis.[20] The nodes involved in these patients were the cervical, supraclavicular or intra-abdominal lymph nodes. The pathology of the various tissues was nonspecific and not diagnostic. Even though some specimens showed positive acid-fast bacilli, they could not be differentiated from tuberculosis, the more common disease. Culture for mycobacteria was more specific and helpful. Four of seven cases had associated Sweet's syndrome that was supported by clinical and histologic evidence. All of them were infected with *M. chelonae/abscessus* group. This finding supports the findings of previous studies[25,26] that reported Sweet's syndrome associated with *M. chelonae/abscessus* group infection. We observed that three of our four cases with Sweet's syndrome had recurrence when there were clinical relapses of lymphadenitis. Our observations and previous data indicate that awareness of infections with rapidly growing mycobacteria is necessary when patients present with lymphadenitis and Sweet's syndrome.

The seven cases presenting with skin and soft tissue infections in our study comprised skin and subcutaneous infections, nodules on tattoo, neck, and breast, and inguinal abscesses. The fact that 41 of 54 patients presented with this entity in an earlier review[20] is evidence that skin and soft tissues are common sites of infection. Acid-fast stain is helpful for recognition of mycobacterial infection. This finding indicates the desirability of doing acid-fast stain in tissue and, particularly, pus from the abscess to achieve rapid diagnosis of mycobacterial infection.

The case of pulmonary infection in our study was a patient with advanced symptomatic HIV. Because the patient had been previously treated for pulmonary tuberculosis and concurrent cryptococcal meningitis, which was the cause of death, the diagnosis of *M. chelonae/abscessus* group pulmonary infection could not definitely be made by the diagnostic criteria of The American Thoracic Society.[21] However, we proposed that pulmonary infection was present, as this patient was a possible case of infection with rapidly growing mycobacteria, especially given the immunocompromised condition.

The case of otitis media and mastoiditis in our study was chronic and did not respond to many conventional antibiotics. The diagnosis was made after mycobacterial infection was detected. The patient had multiple episodes of recurrence despite surgical resection and appropriate medical treatment. This might be another site of infection with rapidly growing mycobacteria that was difficult to treat. The previous study including 21 patients with chronic otitis media caused by rapidly growing mycobacteria had documented that treatment for this entity is difficult, requiring debridement and prolonged antibiotic therapy.[27] This study also proposed that tympanostomy tube placement is a risk factor for this infection.

Three of four cases of eye infection in our study reported previous eye injury, consistent with a previous study of 22 patients, in which 91% had previous eye injury.[11] The 20th case, who had endophthalmitis and needed surgery for nucleation, had a history of penetrating eye injury 3 years prior to the infection. Eye surgery is another risk factor for endophthalmitis, according to previous reports.[28,29]

Treatment of infections with rapidly growing mycobacteria is difficult, because of resistance to conventional antituberculous drugs and many antibiotics, and common clinical relapse. The seventh and sixteenth cases in our study as presented above demonstrate the

difficulty of treatment. Although a prior study suggested that primary treatment should be local excision of the affected lymph nodes,[5] many studies have reported the success of medical treatment with and without surgical treatment.[2–4,6–20] Seventeen cases in our study had received the treatment, and 13 of these had good clinical outcome. The other two cases with fair clinical outcomes and two cases with poor clinical outcomes needed concurrent surgical treatment.

The antimicrobial susceptibilities of *M. chelonae/abscessus* group and *M. fortuitum* group were different.[30] All strains of *M. fortuitum* are susceptible to cotrimoxazole,[30] ciprofloxacin, and ofloxacin,[31] and some strains are susceptible to cefoxitin, doxycycline, and erythromycin,[30] whereas fewer than 20% of *M. chelonae/abscessus* group are susceptible to these drugs.[30,32–34] The susceptibility patterns of these drugs found in our study are similar to these.

A study in 1978 suggested that amikacin is a promising drug for the treatment of both *M. chelonae* and *M. fortuitum* infection,[35] and a study by Swenson has confirmed this. According to the results of our study, all strains of *M. chelonae/abscessus* group and *M. fortuitum* group are susceptible to amikacin and netilmicin. Clarithromycin is another drug that actively inhibits both groups of organisms, and is 10–50 times more potent than erythromycin against *M. chelonae/abscessus* group. Unfortunately, before 1999 we had not tested the susceptibility of the organisms to clarithromycin in clinical practice, because disks were unavailable. However, a previous study that enrolled some patients from our study[36] showed that 91.7% of *M. chelonae/abscessus* group strains and 71.4% of *M. fortuitum* group strains were susceptible to clarithromycin by E-test MIC study. The other 28.6% of *M. fortuitum* group were intermediately resistant to clarithromycin. Imipenem was the only β-lactam active against *M. chelonae/abscessus* group for 39% of strains in a previous study.[32] Seventy per cent of the cases infected by *M. chelonae/abscessus* group in our study were susceptible to imipenem. Because of the variations in susceptibility by and within species subgroups, we recommend susceptibility testing if the test is available.

Clinical therapeutic trials of infections with rapidly growing mycobacteria are scanty. A clinical trial of clarithromycin for cutaneous infection due to *M. chelonae* suggests that clarithromycin may be the drug of choice.[37] However, the later reports of rapid development of resistance to clarithromycin monotherapy for *M. chelonae* infection[38] and quinolone monotherapy for *M. fortuitum* infection[33] suggest that combination therapy is more suitable. Medical treatment of the patients in our study included two- or three-drug combinations. The outcome of treatment varied among each group of diseases. Most of the patients with lymphadenitis had good clinical outcome. The cases with fair and poor clinical outcomes had more involved lymph nodes at first presentation, and they needed surgical resection. This suggests that widespread lymph node involvement may be a poor prognostic sign. Relapse was common in this group, especially in the cases with multiple node involvement. We recommend using at least three drugs to which the organism is susceptible for medical therapy, and continuing treatment long term. Surgical resection, if possible, is helpful for the patient with lymphadenitis.

The patients with cutaneous infection responded well to the treatment, but the extensive skin lesion also needed surgery. If an abscess was present, drainage was indicated. Successful topical amikacin monotherapy for keratitis was reported in one study, but 75% of patients needed early keratectomy.[11] We still recommend using at least two or three topical and systemic drugs for medical therapy. Cases with endophthalmitis may need surgery to control the disease. Since a previous study reported that more patients on concurrent corticosteroid therapy had failed medical therapy,[10] we recommend the avoidance of corticosteroid therapy in these patients.

CONCLUSIONS

Infections with rapidly growing mycobacteria present with variable clinical syndromes. The diseases can occur in apparently normal hosts. Awareness of the organism can lead to diagnosis and suitable treatment. Culture of mycobacteria from clinical specimens is necessary for definitive diagnosis, since the pathology is nonspecific. In our study, clinical responses varied. Relapse was common, particularly in the cases with lymphadenitis. Medical therapy, including two or three drugs to which the organism is susceptible, is recommended. Surgical resection is indicated in cases with failed medical therapy and/or clinical relapse.

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REFERENCES

1. Wallace RJ Jr, Swenson JM, Silcox VA, et al. Spectrum of diseases due to rapidly growing mycobacteria. Rev Infect Dis 1983; 5:657–679.
2. Drabick JJ, Duffy PE, Samlaska CP, et al. Disseminated *Mycobacterium chelonae* subspecies *chelonae* infection with cutaneous and osseous manifestations. Arch Dermatol 1990; 126:1064–1067.
3. Wallace RJ Jr, Brown BA, Onyi GO. Skin, soft tissue, and bone infections due to *Mycobacterium chelonae chelonae*: importance of prior corticosteroid therapy, frequency of disseminated infections, and resistance to oral antimicrobials other than clarithromycin. J Infect Dis 1992; 166:405–412.

4. Fonseca E, Alzate C, Canedo T, Contreras F. Nodudar lesions in disseminated *Mycobacterium fortuitum* infection. Arch Dermatol 1987; 123:1603–1604.
5. Wright JE. Non-tuberculous mycobacterial lymphadenitis. Aust NZ J Surg 1996; 66:225–228.
6. Pesce RR, Fejka S, Colodny SM. *Mycobacterium fortuitum* presenting as an asymptomatic enlarging pulmonary nodule. Am J Med 1991; 91:310–312.
7. Rolston KVI, Jones PG, Fainstein V, Bodey GP. Pulmonary disease caused by rapidly growing mycobacteria in patients with cancer. Chest 1985; 87:503–506.
8. Kesten S, Chaparro C. Mycobacterial infections in lung transplant recipients. Chest 1999; 115:741–745.
9. Gran JT, Eng J, Refvem OK, et al. Monoarthritis due to *Mycobacterium chelonae*. J Rheumatol 1987; 14:852–853.
10. Ford JG, Huang AJW, Pflugfelder SC, et al. Non-tuberculous mycobacterial keratitis in South Florida. Ophthalmology 1998; 105:1652–1658.
11. Huang SCM, Soong HK, Chang JS, Liang YS. Non-tuberculous mycobacterial keratitis: a study of 22 cases. Br J Ophthalmol 1996; 80:962–968.
12. Matoba A. *Mycobacterium chelonae* keratitis. Am J Ophthalmol 1987; 103:595–596.
13. Ambler JS, Meisler DM, Zakov ZN, et al. Endogenous *Mycobacterium chelonae* endophthalmitis. Am J Ophthalmol 1989; 108:338–339.
14. Lowry PW, Jarvis WR, Oberle AD, et al. *Mycobacterium chelonae* causing otitis media in an ear-nose-and throat practice. N Engl J Med 1988; 319:978–982.
15. Austin WK, Lockey MW. *Mycobacterium fortuitum* mastoiditis. Arch Otolaryngol 1976; 102:558–560.
16. Raad II, Vartivarian S, Khan A, Bodey GP. Catheter-related infections caused by the *Mycobacterium fortuitum* complex: 15 cases and review. Rev Infect Dis 1991; 13:1120–1125.
17. Hoy JF, Rolston KVI, Hopper RL, Bodey GP. Mycobacterium fortuitum bacteremia in patients with cancer and long term venous catheter. Am J Med 1987; 83:213–217.
18. Clegg HW, Foster MT, Sanders WE Jr, Baine WB. Infection due to organisms of *Mycobacterium fortuitum* complex after augmentation mammoplasty: clinical and epidemiologic features. J Infect Dis 1983; 147:427–433.
19. Montoliu J, Gatell JM, Ponal J, et al. Disseminated visceral infection with *Mycobacterium fortuitum* in a hemodialysis patient. Am J Nephrol 1985; 5:205–211.
20. Ingram CW, Tanner DC, Durack DT, Kernodle GW Jr, Corey GR. Disseminated infection with rapidly growing mycobacteria. Clin Infect Dis 1993; 16:463–471.
21. Wallace RJ Jr, O'Brien R, Glassroth J, Raleigh J, Dutt A. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. Am Rev Respir Dis 1990; 142:940–953.
22. Heifets LB, Jenkins PA. Speciation of mycobacteria in clinical laboratories. In: Gangadharam PRJ, Jenkins PA, eds. Mycobacteria I: Basic aspects. New York: Chapman & Hall, 1998:308–351.
23. Cynamon MH, Klemens SP. Drug susceptibility tests for *Mycobacterium fortuitum* and *Mycobacterium chelonae*. In: Heifets LB, ed. Drug susceptibility in the chemotherapy of mycobacterial infections. Miami, FL: CRC Press, 1991: 147–160.
24. Woods GL, Washington JA II. Mycobacteria other than *Mycobacterium tuberculosis*: review of microbiologic and clinical aspects. Rev Infect Dis 1987; 9:275–294.
25. 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; 139:107–110.
26. Chetchotisakd P, Mootsikapun P, Anunnatsiri S, et al. 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.
27. Franklin DJ, Starke JR, Brady MT, Brown BA, Wallace RJ Jr. Chronic otitis media after tympanostomy tube placement caused by Mycobacterium abscessus: a new clinical entity? Am J Otol 1994; 15:313–320.
28. Robin JB, Beatty BF, Dunn S, et al. *Mycobacterium chelonei* keratitis after radical keratotomy. Am J Ophthalmol 1986; 102:72–73.
29. Roussel TJ, Stern WH, Goodman DF, Whitcher JP. Postoperative mycobacterial endophthalmitis. Am J Ophthalmol 1989; 107:403–406.
30. Swenson JM, Wallace RJ Jr, Silcox VA, Thornsberry C. Antimicrobial susceptibility of five subgroups of *Mycobacterium fortuitum* and *Mycobacterium chelonae*. Antimicrob Agents Chemother 1985; 28:807–811.
31. Young LS, Berlin OGW, Inderlied CB. Activity of ciprofloxacin and other fluorinated quinolones against mycobacteria. Am J Med 1987; 82(4A):23–26.
32. Wallace RJ Jr, Brown BA, Onyi GO. Susceptibilities of *Mycobacterium fortuitum* biovar *fortuitum* and the two subgroups of *Mycobacterium chelonae* to imipenem, cefmetazole, cefoxitin, and amoxicillin–clavulanic acid. Antimicrob Agents Chemother 1991; 35:773–775.
33. Wallace RJ Jr, Bedsole G, Sumter G, et al. Activities of ciprofloxacin and ofloxacin against rapidly growing mycobacteria with demonstration of acquired resistance following single-drug therapy. Antimicrob Agents Chemother 1990; 34:65–70.
34. Brown BA, Wallace RJ Jr, Onyi GO, DeRosas V, Wallace RJ III. Activities of four macrolides, including clarithromycin, against *Mycobacterium fortuitum*, *Mycobacterium chelonae*, and *M. chelonae*-like organisms. Antimicrob Agents Chemother 1992; 36:180–184.
35. Dalovisio JR, Pankey GA. In vitro susceptibility of *Mycobacterium fortuitum* and *Mycobacterium chelonei* to amikacin. J Infect Dis 1978; 137:318–321.
36. Chittasobhaktra T, Vibhagool A, Prachaktam R. Clinical manifestation and drug susceptibility of rapidly growing mycobacteria. J Infect Dis Antimicrob Agents 1999; 16:109–114.
37. 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; 119:482–486.
38. Tebas P, Sultan F, Wallace RJ Jr, Fraser V. Rapid development of resistance to clarithromycin following monotherapy for disseminated infection in a heart transplant patient. Clin Infect Dis 1995; 20:443–444.