Sixty-three Cases of Mycobacterium marinum Infection
Clinical Features, Treatment, and Antibiotic Susceptibility of Causative Isolates
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Background: Mycobacterium marinum is a nontuberculous mycobacterium responsible for skin infections. Although cases have been seldom reported, no series of M. marinum infection has been recently reported and the treatment is not standardized.

Methods: A national survey was conducted on culture-confirmed M. marinum infections that occurred in France from January 1, 1996, to December 31, 1998. Clinical characteristics and therapeutic data were analyzed, and the minimum inhibitory concentrations of 11 antibiotics were determined against the causative isolates.

Results: Sixty-three cases of M. marinum infection were studied. In 53 (84%) of the patients, inoculation was related to fish tank exposure. The site of infection was mainly the upper limb (in 60 [95%] of the 63 patients), and infection was spread to deeper structures in 18 (29%) of the patients. All patients were treated with antibiotics (median time, 3½ months), and 30 (48%) underwent surgery. Various antibiotic regimens were prescribed, and the initial regimen was modified in 22 (35%) of the patients. Clarithromycin, cyclines, and rifampin were the most commonly prescribed antibiotics. Cure was observed for 55 (87%) of the patients. Failure was related to deep structure involvement (3 of 45 vs 5 of 18 patients; P= .04) but not to any antibiotic regimen. All strains showed the same susceptibility pattern without acquired resistance. The 90% minimum inhibitory concentrations of rifampin and rifabutin were far lower (0.5 and 0.06 µg/mL, respectively) than the 90% minimum inhibitory concentrations of clarithromycin (2 µg/mL) and the cyclines (minocycline, 4 µg/mL; and doxycycline, 8 µg/mL).

Conclusions: Mycobacterium marinum infections are emerging infections related to fish tank hobby. Because of the severity of the cases with spread of infection, clinical awareness of M. marinum infection and its associated risk factors is important so that the diagnosis can be made and therapy can be initiated promptly.

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PATIENTS AND METHODS

PATIENTS

Anonymous standardized forms were sent at the end of 1996 by the NRC to dermatologists, infectious disease specialists, and microbiologists (Azay-Mycobacterium group) of university hospitals all over France. A case patient was defined as a patient with a culture-positive infection with M marinum. All cases diagnosed and treated between January 1, 1996, and December 31, 1998, were reported, and the corresponding strain was sent to the NRC laboratory (Laboratory of Bacteriology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France).

The following information was collected: patient characteristics (sex and age), immune and human immunodeficiency virus status, fish tank and swimming hobbies, injury and contact with fishes, infection history, site and clinical type of the lesions, spread of infection to deeper structures (tendon, joint, or bone), antimicrobial therapy (name of the antibiotic and date of start and discontinuation), surgery, and clinical outcome. Forms were filled in by the clinicians and microbiologists in charge of the patient. Additional data were collected, when needed, by telephone or written correspondence between the NRC and the clinician or microbiologist. An antibiotic regimen was eligible for efficacy evaluation if it had been given for at least 15 days. Outcome was defined as cure when no sign of infection was observed at the end of treatment or significant improvement was noticed at the end of the follow-up, and as failure when no improvement, after effects, or relapse was observed.

STRAINS

The strains of M marinum were grown on Lowenstein-Jensen medium on arrival at the NRC laboratory. They were identified based on the phenotypic characteristics, as previously described, and then stored at -80°C in Youmans broth, supplemented with 20% fetal bovine serum. The minimum inhibitory concentrations (MICs) of 11 antibiotics (rifampin, rifabutin, ethambutol hydrochloride, amikacin, doxycycline, minocycline, clarithromycin, ofloxacin, levofloxacin, ciprofloxacin, and sparfloxacin) were determined by the agar dilution method in Mueller-Hinton agar supplemented with 5% Middlebrook OADC (oleic acid, albumin, dextrose, and catalase [Fisher Scientific International, Elancourt, France]), as previously described.

ANALYSES

Data were computerized and analyzed using computer software (Epi Info 6.1; Centers for Disease Control and Prevention, Atlanta, Ga). When appropriate, differences between categories were analyzed using the χ² test for quantitative values and the t test for qualitative values.

In the laboratory, we determined the in vitro susceptibility of M marinum to antibiotics that were given to the patients to correlate its results to in vivo efficacy.

RESULTS

GENERAL CHARACTERISTICS OF THE PATIENTS

Culture confirmed infection with M marinum was reported for 66 patients from 1996 to 1998 in France. The incidence of M marinum infection in France was, therefore, about 0.04 case per 100,000 inhabitants per year. Three cases were excluded because of insufficient information on patient outcome. The 63 cases included in the study distributed as 10 cases in 1996, 28 in 1997, and 25 in 1998. The patients included 37 males and 26 females, and their median age was 46 years (range, 4-77 years). A total of 31 hospitals, distributed in all areas of France, reported cases. Exposure to a fish tank in a household with indoor or outdoor aquariums was reported for 53 patients (84%), and death of the tank fishes was reported in 15 of the 23 informed cases. Injury or contact with a fish spine or oysters was reported for 5 patients, and swimming pool hobby was reported for 1. The source of infection was unknown for 4 patients. Four patients had the human immunodeficiency virus, including 2 who had the acquired immunodeficiency syndrome.

CLINICAL CHARACTERISTICS

Clinical characteristics by treatment outcome are presented in Table 1. Among the 27 patients with a recorded history of infection, the median time between

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Table 1. Clinical Characteristics of Patients With a Mycobacterium marinum Infection With Regard to the Outcome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Those Cured</th>
<th>Those in Whom Treatment Failed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion site*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>48</td>
<td>42</td>
<td>6</td>
</tr>
<tr>
<td>Arm and forearm</td>
<td>16</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Wrist</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Leg</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Type of skin lesion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nodule</td>
<td>25</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Sporotrichoid</td>
<td>16</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Ulcer</td>
<td>10</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Abscess</td>
<td>9</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Pustule</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Uninformed</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Spread to deeper structures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>18</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>No (adenitis)</td>
<td>45 (10)</td>
<td>42 (9)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Surgical debridement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30</td>
<td>25</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>33</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>55</td>
<td>8</td>
</tr>
</tbody>
</table>

*Some patients have more than 1 lesion site.
inoculation and the appearance of lesions was 16 days (range, 0-292 days). The site of the skin lesions was the upper limb in 60 (95%) of the 63 patients. Only 3 patients had skin lesions on the lower limb: a hospitalized child, an old woman who owns a fish tank but did not do its maintenance herself, and a child who went to a swimming pool. More than 1 skin lesion was observed in 32 (67%) of 48 patients informed about this item. The clinical description of the skin lesions was reported for 61 patients. Nodules were observed in 41 (67%) of the patients, including a sporotrichoid aspect in 16 (39% of the nodules). The other skin lesions were ulcers, abscesses, and pustules. Adenitis was observed in 10 patients. Deep structure infection (tendon, joint, or bone) was reported in addition to skin lesions for 18 patients: tenosynovitis in 15, arthritis in 7, and osteitis in 3 (arthritis being combined with osteitis in 3 patients and with tenosynovitis in 4) (Figure). Deep structure infection was more common in females than in males (11 of 26 females vs 7 of 37 males; \( P = .04 \)) but was not related with other characteristics.

A histologic examination was done in 51 (81%) of the 63 patients. Pathologic typical findings of mycobacterial infection were reported for 29 (81%) of the 36 written results that were transmitted.

**TREATMENT**

All 63 patients received antibiotics. The median duration of antibiotic therapy was 3½ months (range, 1-25 months). The duration was significantly longer for patients with deeper structure infections than for patients with infections limited to the skin and soft tissue (median duration, 7½ vs 4 months; \( P = .004 \)).

One single antibiotic regimen was prescribed for 41 patients, 2 successive regimens were prescribed for 15 patients, and 3 successive regimens were prescribed for 7 patients. The number of successive regimens was not related to general or clinical characteristics (data not shown).

A total of 132 antibiotic prescriptions were given to the 63 patients, ie, a mean of 2 antibiotic prescriptions per patient. The most frequently prescribed antibiotics were clarithromycin, cyclines, including minocycline and doxycycline, rifampin, and ethambutol. All patients received at least 1 of these antibiotics. The antibiotics administered and the number of their courses are listed in Table 2 by treatment outcome and the severity of the infection (spread to deeper structures).

Antibiotic therapy was given as a monotherapy in 23 patients (37%) and as a combination of at least 2 drugs in 40 patients (63%). Antibiotics prescribed as a monotherapy were cyclines for 19 patients (minocycline for 14 and doxycycline for 5) and clarithromycin for 4 patients. Monotherapy was significantly associated with infection limited to skin and soft tissue (20 of 45 vs 3 of 18 patients; \( P = .04 \)). Frequent drug combinations were clarithromycin plus rifampin (\( n = 20 \)), cyclines plus clarithromycin (\( n = 11 \) \( n = 4 \) with doxycycline and \( n = 7 \) with minocycline), rifampin plus ethambutol (\( n = 8 \)), and cyclines plus rifampin (\( n = 6 \) \( n = 3 \) with doxycycline and \( n = 3 \) with minocycline).

Cyclines were prescribed more for infection limited to skin and soft tissue than for infection spread to deeper structures. In contrast, rifamycins (rifampin and rifabutin) and ethambutol were prescribed more for infection spread to deeper structures than infection limited to skin and soft tissue; clarithromycin was equally prescribed in both cases (Table 2).

In addition to antibiotics, 30 patients underwent surgery for excision or debridement, including 17 with infection limited to skin and soft tissue and 13 with infection spread to deeper structures. Conversely, no surgery was performed for 5 patients with deep structure infection (2 with arthritis, 1 with tenosynovitis, 1 with tenosynovitis and arthritis, and 1 with osteitis, tenosynovitis, and arthritis) and for 28 with infection limited to the skin and soft tissue. Surgery was indeed associated with deep structure infection (13 of 18 vs 17 of 45 patients; \( P = .01 \)) but not with other characteristics (sex, age, aspect and site of the lesion, and outcome).

**OUTCOME**

The outcome was evaluated for the 63 patients: 55 (87%) were cured and 8 (13%) experienced treatment failure. The patients in whom treatment failed are described in Table 3. Failure was significantly related to infection spread to deeper structures (3 of 45 vs 5 of 18 patients; \( P = .04 \)) and to the skin lesion aspect of the ulcer (4 of 6 vs 4 of 49 patients; \( P = .02 \)). Infections in human immunodeficiency virus–positive patients (\( n = 4 \)) were not different from those in human immunodeficiency virus–negative patients with regard to the source of infection, clinical characteristics, and outcome.

The efficacy of antibiotic therapy was evaluated by the number of failures according to the number of prescriptions and the severity of the infection (spread to deeper structures). Failure was not related to the prescription of one specific antibiotic or regimen or to the duration of the treatment (median, 6 vs 5 months; \( P = .13 \)).

For infections limited to skin and soft tissue, cure was observed in 42 (93%) of 45 patients, including 20 undergoing monotherapy (16 received cyclines and 4 received clarithromycin). The 3 patients in whom treat-
For infections spread to deeper structures, treatment with a combination of 2 antibiotics, among cyclines, clarithromycin, and rifampin, resulted in cure of most (13 of 18 patients). However, 4 of the 5 patients in whom treatment failed (patients 4, 5, 6 and 8, detailed in Table 3) were also treated with a combination of clarithromycin with rifampin, rifabutin, or cyclines for a minimum of 2 months. Of these 4 patients, 3 had received corticosteroids before the diagnosis. Unfortunately, because we did not record the information on corticosteroid therapy for all the patients, we could not evaluate it as a risk factor.

The MICs were determined for the 11 antibiotics that were given to the patients (rifampin, rifabutin, ethambutol, amikacin, doxycycline, minocycline, clarithromycin, and fluoroquinolones [including ofloxacin, levofloxacin, ciprofloxacin, and sparfloxacin]) against all the strains isolated from the 63 patients but 2 (because of insufficient growth). For each antibiotic, the MICs were distributed in a narrow range, and the modal MIC was close to the 50% MIC and to the geometric mean MIC (Table 4). The MICs of rifampin and rifabutin were lower than the MICs of the other antibiotics (90% MIC of 0.5 and 0.06 µg/mL, respectively). The MICs of the cyclines, clarithromycin,

### Table 2. Antibiotic Courses Given to Patients With a *Mycobacterium marinum* Infection With Regard to the Spread of Infection and the Outcome*

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Total Courses</th>
<th>SSTIs</th>
<th>DSIs</th>
<th>Total Failures</th>
<th>Total Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin</td>
<td>39</td>
<td>24</td>
<td>2</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Minocycline</td>
<td>24</td>
<td>20</td>
<td>2</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>11</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rifampin</td>
<td>21</td>
<td>11</td>
<td>1</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ethambutol hydrochloride</td>
<td>13</td>
<td>5</td>
<td>1</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Sparfloxacin</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Amikacin</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pristinamycin</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Amoxicillin plus clavulanate potassium</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sulfamethoxazole plus trimethoprim</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*One antibiotic course is defined as at least 15 days of therapy. SSTI indicates infection limited to skin and soft tissue; and DSI, infection spread to deeper structures.

### Table 3. Characteristics of Patients With *Mycobacterium marinum* Infection in Whom Treatment Failed*

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Exposure</th>
<th>Type of Skin Lesion</th>
<th>Site</th>
<th>DSI</th>
<th>Antibiotic (MIC)</th>
<th>Duration</th>
<th>Surgery</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/47</td>
<td>Fish tank</td>
<td>Sporotrichoid</td>
<td>Hand</td>
<td>No</td>
<td>Clarithromycin (0.5) and minocycline (0.5)</td>
<td>8 mo</td>
<td>Yes</td>
<td>No improvement</td>
</tr>
<tr>
<td>2/M/49</td>
<td>Fish tank</td>
<td>Ulcer</td>
<td>Hand</td>
<td>No</td>
<td>Ofloxacin (4) and sulfamethoxazole and trimethoprim (16)</td>
<td>15 d</td>
<td>Yes</td>
<td>Relapse</td>
</tr>
<tr>
<td>3/M/40</td>
<td>Fish tank</td>
<td>Papule</td>
<td>Arm</td>
<td>No</td>
<td>Rifampin (0.25) and ethambutol hydrochloride (2) and minocycline (0.25)</td>
<td>5 mo</td>
<td>No</td>
<td>Relapse</td>
</tr>
<tr>
<td>4/M/47</td>
<td>Fish tank</td>
<td>Nodule</td>
<td>Hand</td>
<td>Yes</td>
<td>Clarithromycin (1) and rifampin (0.5) and ethambutol (2), and clarithromycin (0.25)</td>
<td>6 mo</td>
<td>Yes</td>
<td>Relapse</td>
</tr>
<tr>
<td>5/F/39</td>
<td>Oyster contact</td>
<td>Ulcer</td>
<td>Hand</td>
<td>Yes</td>
<td>Rifampin (0.06), ethambutol (2), and clarithromycin (0.5)</td>
<td>2 mo</td>
<td>Yes</td>
<td>Aftereffects</td>
</tr>
<tr>
<td>6/F/49</td>
<td>Fish contact</td>
<td>Abscess</td>
<td>Hand</td>
<td>Yes</td>
<td>Rifampin (0.06) and ethambutol (2) and ethambutol (1), clarithromycin (0.5), rifampin (0.25), and ciprofloxacin (1)</td>
<td>2 mo</td>
<td>Yes</td>
<td>Aftereffects</td>
</tr>
<tr>
<td>7/F/57</td>
<td>Fish tank</td>
<td>Ulcer</td>
<td>Arm</td>
<td>Yes</td>
<td>Clarithromycin (4) and ciprofloxacin (8) and isoniazid (ND), rifampin (0.5), ethambutol (4), and pyrazinamide (ND)</td>
<td>1 mo</td>
<td>No</td>
<td>No improvement</td>
</tr>
<tr>
<td>8/F/24</td>
<td>Unknown</td>
<td>Ulcer</td>
<td>Leg</td>
<td>Yes</td>
<td>Rifabutin (0.015), ciprofloxacin (4), and clarithromycin (0.5)</td>
<td>15 d</td>
<td>No</td>
<td>No improvement</td>
</tr>
</tbody>
</table>

*DSI indicates infection spread to deeper structures; MIC, minimum inhibitory concentration in micrograms per milliliter; and ND, not determined.

**ANTIBIOTIC MICS**

The MICs were determined for the 11 antibiotics that were given to the patients (rifampin, rifabutin, ethambutol, amikacin, doxycycline, minocycline, clarithromycin, and fluoroquinolones [including ofloxacin, levofloxacin, ciprofloxacin, and sparfloxacin]) against all the strains isolated from the 63 patients but 2 (because of insufficient growth). For each antibiotic, the MICs were distributed in a narrow range, and the modal MIC was close to the 50% MIC and to the geometric mean MIC (Table 4). The MICs of rifampin and rifabutin were lower than the MICs of the other antibiotics (90% MIC of 0.5 and 0.06 µg/mL, respectively). The MICs of the cyclines, clarithromycin,
amikacin, and ethambutol were moderate values close to 4 µg/mL. Among the fluoroquinolones, the MICs of sparfloxacin were 2- to 4-fold lower than the MICs of ciprofloxacin, levofloxacin, and ofloxacin.

There was no difference between the geometric mean MICs for strains isolated from patients who were cured and the geometric mean MICs for strains isolated from patients in whom treatment had failed (data not shown). Acquired resistance to an antibiotic was not observed in strains isolated from either cured patients or patients in whom treatment had failed.

**COMMENT**

We reported 63 cases of culture-confirmed *M. marinum* infection during a 3-year period. It is, to our knowledge, the largest series reported in the literature. Infection was more frequent in males than in females. This might be explained by the prescription of corticosteroids before the diagnosis, which is common in the case of female rheumatic disease and might have facilitated the spread of infection.

We reported 63 cases of culture-confirmed *M. marinum* infection during a 3-year period. It is, to our knowledge, the largest series reported in the literature. Infection was more frequent in males than in females. This might be explained by the prescription of corticosteroids before the diagnosis, which is common in the case of female rheumatic disease and might have facilitated the spread of infection.

**Table 4. Minimum Inhibitory Concentrations of 11 Antibiotics Against 61 Strains of *Mycobacterium marinum***

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>50%</th>
<th>90%</th>
<th>Modal</th>
<th>Geometric Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
<td>0.25</td>
<td>0.5</td>
<td>0.125</td>
<td>0.22 ± 0.09</td>
<td>0.125-4</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06 ± 1.50</td>
<td>0.015-0.25</td>
</tr>
<tr>
<td>Ethambutol hydrochloride</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1.8 ± 1.5</td>
<td>1-4</td>
</tr>
<tr>
<td>Amikacin</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2.1 ± 1.9</td>
<td>1-8</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>4</td>
<td>8</td>
<td>8</td>
<td>4.0 ± 2.3</td>
<td>0.125-16</td>
</tr>
<tr>
<td>Minocycline</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2.1 ± 1.8</td>
<td>0.5-8</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>0.5</td>
<td>2</td>
<td>0.5</td>
<td>0.8 ± 2.6</td>
<td>0.25-4</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>4</td>
<td>16</td>
<td>4</td>
<td>5.4 ± 2.1</td>
<td>2-32</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>4</td>
<td>8</td>
<td>4</td>
<td>3.7 ± 1.8</td>
<td>2-32</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>3.1 ± 1.7</td>
<td>1-16</td>
</tr>
<tr>
<td>Sparfloxacin</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>1.0 ± 1.9</td>
<td>0.5-4</td>
</tr>
</tbody>
</table>

* Determined by the agar dilution method in Mueller-Hinton agar supplemented with 5% Middlebrook OADC (oleic acid, albumin, dextrose, and catalase).
has a natural multidrug resistance pattern, as suggested by the in vitro susceptibility results of this study, which showed that *M. marinum* has a natural multidrug resistance pattern, consistent with the literature review.3,12-30

No treatment failure was related to a strain of *M. marinum* with acquired resistance to any antibiotic. Acquired resistance has been described in patients with mycobacterial infections only for drugs with a potent activity, such as streptomycin sulfate in patients with tuberculosis31 or clarithromycin in patients with *Mycobacterium avium* infection.32 Acquired resistance has not been described for *M. marinum* yet. This might indicate that none of the antibiotics given has a potent activity against *M. marinum*. This is confirmed by the in vitro susceptibility results of this study, which showed that *M. marinum* has a natural multidrug resistance pattern, as suggested by the results of other studies.12,13,31

Rifamycins, rifampin, and rifabutin are the only antibiotics that have low MICs and MICs close to those found for *Mycobacterium tuberculosis*. However, this was not fully correlated with the in vivo efficacy because 5 patients (who underwent a total of 5 courses of rifampin and 2 of rifabutin) in whom treatment failed had received rifamycins with a long duration of therapy (9, 7, 6, 4, and 4 months). The MICs of minocycline, doxycycline, clarithromycin, and amikacin were moderate values close to those reported for other atypical mycobacteria. Comparable values of MICs were observed for clarithromycin and amikacin against *M. avium* and for cyclines and amikacin against rapidly growing mycobacteria.12-35,33,34,35 which have been correlated with in vivo efficacy.32,30 Only 2 treatment failures were observed with cyclines, but most of the patients treated by cyclines, and especially by cyclines alone, had received rifamycins limited to the skin and soft tissue. The MICs of ethambutol, ciprofloxacin, ofloxacin, and levofloxacin were far above the concentration break points and, consequently, in vivo efficacy was less probable. Failure was indeed observed in half of the patients treated with these antibiotics. The activity of the new fluoroquinolone, sparfloxacin (even its MICs were lower than those of the classic fluoroquinolones), has still to be demonstrated; in our study, 3 patients were treated with sparfloxacin, and treatment failed in 1.

Surgery seemed frequently inadequate to Chow et al.27 In our study, surgery was consistently done for most of the infections spread to deeper structures, except for the patients in whom treatment failed. In these latter patients, the duration of treatment was too short.

To draw recommendations for a standardized treatment, we sought to evaluate the outcome by antibiotic regimens. Fifty-five (87%) of the patients were cured after therapy that included clarithromycin, rifampin, or cyclines. However, patients in whom treatment failed were observed among those treated with the same antibiotics. Consequently, a favorable treatment outcome could not be related to any specific antibiotic, consistent with the literature review.3,12-30

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REFERENCES


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3. Swift S, Cohen H. Granulomas of the skin due to *Mycobacterium balnei* after abra-
synovitis produced by *Mycobacterium marinum* in a fisherman. *J Clin Mi-
5. Harth M, Ralph E, Farawi R. Septic arthritis due to *Mycobacterium marinum.*
911.
7. Parent LJ, Saito MM, Appelbaum PC, Dossett JH. Disseminated *Mycobacter-
um marinum* infection and bacteremia in a child with severe combined immu-
8. Saubolle M. Nontuberculous mycobacteria as agents in human disease in the
10. Saito H, Tomioka H, Sato K, Dekio S. In vitro and in vivo antmycobacterial ac-
2877-2882.
11. Wallace R, Wiss K. Susceptibility of *Mycobacterium marinum* to cyclines and
12. Bernoch P, Ems-RK, Saubolle MA, Wallace RJ. Laboratory diagnosis of the my-
American Society for Microbiology; 1994:1-36.
13. Aubry A, Jarlier V, Escalona S, Truffot-Perrin C, Cambau E. Antibiotic suscep-
44:3313-3318.
14. Ang P, Rattana-Apimayakij N, Goh CL. Retrospective study of *Mycobacter-
15. Casal M, Casal MM. Multicenter study of incidence of *Mycobacterium marinum*
16. Dobos KM, Quinn FD, Ashford DA, Horsburgh CR, King CH. Emergence of a unique
17. Jernigan JA, Farr BM. Incubation period and sources of exposure for cutaneous
*Mycobacterium marinum* infection: case report and review of the literature. *Clin
18. Bonafé J, Grigorieff-Larrue N, Bauriaud R. Les mycobactérioses cutanées atyp-
iques: résultats d’une enquête nationale. *Ann Dermatol Venereol.* 1992;119:463-
470.
19. Gombert M, Goldstein E, Corrado M, Stein A, Butt K. Disseminated *Mycobacte-
rium marinum* infection after renal transplantation. *Ann Intern Med.* 1981;94:
486-487.
20. Zukeran P, Canillet S, Gayraud L. Infection sporotrichoı¨de à *Mycobacterium mari-
num* chez un sujet porteur du virus de l’immunodéficience humaine (VIH). *Ann
des mycobactéries atypiques dans l’eau d’une piscine. *Rev Epidemiol Sante Pub-
22. Hamner D, Pittik S, Block C, Kaufman L, Amit S, Rosenfeld J. *Mycobacterium mari-
19:539-543.
*Mycobacterium marinum* infection in a patient with systemic lupus erythema-
26. Black MM, Ekyon SJ. The successful treatment of tropical fish tank granuloma
(*Mycobacterium marinum*) with co-trimoxazole. *Br J Dermatol.* 1977;97:689-
692.
and wrist: results of conservative treatment in twenty-four cases. *J Bone Joint
28. Iijima S, Saito J, Otaka F. *Mycobacterium marinum* skin infection successfully
29. Kazin SH, Bishop AT. Atypical *Mycobacterium* infections of the upper extremity.
30. Donat ST, Smith PW, Levitz RE, Quintiliani R. Therapy of *Mycobacterium mari-
um* infections: use of cyclines vs rifampin. *Arch Intern Med.* 1986;146:902-
904.
769-785.
*Mycobacterium avium* infection in patients with acquired immune deficiency syn-
33. Sanders W, Wolinsky E. In vitro susceptibility of *Mycobacterium marinum* to eight
chemical patterns of the unnamed third biovariant complex of *Mycobacter-
35. Watt B, Rayner A, Harris G. Comparative activity of azithromycin against clinical
cutaneous (disseminated) infection due to *Mycobacterium chelonae*. *Ann Intern