Short Communication

*Mycobacterium marinum* Tenosynovitis: Three Case Reports and Review of the Literature

Hung-Chin Tsai1,2,4, Susan Shin-Jung Lee1, Shue-Ren Wann1, Yao-Shen Chen1, Yu-Wen Liu2 and Yung-Ching Liu1,4*

1Section of Infectious Diseases, Department of Medicine, Kaohsiung Veterans General Hospital; 2Graduate Institute of Medicine and 3College of Medicine, Kaohsiung Medical University, Kaohsiung; and 4National Yang-Ming University, Taipei, Taiwan, Republic of China

(Received May 1, 2006. Accepted July 24, 2006)

SUMMARY: *Mycobacterium marinum* is one of the nontuberculosis mycobacteria responsible for skin infections. There have been very few case series of *M. marinum* infections reported in the English literature. Herein, we describe three patients with *M. marinum* tenosynovitis. All patients had positive cultures and were exposed to pricking by a fishbone. The incubation period ranged from 7 to 60 days. Key elements in the diagnosis of this infection were a high index of suspicion raised by negative bacterial tissue cultures, poor response to conventional antibiotics treatment, a history of exposure to tropical fish and tissue biopsy for culture and histology. The treatment is essentially antimicrobial therapy supplemented by an appropriate surgical debridement, especially when deep structures are involved.

*Mycobacterium marinum* is a well-known cause of cutaneous infection manifested by skin ulcers and nodular lymphangitis. It can spread to deeper structures, resulting in tenosynovitis, arthritis and osteomyelitis (1,2). It was first described as swimming-pool granuloma (3) and is often acquired from aquarium maintenance and hence called fish tank granuloma (4). *M. marinum* causes disease in many fish species from cold or warm, fresh or saltwater, and human infection follows contact with affected fish or contaminated water (5). The diagnosis of *M. marinum* is often delayed due to lack of clinical suspicion, which would lead to the special diagnostic procedures required to accurately identify and diagnose this seemingly uncommon entity (6). We present our experience with 3 cases of tenosynovitis due to *M. marinum* and review other recent studies on treatment of the disease, to provide recommendations for current management of infections due to *M. marinum*.

The first patient was a 53-year-old, immunocompetent, male resident of southern Taiwan, who worked as a vendor of ice for years. He had no history of medical illness and also had no risk factors for HIV infection. In April 2004, the patient developed swelling, tenderness and erythematous lesions with exudation on the palmar side of his left hand. He sought medical attention for the lesion, and over the ensuing 4 weeks, several courses of antibiotics were prescribed at a regional medical attention for the lesion, and over the ensuing 4 weeks, with exudation on the palmar side of his left hand. He sought medical attention for the lesion, and over the ensuing 4 weeks, several courses of antibiotics were ineffective. The lesions on his palm gradually deteriorated, with ulcerations and discharge, and extended to the palmar side of the hand and fingers. The patient was referred by his general practitioner in January 2005 with a complaint of left wrist swelling for 1 week. This had started as an edematous change in the wrist joint which spread into the second and third fingers and dorsum of the hand. There was no history of trauma or foreign body present in the hand.

On examination, there was redness and swelling of the wrist, extending to the dorsum of the hand and fingers. The function of the hand and wrist was limited. Plasma sugar was 190 mg/dl. Tenosynovectomy was performed, and the histopathology disclosed infiltrations of acute and chronic inflammatory cells with formation of granulation tissue and fibrinous exudates. Acid-fast bacilli were identified. *M. marinum* was identified as the causative pathogen by mycobacterial culture, polymerase chain reaction (PCR) for 65 kD heat shock protein gene and HanlIII, BsuI restriction enzyme digestion. The patient was initially treated with antituberculous drugs, and the regimen was changed to rifampin, ethambutol and clarithromycin after diagnosis. Gradual improvement occurred, but therapy continued for 7 months before the lesion healed completely.

The second patient was a 59-year-old man with a history of diabetes mellitus for 5 years, controlled with metformin. He was referred by his general practitioner in January 2005 with a complaint of left wrist swelling for 1 week. This had started as an edematous change in the wrist joint which spread into the second and third fingers and dorsum of the hand. There was no history of trauma or foreign body present in the hand.

On examination, there was redness and swelling of the wrist, extending to the dorsum of the hand and fingers. The function of the hand and wrist was limited. Plasma sugar was 190 mg/dl. Tenosynovectomy was performed, and the histopathology examination revealed chronic granulomatous inflammation with caseous necrosis and Langhans cells. A Ziehl-Neelsen stain for acid-fast bacilli was positive. Routine bacterial cultures were negative, and *M. marinum* was isolated from mycobacterial cultures after 6 weeks’ incubation. The patient was a fishmonger and admitted to being frequently pricked by fishbones, since he handled the fish bare-handed.

A combination of isoniazid, rifampicin, pyrazinamide and ethambutol was started postoperatively and was continued for 6 months despite the mycobacterial culture results. The lesions improved significantly. The patient remained under observation in the outpatient department during the 6-month period.

The third patient was a 58-year-old man who was admitted via the emergency department in January 2005 with an infection of the right 4th finger. He was pricked by a fishbone...
spine 2 months previously while preparing fish in the kitchen. The infection had been treated with cefazolin followed by ampicillin/sulbactam for 3 weeks, but the response was poor. On examination, the right 4th finger was inflamed and swollen with painful ulcers over the proximal portion of his finger. Tenosynovectomy was performed, and the pathological examination showed chronic synovitis. No acid-fast bacilli were identified, and routine bacterial cultures were negative. 

\textit{M. marinum} was isolated from the 7H11 culture plate at 30°C after 4 weeks' incubation. The species identification was made by PCR for 65 kD heat shock protein gene and restriction enzyme analysis. The patient was treated initially with a combination of four tuberculosis agents. After 2 months of therapy, a second synovectomy was performed due to incomplete clinical response. Histological examination of the tissue showed the presence of granulomas with caseous necrosis and many Langhans cells. Acid-fast bacilli were present. The same treatment regimen was continued for 5 months, and the lesion slowly improved. The patient remains under observation in the outpatient department.

Tenosynovitis is defined as an inflammation of a tendon sheath (7). Acute flexor tenosynovitis due to \textit{Staphylococcus aureus} is the most common tendon sheath infection, usually secondary to penetrating injury (8). Chronic tenosynovitis caused by \textit{M. marinum} infections is relatively rare and is often a cause of extensive, localized soft-tissue infection (1). There are only sporadic reports of this disease in the literature. All the cases reported illustrate the difficulty in diagnosis, resulting in delay of treatment (9-11). In our experience, treatment is often delayed and the most efficacious method of curing these infections remains controversial. We review the current literature with the aim of describing the clinical manifestations, pathological findings and therapeutic management of mycobacterial soft tissue infection caused by \textit{M. marinum}.

Using the MEDLINE database with key words “\textit{Mycobacterium marinum}” and a bibliographic review of relevant clinical articles, we searched the literature for reports referring to \textit{M. marinum} infection between 2000 and 2005. A total of 166 patients were reviewed (including the 3 patients in our series) (Table 1). Seventy percent (117/166) occurred in men. Their age ranged from 4 to 85 years old (mean 47 years old). The incubation period ranged from a few hours to 8 years (mean 6.8 months). The presumed sources of exposure for 70% of the infections reported were related to aquarium handling, fish or shellfish injuries, saltwater or brackish water contamination or swimming pool-associated injuries. A histological examination was done in 135 (81%) of the 166 patients. Granulomatous inflammation, a typical finding of mycobacterial infection, was reported for 102 (76%) of the 135 specimens examined. However, only 31% of the specimens examined showed the presence of acid-fast bacilli. This corresponded to the low detection rate of acid-fast bacilli reported in other studies (9%, 13.2%) (3,19). All 166 patients received antibiotics. The duration of antibiotic therapy ranged from 1 to 14 months. The outcome was a cure or improvement at the end of the follow-up in 85% (141/166) of the patients. Treatment failure occurred in 10% (12/115).

The correct diagnosis of cutaneous \textit{M. marinum} infection can be difficult for the clinician and is commonly delayed, because the presentation is often insidious and nonspecific, and key historical information may not be obtained. The mean duration of symptoms before correct diagnosis in our review was 6.8 months. This is of clinical importance since untreated \textit{M. marinum} infections can result in significant morbidity, including extension to cause tenosynovitis and loss of joint mobility due to osteomyelitis, and can even result in amputation of the affected extremity (22,20-21). Clinical clues in the patient’s history (skin injuries associated with fish, aquariums, swimming pools or natural bodies of freshwater or saltwater) and poor response to conventional antibiotics treatment are the most important clues to \textit{M. marinum} infections, and nothing these clues can expedite diagnosis and therapy in cases presenting with cutaneous infections.

Optimal treatment for \textit{M. marinum} infection has not yet been established. The infection probably resolves spontaneously in some cases, although complete resolution may take up to 2 years (1). In the study of Chow et al. (20), antibiotic therapy alone was enough to cure most patients, and additional surgical debridement cured the remaining cases. In our study, all patients were treated with antibiotics. At present, no study has compared different antibiotic regimens due to the small number of cases and the difficulty and delay in making a correct diagnosis (1). In the literature, various antibiotic combinations have been described, including cyclines, sulfamethoxazole/trimethoprim, rifampin, ethambutol, clarithromycin, levofloxacin and amikacin (1,3,22,23). The optimal duration of treatment varied from 6 weeks to 18 months (1). In our study, the duration of treatment ranged from 5 to 7 months. This duration was considered short for treatment of infections extending to deeper skin structures; however, all patients had a favorable outcome.

There are a few didactic points that are worth mentioning in our three cases. First, all of the pathologic specimens examined in our patients showed the presence of acid-fast bacilli in contrast to the low detection rate reported in the literature. Second, all three cases were treated successfully with regimens that included rifampin and ethambutol. Atypical mycobacterial infection is not routinely identified to the species level in Taiwan. The incidence of \textit{M. marinum} may be underestimated because some patients may be diagnosed as having tuberculosis based on the presence of acid-fast bacilli. The most common incorrect diagnoses reported in the literature include sporotrichosis, gout, rheumatoid arthritis, foreign reactions and epithelioid sarcoma (9,23). Third, the duration of symptoms before correct diagnosis was relatively short (7-60 days) in our patients. This is primarily due to the high clinical suspicion raised by a history of fish bone injury. Rapid diagnosis with PCR for 65 kD heat shock protein and restriction enzyme analysis shortens the duration to reach a correct diagnosis.

Physicians should be aware that the history from exposure to development of cutaneous \textit{M. marinum} infection can be very long. Accurate diagnosis cannot be made if patients were not questioned about potential exposures before the onset of symptoms. Those patients who had atypical cutaneous infections with poor treatment response to conventional antibacterial antibiotics should be questioned about skin injuries associated with aquariums, fish, shellfish, saltwater or brackish water, swimming pools or natural bodies of freshwater that may have occurred recently or many months before the onset of symptoms. Such questions may identify exposures that would otherwise be overlooked and might therefore prevent unnecessary complications by expediting diagnosis and appropriate therapy.
REFERENCES


<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Male/ Female</th>
<th>Age range (mean)</th>
<th>Duration of disease before presentation (mean)</th>
<th>Exposure1 (%)</th>
<th>Pathology</th>
<th>Duration of treatment (mean)</th>
<th>Outcome2</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ang et al.</td>
<td>38</td>
<td>30/8</td>
<td>14 - 85 (44.7)</td>
<td>1 - 132 mo (19)</td>
<td>17/38 (45)</td>
<td>Granulomatous inflammation (100%), Acid-fast bacilli positive 5/38 (13.2%), Mycobacterial culture 1/35 (2.9%)</td>
<td>4 - 38 wk (14.9)</td>
<td>Improvement 26/38 (68.4%), Failure 2/38 (5.3%), Loss of follow-up 10/38 (26.3%)</td>
<td>(12)</td>
</tr>
<tr>
<td>Bhatt et al.</td>
<td>3</td>
<td>2/1</td>
<td>23 - 84 (52.3)</td>
<td>0.75 - 6 mo (2.9)</td>
<td>2/3 (67)</td>
<td>Granulatation tissue (1), Granulomatous (1), Acute on chronic inflammation (1)</td>
<td>6 - 36 wk (16.6)</td>
<td>Improvement 1/3 (33%), Cure 2/3 (67%)</td>
<td>(9)</td>
</tr>
<tr>
<td>Timothy et al.</td>
<td>1</td>
<td>M 49</td>
<td>5 mo</td>
<td>1 (100)</td>
<td>NA</td>
<td>Granulomatous inflammation 10/10 (100%), Acid-fast bacilli positive 9/14 (64%)</td>
<td>≤3 mo</td>
<td>Improvement 1/3 (33%), Cure 2/3 (67%)</td>
<td>(13)</td>
</tr>
<tr>
<td>Wu et al.</td>
<td>14</td>
<td>8/6</td>
<td>9 - 72 (49)</td>
<td>2 mo</td>
<td>7/14 (50)</td>
<td>Granulomatous inflammation 10/10 (100%), Acid-fast bacilli positive 9/14 (64%)</td>
<td>≤3 mo</td>
<td>Improvement 1/3 (33%), Cure 2/3 (67%)</td>
<td>(14)</td>
</tr>
<tr>
<td>Rajadhyaksha et al.</td>
<td>1</td>
<td>M 59</td>
<td>3 mo</td>
<td>none</td>
<td>Chronic inflammation</td>
<td>≤6 wk</td>
<td>Improvement</td>
<td>(15)</td>
<td></td>
</tr>
<tr>
<td>Enzensberger et al.</td>
<td>1</td>
<td>F 60</td>
<td>8 mo</td>
<td>1 (100)</td>
<td>Non-caseous granuloma, Acid-fast bacilli positive</td>
<td>long-term ≤4 mo</td>
<td>Improvement</td>
<td>(10)</td>
<td></td>
</tr>
<tr>
<td>Aubry et al.</td>
<td>63</td>
<td>37/26</td>
<td>4 - 77 (46)</td>
<td>16 days (range 0-292 days)</td>
<td>53/63 (84)</td>
<td>Granulomatous inflammation 29/36 (81%)</td>
<td>3.5 mo (median)</td>
<td>Cure 55/63 (87%), Failure 8/63 (13%)</td>
<td>(1)</td>
</tr>
<tr>
<td>Hess et al.</td>
<td>29</td>
<td>26/3</td>
<td>28 - 70 (50)</td>
<td>5.2 mo</td>
<td>20/29 (69)</td>
<td>Granuloma 36%, Acid-fast bacilli positive 22%</td>
<td>6 mo (4-12)</td>
<td>Cure (100%)</td>
<td>(16)</td>
</tr>
<tr>
<td>Lim et al.</td>
<td>1</td>
<td>M 34</td>
<td>3 mo</td>
<td>1 (100)</td>
<td>Granulomatous inflammation, Acid-fast bacilli positive</td>
<td>8 wk</td>
<td>Cure</td>
<td>(17)</td>
<td></td>
</tr>
<tr>
<td>Lewis et al.</td>
<td>8</td>
<td>4/4</td>
<td>25 - 59 (45)</td>
<td>NA</td>
<td>Granuloma 6/8 (75%), Acid-fast bacilli positive 3/8 (37.5%)</td>
<td>2 - 14 mo</td>
<td>Cure (100%)</td>
<td>(5)</td>
<td></td>
</tr>
<tr>
<td>Thariat et al.</td>
<td>1</td>
<td>M 22</td>
<td>2 wk</td>
<td>1 (100)</td>
<td>Tuberculoid granulomatous caseous necrosis</td>
<td>4 mo</td>
<td>Cure</td>
<td>(18)</td>
<td></td>
</tr>
<tr>
<td>Wongworawat et al.</td>
<td>1</td>
<td>M 30</td>
<td>8 yr</td>
<td>1 (100)</td>
<td>Non caseous granulomatous inflammation, Acid-fast bacilli positive</td>
<td>6 mo</td>
<td>Cure</td>
<td>(2)</td>
<td></td>
</tr>
<tr>
<td>Amrami et al.</td>
<td>2</td>
<td>2/0</td>
<td>42, 61</td>
<td>6 - 12 mo</td>
<td>2 (100)</td>
<td>Non caseous granuloma 1/2 (50%)</td>
<td>3 mo, NA</td>
<td>Improvement 1/2 (50%), Cure 1/2 (50%)</td>
<td>(11)</td>
</tr>
<tr>
<td>Present study</td>
<td>3</td>
<td>3/0</td>
<td>53 - 59 (57)</td>
<td>7 - 60 days</td>
<td>Granulomatous inflammation 100%, Acid-fast bacilli positive 100%, Mycobacterial culture 100%</td>
<td>5 - 7 mo (6)</td>
<td>Cure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1): Exposure history include exposure to a fish tank in a house-hold with indoor or outdoor aquariums, death of the tank fishes, injury or contact with a fish spine or oysters and swimming pool hobby.
2): Outcome was defined as cure when signs of infection were absent at the end of treatment. Improvement was defined as absence of observable signs of infection at the end of the follow-up. Failure was considered when no improvement occurs, or relapse occurred after initial improvement.

NA, not available.

REFERENCES