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Osteomyelitis and Synovitis Produced by *Mycobacterium marinum* in a Fisherman

RICHARD B. CLARK,[1]* HARVEY SPECTOR,[1] DONALD M. FRIEDMAN,[2] KIMBERLY J. OLDRATI,[1] CHRISTINE L. YOUNG,[1] AND STEPHEN C. NELSON[3]

Departments of Pathology,[1] Rheumatology,[2] and Infectious Diseases,[3] Crozer-Chester Medical Center, Upland, Pennsylvania 19013

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We report a case of osteomyelitis and synovitis produced by *Mycobacterium marinum* in the left index finger of a fisherman. A combination of surgical intervention and antimicrobial therapy with minocycline, rifampin, and ethambutol was efficacious.

Mycobacterium marinum has long been recognized as a cause of swimming pool or fish tank granulomata. Most cases are observed after an individual has received minor trauma in association with contaminated fresh or salt water (4).

Most *M. marinum* infections do not invade beyond the superficial cooler regions of the skin since the organism grows well at 30 to 32°C but usually not at 37°C (15). In recent years, however, the organism has been shown to produce more deeply invasive infections of the tendon sheaths, joints, and even bones (3, 10). Most of these infections have involved the hands and fingers. Possibly, the internal core temperature in body regions such as the hands and fingers is significantly lower than 37°C in some individuals, allowing growth of *M. marinum* in vivo. The resultant *M. marinum* infection may permanently limit the motion range of the affected appendage or even require the amputation of a finger to cure progression (3, 10).

Case report. The patient was a 56-year-old male who presented with an index finger swollen for at least 1 year. The finger was moderately painful to the touch and had a limited range of motion. The patient was known to be an avid fisherman in the Chesapeake Bay but upon close questioning was unable to remember any previous trauma to his left index finger. On an outpatient basis, two injections of corticosteroids were administered to his left index finger, at 2 months and 1 month before presentation. Fluid removed for cultural analysis 1 month earlier was negative for pyogenic bacteria.

The patient was admitted with a provisional diagnosis of synovitis of the left index finger. Serologic tests for rheumatoid factor, syphilis, and Lyme disease were all negative. Results of a technetium scan of the left index finger were consistent with osteomyelitis. The patient was taken to the operating room, where soft tissue, synovium, and bone of the left index finger were debrided.

Histologic examination of the synovium and soft tissue revealed a marked inflammatory reaction, with both chronic inflammatory cells and granulation tissue. There were scattered small, well-formed, epithelioid, noncaseating granulomata with Langhans giant cells, as well as a poorly formed granulomatous reaction showing caseating necrosis. Focal microabscesses infiltrated with polymorphonuclear leukocytes were observed. These abscesses were in direct association with the granulomatous inflammation. Examination of the bone revealed osteomyelitis with granulomatous inflammation. Dead bone (sequestrum) was surrounded by granulation tissue and chronic inflammatory cells. There was no evidence of new bone formation. Kinyoun acid-fast stains of the synovium, soft tissue, and bone revealed numerous elongated, beaded, nonbranching, acid-fast bacilli. Special tissue Gram and fungal stains were negative for other microorganisms.

Bone and soft tissue specimens from the left index finger were plated onto two slants each of Lowenstein-Jensen and 7H11 media. One culture set of Lowenstein-Jensen and 7H11 media was incubated at 30°C, and the other was incubated at 37°C. After 3 weeks of incubation, a photochromogenic mycobacterium was recovered on both Lowenstein-Jensen and 7H11 media from the soft tissue specimens incubated at 30°C but not from those incubated at 37°C. Both the 7H11 and the Lowenstein-Jensen slants inoculated with the bone specimen were overgrown with an *Aspergillus* species, a common contaminant in our laboratory during this time period. The mycobacterium was identified by routine methods as *M. marinum* (15) and confirmed as this species by the Pennsylvania Department of Health. Susceptibility testing at the Pennsylvania Department of Health was performed by the proportional plate method. Standardized inocula of the *M. marinum* strain were plated onto control and drug-impregnated 7H10 agar plates and incubated at 28°C. Resistance was determined by using the 1% endpoint. *Mycobacterium tuberculosis* $H_{37}Rv$ was used as the control organism and incubated at 35°C. The *M. marinum* isolate, by the proportional plate method, was susceptible to ethambutol (10 μg/ml), rifampin (1.0 μg/ml), and ansamycin (1.0 μg/ml) but resistant to isoniazid (0.2 and 1.0 μg/ml) and streptomycin (2.0 μg/ml). Susceptibility testing by a standard microbroth method (16) at the Centers for Disease Control showed the following MICs for the *M. marinum* strain (in micrograms per milliliter): amikacin, 0.5; cefoxitin, 2; tobramycin, 2; kanamycin, 0.5; doxycycline, 0.25; minocycline, 0.25; erythromycin, 0.25; sulfamethoxazole, 256; capreomycin, 4; imipenem, 0.25; ciprofloxacin, 1; and amoxicillin-clavulanic acid, 1.

The patient was placed on therapy with minocycline, rifampin, and ethambutol. He responded to both surgical and antibiotic therapies. A draining sinus tract that formed after surgery has closed, and the patient has an increased range of motion with his finger. Chemotherapy will be given for a total of 9 months.

* Corresponding author.

Discussion. Histologic examination of the bone revealed marked destruction and a chronic osteomyelitis with acid-fast bacilli. The *M. marinum* isolate was recovered from soft tissue adjacent to the bone but was not isolated from the bone because of overgrowth with the contaminating *Aspergillus* species. Even though the patient did not recall any specific trauma to his finger, he was frequently exposed to fish and potentially contaminated fresh and salt water. The infection may have progressed to synovitis and osteomyelitis because of the delay in diagnosis; however, not all patients with *M. marinum* infections greater than 1 year in duration develop the more invasive synovitis or osteomyelitis seen in our patient (10).

Two cases of *M. marinum* osteomyelitis have been described previously in the literature. In the first case, *M. marinum* osteomyelitis was observed in a 36-year-old male who had lacerated his right third finger with a cable contaminated with water from the Mississippi River (10). Like our patient, this particular individual presented with both osteomyelitis and synovitis. Even though details of the patient's history were lacking, the diagnosis of osteomyelitis was confirmed by histologic studies. Amputation of the affected finger was required to cure the infection. In their original study (10), Jolly and Seabury mentioned the occurrence of one additional case of *M. marinum* osteomyelitis; no specific information was provided since this particular individual presented after the preparation of their original manuscript.

Synovitis due to *M. marinum* was initially thought to be quite rare. No cases of synovitis were reported in the largest common-source outbreak of *M. marinum* infections, which involved 290 patients (14). However, in recent years the number of reported synovitis cases either as single case reports or as a series of cases has dramatically increased (1, 2, 3, 4, 7, 9–12, 17–19). Nine studies with at least three cases per report have been published (2, 3, 4, 7, 9–11, 17–19); six of the nine studies have been reported since 1983 (2, 3, 4, 9, 11, 17). Of the patients described in these studies, most had sustained puncture wounds while in contact with fish, crabs, shrimp, or other marine life or had a history of frequent exposure to fish. All but two of the infections were limited to the hands, fingers, or wrist area. The remaining two cases involved the knees (17). Of these nine reports involving 64 patients with synovitis, only the 1 patient described by Jolly and Seabury presented with a concomitant osteomyelitis (10).

There is a wide range of inflammatory changes associated with synovitis produced by *M. marinum* (2, 6, 17). As with our patient, histologic studies have indicated that the infected synovium shows extensive ulceration with destruction of much of the synovial architecture. Acid-fast-staining bacilli were observed in most of the cases reported earlier and appear, as in our report, slender, curved, and beaded. The organisms are located most often on the surfaces of the tissues and not in the granuloma itself.

The optimal form of therapy for an *M. marinum* infection is dependent upon the specific infection site. Superficial cutaneous infections may resolve spontaneously without therapy. Deeper *M. marinum* infections such as synovitis or osteomyelitis may be more destructive and resistant to therapy (3, 4, 18). One recent report (3) advocates initial therapy of *M. marinum* synovitis with antibiotics; 14 of 24 patients were cured by chemotherapy alone. The 10 remaining patients required debridement after antibiotic therapy failed. Other studies report the use of surgical intervention combined with antibiotic therapy to cure the synovitis (9, 11, 19). One report, however, described an unusually aggressive *M. marinum* synovitis that progressed despite surgical and antibiotic therapies; amputation of the affected finger was required to control the infection (18). One of the patients described earlier with *M. marinum* osteomyelitis also required an amputation to prevent disease progression (10). Therefore, not all patients with deep *M. marinum* infections may respond to conventional surgical and antibiotic therapies.

Most investigators report the use of rifampin and ethambutol, the tetracyclines, and trimethoprim-sulfamethoxazole to treat *M. marinum* infections. Some authors believe that rifampin coupled with ethambutol is the preferred antimicrobial therapy for *M. marinum* infections (7). Our particular patient was treated with this combination along with minocycline. This antibiotic regimen was selected because of its excellent tissue penetration and its lack of resistance to these drugs as determined by in vitro susceptibility testing and because our patient met a number of prognostic criteria that might have predicted poor outcome as suggested by Chow et al. (steroid injections, pain in addition to swelling, and a postsurgically draining sinus) (3). Resistance to the tetracycline class of antibiotics has been described for *M. marinum* and may have been responsible for several infections that failed to respond to these drugs (8, 13). Isolates should be tested with the tetracyclines before therapy is restricted to these antibiotics. Other drugs, such as ciprofloxacin and other quinolones, show good in vitro activities against *M. marinum* (5).

In summary, we report a case of *M. marinum* osteomyelitis and synovitis in a fisherman. The infection has responded to surgical and antimicrobial therapies. *M. marinum* should be suspected in patients with a history of cutaneous infections that do not respond to conventional therapies.

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