Sporotrichoid presentation of Mycobacterium marinum infection of the upper extremity. A case report

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ABSTRACT

Background: *Mycobacterium marinum* is a human opportunistic pathogen that is known to inhabit swimming pools, home aquariums, and natural bodies of salt and fresh water. Epidemic cases involving swimming pools are easily recognized, but sporadic cases are frequently misdiagnosed.

Objective: A 42-year-old male presented with a 2-month history of the appearance of livid, verrucous, painless nodules on his right upper extremity. He had cleaned an aquarium with tropical fish for the past 2 years.

Methods: A histopathological examination suggested a granulomatous inflammation. After incubation on Löwenstein-Jensen medium, *Mycobacterium marinum* was identified using biochemical methods and the PCR technique.

Results: Systemic therapy with rifampicin, ethambutol, and clarithromycin over a period of 6 months led to complete resolution of the skin lesions with some residual scars.

Conclusion: Knowledge of this condition is very important to avoid unnecessary diagnostic procedures and improper treatment.

KEY WORDS

***Mycobacterium marinum*, sporotrichoid skin infection, aquariumborne, diagnosis, treatment**

Introduction

Mycobacterium marinum (*M. marinum*) infection in humans was first described in 1954 by Linell and Norden. They reported on 80 patients involved in a swimming pool epidemic in Sweden (1). *M. marinum* is the causative pathogen of skin infections that have been called "swimming pool granuloma" and "fish tank granuloma." Most infections are acquired in swimming pools, beaches, rivers, and lakes, or by cleaning aquariums. Vectors of infection include fresh- or saltwater fish, snails, shellfish, dolphins, and water fleas. Infection may be acquired by direct inoculation through injured skin in an aquatic environment. Risk factors include skin injuries and water/fish related hobbies or occupations (2–4).

Three types of lesions are recognized: 1. a solitary granulomatous verrucous papule that may occasionally ulcerate and show purulent discharge; 2. ascending lymphatic sporotrichoid lesions; 3. rare cutaneous dis-

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seminated lesions, which occur frequently in immunosuppressed patients. Lesions are painful in less than one-half of cases, lymphadenopathy is rare and typically mild, and systemic symptoms are unusual (5–14).

The clinical presentation is often insidious and nonspecific and key anamnestic data may be missed; for this reason the diagnosis is often delayed. This is clinically relevant because untreated *M. marinum* infections can result in significant morbidity, including loss of joint mobility due to osteomyelitis and even amputation of the affected appendage. Because this infection is relatively rare, an optimal treatment has not been established (15–16).

Case report

A 42-year-old man presented with a history of painless, livid, verrucous nodular skin lesions on the right forearm and upper arm (Figure 1). The first skin lesion had appeared on the extensor side of the wrist 2 months before he was examined and admitted to our department. Small amounts of yellowish fluid were intermittently discharged from the lesion. Despite the treatment with short-course antibiotics (amoxicillin, ciprofloxacin), the nodule on the wrist enlarged and new lesions turned up rapidly on the flexor side of the right forearm and upper arm. Regional lymphadenopathy was absent. There were no systemic complaints. The patient denied an injury at the site of the first lesion. He did not take any medications and had no contact with domestic animals. He had never been in the tropics, but he had owned an aquarium with tropical fish for the past 2 years and cleaned it regularly himself. There were no risk factors for HIV infection. Family history of skin diseases was negative.

Clinically, a long, painless, solid, livid, verrucous infiltrate 30 × 10 mm in diameter was localized on the extensor side of the right wrist (Figure 2). Four similar pea-size lesions were also expressed on the medial side of the lower third of the right forearm, and on the flexor side of the upper third of the right forearm, as well as on the medial aspect of the lower third of the upper arm. The complete blood screening and biochemical tests, immunoglobulins, serum complement, and angiotensin converting enzyme (ACE) were within normal limits. Serological tests for *Bartonella henselae* and *Bartonella quintana* were negative, as were the Venereal Disease Research Laboratory (VDRL) test and the *Treponema pallidum* hemagglutination assay (TPHA). The chest X-ray was normal. The tuberculin skin test resulted in an induration 20 mm in diameter.

Skin biopsies were taken for fungal isolation, histological, and mycobacterial examination. The histopathology suggested a granulomatous inflammation, but no organisms were identified (Figure 3). A culture on Sabouraud medium was negative. A 4-week incubation on Lowenstein-Jensen medium at 31° C yielded an acid-fast bacterium, identified using biochemical and molecular methods as *M. marinum* (Figure 4).

Susceptibility tests showed resistance to isoniazid but susceptibility to rifampicin, ethambutol, ciprofloxacin and clarithromycin. Three-drug combination therapy including rifampicin and ethambutol over a period of 6 months, as well as clarithromycin over a period of 4 months, was initiated. Four months after starting treatment a complete resolution of skin lesions was observed with some residual scars.

Discussion

M. marinum is a human opportunistic pathogen that is known to inhabit swimming pools, home aquariums and natural bodies of salt and fresh water. The distribution of this "mycobacterium other than tuberculosis (MOTT)" is worldwide, and it is prevalent in heated water in temperate climates and in the sea and natural pools in warmer regions. The infection is not transferable from human to human. Epidemic cases involving swimming pools are easily recognized, but sporadic cases are frequently misdiagnosed. The diagnosis of cutaneous *M. marinum* infection is mainly clinical, with supporting evidence from histopathology and response to therapy. Conventional detection and culture methods are laborious and technically difficult. Molecular methods such PCR techniques may play a more important role in the diagnosis of "MOTT" infections (17, 18).

Deep infections such as tenosynovitis, osteomyelitis, arthritis, bursitis, and carpal tunnel syndrome are rare. They result from a direct extension of the cutaneous infection and may be very resistant to treatment (19).

Physicians should be aware that the incubation period for cutaneous *M. marinum* infection, although usually less than 4 weeks, can be as long as 9 months (20).

Before 1962 most cutaneous *M. marinum* infections reported in the literature involved swimming pool-associated injuries, including two large outbreaks involving almost 350 patients. A possible explanation for the decline in reported pool-associated cases is the improvement in swimming pool water disinfection practices in recent decades (21).

A diagnosis of *M. marinum* skin infection is best established by obtaining at least a 4 mm punch skin biopsy specimen of the granuloma. The specimen must be bisected, with one half used for hematoxylin-eosin and acid fast stains and the other half for inoculation on Löwenstein-Jensen media. The specimen should be incubated at 30–33° C for optimal growth. Growth generally takes 2 to 5 weeks. *M. marinum* is a photochromogen; that is, the colonies form a yellow pigment when exposed to light. In lesions reminiscent of sporotrichosis, culture of a tissue specimen on Sabouraud medium must be performed to rule out a deep fungal infection.

Figure 1. *M. marinum* cutaneous infection: Sporotrichoid lesions on the right forearm and upper arm

Figure 2. *M. marinum* cutaneous infection: Clinical aspect of the first skin lesion on the extensor side of the right wrist.

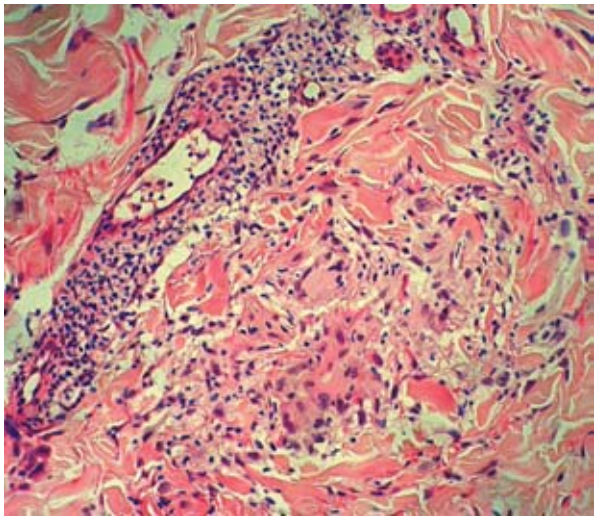

Figure 3. *M. marinum* cutaneous infection: The histopathology shows a granulomatous inflammation.

The histopathologic findings vary depending on the duration of the lesion obtained at biopsy. Lesions younger than 3 months show a nonspecific mixed inflammatory infiltrate, but acid-fast stains typically reveal bacilli. Older lesions show characteristic tuberculoid granulomas. The epidermis frequently shows papillomatosis, hyperkeratosis, ulceration, and an acute inflammatory infiltrate. Acid-fast bacilli may often be present in the necrosis at the center of the granuloma.

Patients infected with *M. marinum* frequently have persistently positive tuberculin tests. Because of the high incidence of cross-reactivity and low sensitivity, skin testing should not be considered as a diagnostic criterion for present or past infections with *M. marinum*. Evaluation for tuberculosis always should be performed in patients with positive tuberculin skin tests and treatment should be provided on the basis of current guidelines. However, positive tuberculin reactions in patients with *M. marinum* infection can be attributed to this infection and should not always be considered an indication for treatment of latent tuberculosis. The cross reactions to tuberculin observed in patients with *M. marinum* infection were stronger than those observed in patients with *Mycobacterium avium* complex disease. This is consistent with genetic studies showing that *M. marinum* is closely related to *M. tuberculosis* (22).

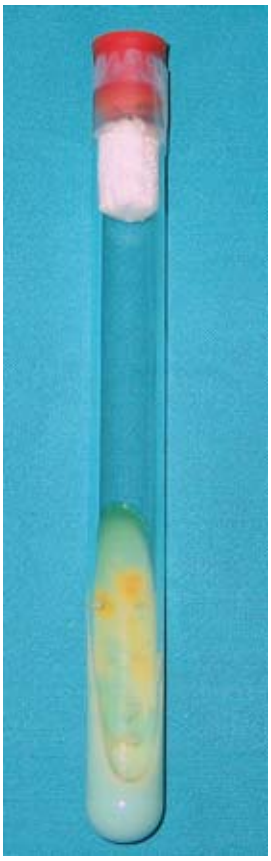

Figure 4. *M.marinum* cutaneous infection: Culture of *Mycobacterium marinum* on Löwenstein-Jensen medium.

The main differential diagnosis of *M. marinum* cutaneous granuloma is sporotrichosis. A foreign body granuloma should be considered. Some other clinical entities possibly mimicking *M. marinum* infection include cutaneous leishmaniasis, psoriasis, verrucous lichen planus, verruca vulgaris, iodine and bromine granulomas, sarcoidosis, syphilis, gout, and chronic pyogenic infections. In addition, *Pasteurella tularensis*, *Scopulariopsis blochi*, and *Nocardia brasiliensis* infections must be considered in the differential diagnosis (23).

In our case, the infection, acquired from an aquarium,

presented in a sporotrichoid distribution due to proximal spread through the lymphatics up to the regional lymph nodes.

Because the infection is relatively rare, data on optimal treatment are rather scarce. The choice of agents is based mainly on experience of anecdotal reports, findings from case series, and the results of susceptibility testing. In many patients with a mild form of the disease, the infection probably would resolve spontaneously, although complete resolution may take up to 2 years. However, most infections persist, sometimes for years, and spread along lymphatic channels or, rarely, disseminate. Sporotrichoid forms of infection usually do not show a tendency to spontaneous healing. Surgical excision, cryotherapy, irradiation, grenz-ray and X-ray treatment, and electrodessication have been used occasionally (24, 25).

However, antibiotic therapy appears to be necessary in most patients with cutaneous *M. marinum* infection. A wide spectrum of antibiotic regimens has been used successfully, including amikacin, potassium iodide, tetracycline, sulfamethoxazole-trimethoprim, minocycline, doxycycline, and ethambutol plus rimfampicin. Minocycline, doxycycline, and ethambutol plus rifampin have been most frequently recommended. Clarithromycin, minocycline, co-trimoxazole, or rifampicin plus ethambutol have been suggested as being useful. Some new reports recommend monotherapy with low side-effect antibiotics, based on sensitivity tests (26–29).

In line with principles for treatment of other mycobacterial infections, monotherapy should be avoided for extensive *M. marinum* infection. Drug therapy should be preceded by in vitro sensitivity studies because different strains may vary in their responses. Resistance to isoniazid and para-aminosalicylic acid is typical. Patients with disseminated disease should be treated for 9 to 12 months. Surgical debridement is often required when the deep structures of the hand are involved. In contrast to superficial forms of the disease, deeper infection, most often affecting the hand and arm, usually requires both antibiotic and surgical treatment. Steroid injections worsen the clinical outcome and should be avoided (30).

Recommendations on the optimum duration of therapy also vary markedly according to the literature, ranging from a few months to 1.5 years. Treatment should be performed for a minimum of 6 months, or at least 2 months after the lesions have disappeared.

Fish tank exposure is the source of most cases of cutaneous *M. marinum* infections. Patients with open skin lesions or immunosuppression should avoid cutaneous contact with fish tanks or use waterproof gloves.

In conclusion, the diagnosis of cutaneous *M. marinum* infection is mainly clinical, with supporting evidence from histopathological features and the response to therapy. Specimens to detect *M. marinum* or other pathogens by culture should also be obtained. Epidemic cases are easily recognized, but sporadic cases are frequently misdiagnosed (31).

Knowledge of this rare condition is important to avoid unnecessary diagnostic procedures and to start adequate treatment early.

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