Mycobacterium marinum Infection: A Case Report and Review of the Literature

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GOAL

To understand *Mycobacterium marinum* infection to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Identify causes of *M marinum* infection.
2. Describe methods for diagnosing *M marinum* infection.
3. Discuss treatment options for *M marinum* infection.

CME Test on page 50.

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Mycobacterium marinum *is a nontuberculous mycobacteria that is often acquired via contact with contaminated salt or fresh water. We present a case of a 67-year-old man who developed several solitary nontender nodules on his hands and forearm after working on the underside of his boat. In addition, we provide a review of the literature and discuss how this infection is acquired, the underlying pathogenesis, the cutaneous and histologic findings, the differential diagnosis, the diagnostic methods, and the various treatment options.*

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Case Report

An otherwise healthy 67-year-old white man presented to the dermatology clinic with a 10-day history of multiple red scaly lesions on his hands and forearm. The patient recalled that the lesions appeared one week after he had scraped his hands on barnacles while cleaning the underside of his boat. On physical examination, the patient had multiple well-circumscribed, nontender, erythematous subcutaneous nodules with central crusting and scaling located on the dorsal aspect of both hands and his left forearm (Figure 1). There was no lymphadenopathy, and the patient denied fever, painful joints, or any other systemic symptoms.

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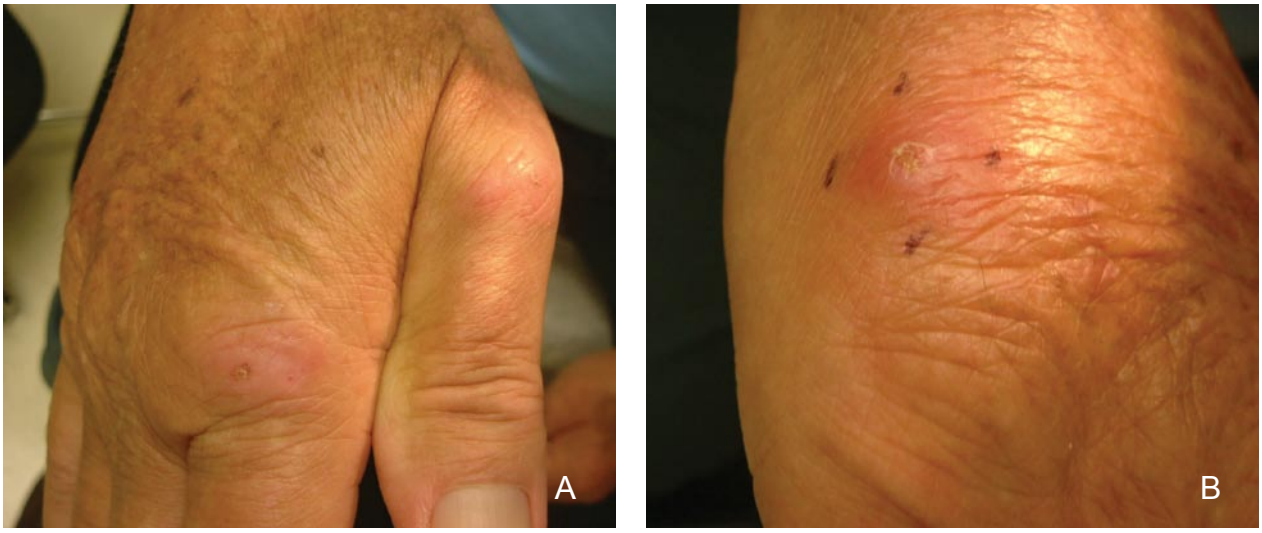

Figure 1. A well-circumscribed, nontender, erythematous subcutaneous nodule with central crusting and scaling (A and B).

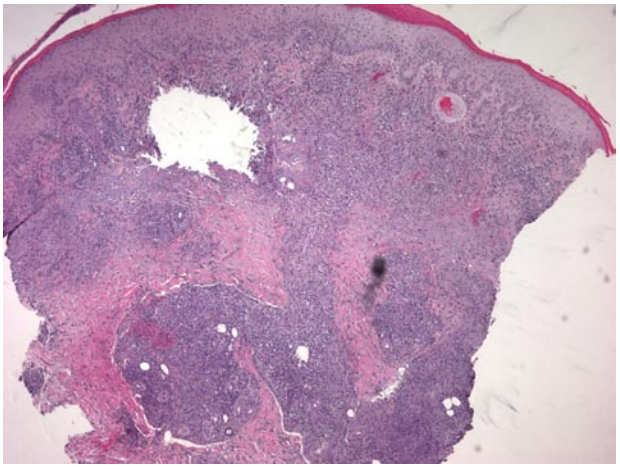

Figure 2. A mixed dense acute, chronic, and granulomatous infiltrate from a punch biopsy of one of the lesions (H&E, original magnification ×10).

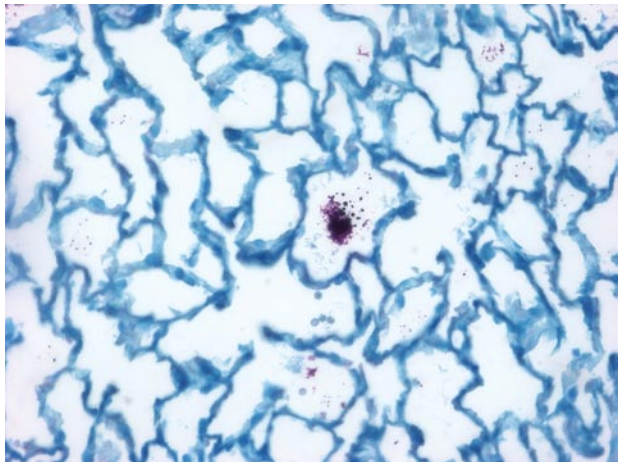

Figure 3. Results of a Fite stain are positive for numerous acid-fast bacteria (original magnification ×10).

Results from a punch biopsy of one of the lesions on the right dorsal hand were characterized as a mixed dense acute, chronic, and granulomatous infiltrate (Figure 2). Numerous acid-fast bacteria were seen on both Ziehl-Neelsen and Fite stains (Figure 3). In addition, a direct smear fluorochrome stain for acid-fast bacilli was positive. The patient was empirically treated with clarithromycin and ethambutol hydrochloride. Two weeks later, the acid-fast bacilli culture grew out *Mycobacterium marinum* sensitive to clarithromycin, ethambutol hydrochloride, and rifampin. After 2 months of treatment, his lesions had completely resolved.

Comment

M marinum is a nontuberculous atypical *Mycobacterium* that can cause cutaneous infection of sites of prior wounds exposed to contaminated fresh or salt water. Known originally as *swimming pool granuloma,* this infection was first described in 1951 after large outbreaks of cases involving swimming pools.[1,2] After widespread pool chlorination in the 1960s, most reported cases were in fishermen and aquarium owners, giving rise to the term *fish tank granuloma*.[3] Ornamental fish such as the Siamese fighting fish *Betta splendens* and the snakehead *Channa striata* are common hosts of the mycobacteria.[4] With improper chlorination and emergence of chlorine-resistant organisms, swimming pool–associated infections have reemerged.[3]

After entering through an open wound, *M marinum* usually causes a tender erythematous nodule or pustule at the site of inoculation. Although the infection typically occurs on the dominant hand, any extremity may be affected. The average incubation period is approximately 2 to 4 weeks but

can last as long as 9 months.[3,5] With time, the lesion can evolve into a crusted ulcer with an underlying suppurative abscess or a verrucous nodule or plaque. As the infection spreads, multiple nodules can appear following the course of the draining lymphatics. This pattern is commonly known as sporotrichoid spread (Table) because of its resemblance to the ascending lymphangitis of sporotrichosis.[2,6] With deeper infections, tenosynovitis may occur and can progress to septic arthritis and osteomyelitis.[7] As with other atypical mycobacterial infections, the disease can disseminate and become fatal in immunocompromised patients.

The histopathology findings in patients with M *marinum* infections can range from acute and chronic inflammation to ill-defined suppurative granulomas, which is similar to findings seen with other types of mycobacterial infections. The granulomas are characterized by surviving organisms contained within a mixture of surrounding histiocytes and lymphocytes. In addition, suppurative granulomas are formed in response to the presence of multiple reactive neutrophils. The organisms rarely are seen on routine hematoxylin and eosin stain but may become positive on acid-fast stains such as Ziehl-Neelsen or Fite.[2,8] Epidermal changes, including ulceration and pseudoepitheliomatous hyperplasia, can be seen in chronic lesions.[2]

Strain characteristics may play a critical role in the pathogenicity of M *marinum*.[9] Several virulence factors now have been identified by using a research model for the pathogenesis in *Mycobacterium tuberculosis* infection. Factors that are required for intracellular survival of the mycobacteria in macrophages include the exported repetitive protein and the protein encoded by the macrophage-activated gene 24-1.[10,11] In addition, the invasion and intracellular persistence protein A is essential for initial invasion of M *marinum* into macrophages and also allows for the intracellular survival of these organisms.[10-12]

Results from a purified protein derivative test can be positive in some cases but is not a reliable test for M *marinum*. Cultures grown at 30°C to 33°C may take at least 2 to 4 weeks and are positive in only 70% to 80% of cases.[6] Polymerase chain reaction (PCR) may be used to confirm the diagnosis in culture-negative cases.[13] Confirmatory tests such as culture and PCR help rule out other diseases that may present with similar clinical and histologic findings (ie, other atypical mycobacterial infections, sporotrichosis, deep fungal infections, leishmaniasis, catscratch disease, and tuberculosis verrucosa cutis). Most recently, via PCR, Cai et al[14] has detected that heat shock protein 65 kD gene was present in all lesions containing M *marinum*. This important finding could lead to an earlier detection of this infection.

With time, single lesions often can remit spontaneously, but it may take up to 3 years. During that time, the patient remains at high risk of developing tenosynovitis, septic arthritis that may mimic rheumatoid arthritis,[15] osteomyelitis, and dissemination in immunocompromised patients, all of which prompt immediate treatment.[2,7]

No clinical trials exist for the treatment of M *marinum* infections because of the small number of patients with this disease. However, trimethoprim-sulfamethoxazole, minocycline, and clarithromycin all are effective treatments.[5] Success with minocycline is particularly well-documented in the dermatology literature, even in cases complicated by delayed diagnosis and systemic immunosuppression.[16] Anecdotal reports suggest that, despite the similarity in the mechanism and sensitivities of different second-generation tetracyclines, minocycline may be the most effective treatment option.[13] On the other hand, clarithromycin

Differential Diagnosis of Cutaneous Nodules Following Sporotrichoid Spread

Deep fungal infections
Leishmaniasis
Mycobacterium marinum
Nocardiosis
Other atypical mycobacterial infections
Sporotrichosis
Tularemia

is favored as a first-line treatment in the infectious diseases literature.[6] Ethambutol hydrochloride and rifampin may be added to treat resistant strains. This combination has been proven to be more effective against M *marinum* than any single antibiotic regimen.[5] Unfortunately, determining antibiotic sensitivity of M *marinum* is difficult because the organism often responds differently in vivo than in vitro.[13] Refractory cases may require surgical debridement.[2] The disease can be prevented by wearing gloves while working in fish tanks and immediately cleaning any abrasions or injuries that occur while working in contaminated water.[6] Immunocompromised individuals should avoid aquariums completely.

Conclusion

M *marinum* is present in both salt and fresh water environments. Infection with the organism usually presents on an extremity as a painful cutaneous nodule with various secondary skin changes and can spread in a sporotrichoid pattern. Because the organism can take several weeks to culture, patients with a presumptive diagnosis of M *marinum* infection should be initially treated with the appropriate antibiotics. Complications can range from tenosynovitis, septic arthritis, and osteomyelitis to disseminated disease in immunocompromised patients.

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