Short course monotherapy with clarithromycin for localized *Mycobacterium marinum* skin infection

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*Mycobacterium marinum* is an uncommon, but well recognized, human pathogen that causes persistent skin infections. Optimal therapy has not been established, and no controlled studies have been performed. The organism is sensitive in vitro to a variety of agents including trimethoprim-sulfamethoxazole (TMP-SMX), tetracyclines, rifampin, ethambutol, amikacin and ciprofloxacin (1-4), all of which have been used alone or in combination clinically. Recently clarithromycin has been shown to have in vitro activity against *M marinum* and has had promising clinical responses (5-7). However, the optimal dose and duration of therapy are still unclear. We report a case of cutaneous infection with *M marinum* that responded promptly to a short course of low dose monotherapy with clarithromycin.

**CASE REPORT**

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MR WEINSTEIN, DE LOW, T MAZZULLI. Short course monotherapy with clarithromycin for localized *Mycobacterium marinum* skin infection. Can J Infect Dis 1997;8(3):164-166. In vitro studies have shown that *Mycobacterium marinum* is usually susceptible to clarithromycin. However, there are limited published data on the clinical use of clarithromycin for the treatment of *M marinum* infections. This report describes a previously healthy 58-year-old man who developed a chronic soft tissue infection of his right hand caused by *M marinum*. He responded to four weeks’ therapy with clarithromycin. Follow-up at six months showed no relapse. Our experience and review of the literature suggest that short course monotherapy with clarithromycin may be quite effective for uncomplicated soft tissue infections caused by *M marinum*.

**Key Words:** Clarithromycin, *Mycobacterium marinum*

**Monothérapie brève à la clarithromycine pour infection cutanée localisée à *Mycobacterium marinum***

RÉSUMÉ : Des études in vitro ont démontré que *Mycobacterium marinum* est sensible à la clarithromycine. Toutefois, les données publiées sur l’emploi clinique de la clarithromycine en traitement des infections à *M. marinum* sont limitées. Ce rapport décrit le cas d’un homme de 58 ans auparavant en bonne santé qui a développé une infection chronique des tissus mous à la main droite causée par *M. marinum*. Il a répondu à quatre semaines de traitement à la clarithromycine. Le suivi de six mois a permis de constater l’absence de rechute. Notre expérience et notre revue de la littérature nous donnent à penser que la clarithromycine en monothérapie brève peut être efficace contre les infections non compliquées des tissus mous provoquées par *M. marinum*.

*Mycobacterium marinum* is an uncommon, but well recognized, human pathogen that causes persistent skin infections. Optimal therapy has not been established, and no controlled studies have been performed. The organism is sensitive in vitro to a variety of agents including trimethoprim-sulfamethoxazole (TMP-SMX), tetracyclines, rifampin, ethambutol, amikacin and ciprofloxacin (1-4), all of which have been used alone or in combination clinically. Recently clarithromycin has been shown to have in vitro activity against *M marinum* and has had promising clinical responses (5-7). However, the optimal dose and duration of therapy are still unclear. We report a case of cutaneous infection with *M marinum* that responded promptly to a short course of low dose monotherapy with clarithromycin.
CASE PRESENTATION

A previously healthy 58-year-old man suffered a minor scrape on the dorsum of his right hand while removing barnacles from the side of his boat in south Florida. The skin was abraded over the extensor surfaces of the second, third, and fourth proximal phalanges. Two weeks later he developed pain, erythema with a fusiform swelling of the second digit and swelling on the palmar aspect of the hand. A 0.5 cm violaceous papule was present over the middle phalanges. A lesser amount of swelling was present over the third digit. Movement was restricted at the second proximal interphalangeal and metacarpophalangeal joints. There were no ulcerations, nodules, lymphangitis or adenopathy. He was taking no medications.

Initially the patient was treated over a three-month period with courses of oral penicillin and ampicillin with no improvement. An infectious disease consult suggested a biopsy of the papular lesion. Microscopy revealed a focal aggregate of macrophages underlying the squamous epithelium. Adjacent tissue contained lymphocytes, plasma cells and macrophages. Staining of the specimen for mycobacteria was negative, but a photochromogenic mycobacterium growing optimally at 30°C was cultured at seven days. This was confirmed as _M. marinum_ by standard laboratory methods. The isolate was susceptible to minocycline, doxycycline, imipenem, rifampin, ciprofloxacin, ethambutol, clofazamine, amikacin and clarithromycin (minimum inhibitory concentration less than 2.0 mg/L), and resistant to TMP-SMX, erythromycin, cefoxitin and streptomycin. The patient was treated with clarithromycin 500 mg twice daily for four weeks. Within one week he began responding, with a decrease in the swelling and tenderness. By the end of therapy, his skin lesions had completely resolved. Follow-up to six months showed no relapse.

DISCUSSION

_M. marinum_ is a well known cause of cutaneous infection following contact with contaminated fresh or salt water, or infected fish. The most common exposures lead to the descriptions ‘swimming pool’ and ‘fish tank’ granuloma. Disease can include a local papulonodular or noduloulcerative granuloma, sporotrichoid lesions or deep tissue infections of the tendons and bone (1-4). Disseminated disease is rare but has been described in immunocompromised hosts.

Cutaneous infection may be self-limiting (8,9), but healing is usually quite slow. Most cases of _M. marinum_ cutaneous infection respond well to treatment with TMP-SMX, tetracyclines or rifampin with or without ethambutol (1-4,10-12). Optimal regimen and duration of therapy are still not clear. All recommendations come from retrospective case series and often represent the personal experience of individual authors. Few studies have compared the success of different treatment regimens (1). Edelstein (1) noted that the combination of ethambutol and rifampin had a superior response to minocycline alone for local extremity lesions (five of five versus 10 of 14), but the number of treated cases was small.

Huminer et al (4) reviewed 45 cases of aquarium related _M. marinum_ infection with either a nodular or sporotrichoid pattern. TMP-SMX had a satisfactory response in 76% (13 of 17), and ethambutol and rifampin in 89% (eight of nine). Duration of therapy ranged from four to 24 months. Edelstein (1) has recommended a minimum of six months of therapy or two months after lesions have disappeared. The American Thoracic Society recommends a minimum of three months of therapy (2). The Standards Committee of the Canadian Thoracic Society (13) also notes that rifampin and ethambutol is nearly always curative after three to six months of therapy. However, no definitive recommendations were made.

Clarithromycin has in vitro activity against _M. marinum_ (14,15) with minimum inhibitory concentrations that are easily achievable with the orally administered drug. A few case reports have described the clinical use of clarithromycin for _M. marinum_ infections alone or in combination with another agent and at varying dosages (5,6). Bonnet et al (5) described two cases. In one, a woman with advanced chronic human immunodeficiency virus infection, who had cutaneous _M. marinum_ skin abscesses, failed therapy with minocycline and ofloxacin, and then with amikacin, ciprofloxacin and rifampin. She subsequently responded when given clarithromycin 2 g/day for 50 days. A second patient with subcutaneous nodules on his arm responded to one month of clarithromycin and ethambutol in combination. Kuhn et al (6) reported a case of _M. marinum_ facial abscess in a five-year-old that responded to a five-month course of clarithromycin and rifampin. Laing et al (7) reported a man with a sporotrichoid pattern that failed therapy with TMP-SMX, ciprofloxacin and ethambutol (7). Lesions improved on clarithromycin (500 mg/day), but therapy had to be stopped because of nausea. There was finally complete resolution with rifabutin for four months.

CONCLUSIONS

We presented a case of _M. marinum_ soft tissue infection of the hand that responded promptly to clarithromycin monotherapy, after worsening for three months on inappropriate therapy. The use of clarithromycin for this infection has only been reported in three previous case reports, where it was used in combination, at higher dosages or could not be tolerated due to gastrointestinal intolerance. We found that monotherapy with 500 mg twice daily for four weeks was well tolerated and highly effective. For uncomplicated cutaneous infections this seems to be a promising regimen and should be studied further. Combination therapy or more prolonged treatment may still be necessary in immunosuppressed patients or in those with disseminated disease.

REFERENCES


