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

Mitchell R Weinstein MD FRCPC, Donald E Low MD FRCPC, Tony Mazzulli MD FRCPC

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 issue 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.

Department of Microbiology, Mount Sinai Hospital and University of Toronto, Toronto, Ontario
Correspondence and reprints: Dr T Mazzulli, Department of Microbiology, Mount Sinai Hospital, 600 University Avenue Hospital, Toronto, Ontario M5G 1X5. Telephone 416-586-4695, fax 416-586-8746, e-mail tmazzulli@mtsinai.on.ca
Received for publication August 21, 1996. Accepted December 4, 1996

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 phalanx. 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.

Hummer 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

1. Edelstein H. *Mycobacterium marinum* skin infections. Report of 31 cases and review of the literature. Arch Intern Med 1994;154:1359-64.
2. American Thoracic Society. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. Am Rev Respir Dis 1990;142:940-53.
3. Wolinsky E. Mycobacterial diseases other than tuberculosis. Clin Infect Dis 1992;15:1-12.
4. Hummer D, Pitlik SD, Block C, Kaufman L, Amit S, Rosenfield J. Aquarium-borne *Mycobacterium marinum* skin infection, report of a case and review of the literature. Arch Dermatol 1986;122:698-703.

5. Bonnet E, Debat-Zoguereh D, Petit N, Ravaux I, Gallais H. Clarithromycin: A potent agent against infections due to *Mycobacterium marinum*. Clin Infect Dis 1994;18:664-6.
 6. Kuhn SM, Rosen W, Wong A, Jadavji T. Treatment of *Mycobacterium marinum* facial abscess using clarithromycin. Pediatr Infect Dis J 1995;14:631-2.
 7. Laing RBS, Wynn RF, Leen CLS. New antimicrobials against *Mycobacterium marinum* infection. Br J Dermatol 1994;131:914.
 8. Swift S, Cohen H. Granulomas of the skin due to *Mycobacterium balnei* after abrasions from a fish tank. N Engl J Med 1962;267:1244-6.
 9. Philpott JA, Woodburne AR, Philpott OS, et al. Swimming pool granuloma. Arch Dermatol 1963;88:94-8.
 10. Iredell J, Whitby M, Blacklock Z. *Mycobacterium marinum* infection: epidemiology and presentation in Queensland 1971-1990. Med J Aust 1992;157:596-8.
 11. Chow SP, Ip FK, Lau JHK, et al. *Mycobacterium marinum* infections of the hand and wrist. J Bone Joint Surg 1987;69A:1161-8.
 12. Donta ST, Smith PW, Levitz RE, et al. Therapy of *Mycobacterium marinum* infections. Use of tetracyclines vs rifampin. Arch Intern Med 1986;1146:902-4.
 13. Nontuberculous mycobacteria. In: Fitzgerald JM, ed. Canadian Tuberculosis Standards, 4th edn. Gloucester: Canadian Lung Association, 1996.
 14. Brown BA, Wallace RA, Onyi GO. Activities of clarithromycin against eight slowly growing species of nontuberculous mycobacteria, determined by using a broth microdilution MIC system. Antimicrob Agents Chemother 1992;36:1987-90.
 15. Forsgren A. Antibiotic susceptibility of *Mycobacterium marinum*. Scand J Infect Dis 1993;125:779-82.
-
-