

# *Mycobacterium Chelonae*: Nonhealing Leg Ulcers Treated Successfully With an Oral Antibiotic

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**Background:** *Mycobacterium chelonae* is an important human pathogen and should be considered when a physician is faced with nonhealing cutaneous wounds, including ulcers of the lower leg.

**Methods:** The medical literature was searched from 1965 to the present using the key words "*Mycobacterium chelonae*" and "leg ulcers." A case of *Mycobacterium chelonae* infection is reported.

**Results and Conclusion:** Clarithromycin as single-agent oral therapy has been effective in treating these infections once the proper diagnosis is established. Diagnosis of *M chelonae* infection requires being alert to this infectious agent and obtaining cultures for mycobacteria. Aggressive surgical debridement with direct excision of the wound might now be unnecessary because of the effectiveness of oral clarithromycin administered as a single oral agent. (J Am Board Fam Pract 2001;14:457–61.)

Leg ulcers plague mankind with prolonged suffering and disability. The differential diagnosis is broad, and major causes include circulatory disorders, neuropathies, and infectious diseases. In the absence of a circulatory disturbance or neuropathy, and when conventional aerobic and anaerobic cultures are negative, the diagnosis of a mycobacterial infection should be considered. We report on an uncommon but treatable cause of leg ulcers, *Mycobacterium chelonae* infection.

## Methods

We searched the medical literature from 1965 to the present, using the key words "*Mycobacterium chelonae*" and "leg ulcers." A descriptive case is reported.

## *Mycobacterium chelonae* Infection

*M chelonae* is a rapidly growing atypical mycobacterium that can cause both systemic and cutaneous infections as a human pathogen.<sup>1,2</sup> The organism is classified as a Runyon group IV mycobacterium that forms nonpigmented rough, smooth, or mixed

colonies at 25°C to 40°C.<sup>3</sup> This saprophyte is ubiquitous in the environment and has been found in soil, water, and dust particles.<sup>4</sup> It is distinguished from the closely related species *M fortuitum* by its inability to produce the enzyme arylsulfatase.<sup>1</sup>

Although *M chelonae* can be found in many cutaneous sites, infection occurs most commonly after skin trauma from surgery, injections, or minor injuries.<sup>2,4,5</sup> In immunocompetent patients the infection is more frequently localized as a cellulitis or a nodule, whereas in the immunocompromised patient, dissemination (more than five lesions) can occur.<sup>1,3,5</sup> Because the organism is resistant to antituberculosis medications and most other antimicrobial drugs,<sup>1</sup> abscess progression can develop along a chronic, indolent course. Spontaneous resolution requires several months.<sup>1,4,6,7</sup>

## Case History

Our patient was an 80-year-old woman with a 15-year history of diabetes mellitus and right-sided paresis after a carotid endarterectomy. She was referred to the plastic and reconstructive surgery service during her third admission for a persistent cellulitis of her right lower extremity. She had been admitted twice during the previous 30 days for the same complaint.

Her initial cellulitis developed after a cat scratch injury to her right anterior and medial leg. After an outpatient trial of oral amoxicillin-clavulanate did not provide clinical improvement, she was admitted to the hospital and given intravenous cefazolin for

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4 days. She was released on an oral amoxicillin-clavulanate combination of 500 mg three times a day.

After making good initial progress, she returned 3 weeks later with increasing erythema, pain, and fluctuance in the area, but no fever. Two 2×2-cm abscesses were noted on the medial and posterior aspects of her leg. There were no palpable cords, pulses were normal for the patient, and Homans sign was negative. She had no loss of sensation to touch or pinprick. She was admitted a second time and was given intravenous ticarcillin-clavulanate. A surgeon was consulted, and her abscesses were incised and debrided. She continued taking intravenous ticarcillin-clavulanate, and her open wounds were managed with wet-to-dry dressing changes. Her clinical course continued to improve; her erythema approached resolution, and there was considerable decrease in purulent drainage. Her drug regimen was changed to oral cephalexin, and she was released from the hospital with instructions to continue the wet-to-dry dressing changes at home. Aerobic and anaerobic cultures of specimens taken during the admission had failed to show any organism. Results of cultures obtained for fungi, *Nocardia* species, and atypical mycobacteria were still pending at that date.

Four days later the patient returned for a follow-up visit complaining of increasing pain and redness. There was a wide margin of erythema around the wound, purulent discharge from the previous incision and drainage sites, and a new pustular lesion slightly distal to the originally involved areas (Figures 1 and 2). She was admitted to the hospital and given intravenous vancomycin and ticarcillin-clavulanate. The final acid-fast bacteria report from cultures drawn during her second admission were positive for rapid-growing acid-fast bacteria. A presumptive diagnosis of *M chelonae* infection was made, and an infectious disease specialist was consulted.

Based on the consultant's recommendations, the patient's antibiotics were changed to amikacin and cefoxitin. A DNA probe of the acid-fast bacteria cultures was ordered for definitive species identification. A second specimen was sent to R. Wallace, MD, of the University of Texas Health Center (Tyler, Tex) for further sensitivity studies.

The patient's pain and erythema decreased during the first few days of this admission, but shortly thereafter the wound again began to drain purulent fluid. It was thought that a deeper and wider de-



**Figure 1. Multiple leg ulcers were resistant to conventional antibiotics and wound care. Patient before oral therapy with clarithromycin.**

bridement was necessary to decrease the wound bacterial content.

The recommendation after the patient's condition was evaluated was to continue her intravenous antibiotics and wet-to-dry dressing changes, delaying the wider debridement until the species identification and sensitivity studies were done. Four days later these studies confirmed the organism as *M chelonae* sensitive to clarithromycin. The patient was then given oral clarithromycin 500 mg twice a day as a single agent. The patient responded rapidly, and 2 days later she was released from the hospital on oral therapy. At a follow-up visit 1 week later, the cellulitis had resolved, and her open wounds were healing well. At extended follow-up visits, healing was complete and there was no recurrence of the lesions (Figure 3).

## Discussion

### *Clinical Descriptions*

Reports of *M chelonae* as a human pathogen are not uncommon in the literature. More typically recog-



**Figure 2.** The appearance of the largest ulcer by *Mycobacterium chelonae* infection shows a rolled margin.

nized as causing localized cutaneous lesions, the organism has been implicated in disseminated disease as well.<sup>1,3</sup> In particular, mycobacterial pulmonary disease,<sup>3</sup> endocarditis,<sup>1</sup> osteomyelitis,<sup>7-9</sup> ear infections,<sup>7</sup> and keratitis<sup>3</sup> have all been documented. In many such cases of disseminated disease, patients so affected had been previously immunocompromised and often do not have a primary point source of infection.<sup>4,5</sup> A least one case of disseminated subcutaneous nodular infection occurring in the left upper extremity of an immunocompetent patient has been published, however.<sup>10</sup> Cutaneous disease is typically associated with injury to the skin as a result of trauma, injection, or surgery. The disease can be recognized when a wound fails to heal or a previously healed wound breaks down.<sup>3</sup> Cellulitis, abscesses, or individual nodular lesions most commonly appear 3 to 6 weeks after a penetrating skin injury.<sup>1,3</sup> Nosocomial cutaneous disease has been noted to occur after injections of diphtheria-pertussis-tetanus



**Figure 3.** Follow-up examinations revealed complete healing without recurrence of the lesions.

(DPT) vaccine and insulin, open-heart surgery, augmentation mammoplasty, and catheter-related infections, and it has even been linked to use of a contaminated gentian violet solution.<sup>1,7,11-14</sup>

Multiple clinical diagnostic descriptions of cutaneous infection have been reported. Frequently the disease begins as a localized cellulitis that progresses to multiple, recurrent skin abscesses and fluctuant nodules which fail to heal.<sup>1,3</sup> The inflammation is often located on the extremities, and the area might be only minimally tender.<sup>3,4</sup> The chronic ulcerative lesions that can develop have been described as possessing violaceous edges, a nongranulating base, rolled margins, and extensive subcutaneous necrosis that often is realized only during wound debridement.<sup>15</sup> These lesions can be single or multiple, and most commonly they are surrounded by areas of scarred, indurated skin.<sup>1</sup> A great amount of serous discharge is typically seen.

Histologically, biopsy specimens usually show signs of acute inflammation superimposed on chronic dermal and subcutaneous inflammatory

changes.<sup>1</sup> Polymorphonuclear leukocyte infiltration is considerable and can be associated with signs of granulomatous inflammation.<sup>3,4</sup> Necrosis is commonly observed, but true caseation is infrequent.<sup>3</sup> Although foreign body giant cells, Langerhans cells, and histiocytes are often present, acid-fast bacilli are found in less than one third of cases.<sup>3</sup>

Antibiotics, surgical intervention, and controlled localized heating, each attempted alone or in combination, have provided the mainstay of treatment intervention. Until recently, no one treatment modality clearly provided the best disease resolution.

### **Surgical Management**

The surgical literature reporting treatment of *M chelonae* infection stresses adequate debridement of all affected skin and tissues through wide-margin excision and aggressive irrigation.<sup>15,16</sup> After removal of all abscess material, the wound is initially left open and managed with frequent dressing changes.<sup>6</sup> Wide excision is indicated. Local procedures involving only sparse tissue removal have resulted in reemergence of the infection even up to 3 months after surgery.<sup>16</sup> Violaceous macules adjacent to the debridement site are typically the earliest sign of persistent infection.<sup>15</sup> Success of debridement procedures can be difficult to assess because of the slow, progressive nature of mycobacterial growth.<sup>15</sup> It is for this reason that large open wounds must be carefully observed clinically for some time before considering secondary coverage.<sup>6</sup>

Another treatment modality used before the introduction of clarithromycin is controlled localized heating, which has also been successfully shown to eradicate cutaneous mycobacterial disease.<sup>4</sup> In this intervention, a hand-held radio-frequency heat generator uses innate skin resistance to electrical current to elevate surface temperatures. In one study, the generator was used to produce 50°C surface temperatures for 30-second intervals across the dorsum of a hand infected with *M chelonae*.<sup>4</sup> The heat was applied in overlapping fields to allow relative sparing of the normal tissue, and two treatments, 1 week apart, were successful in clearing the infection. At 4 weeks reepithelialization was complete, and at 8 weeks only a minimal scar was seen.<sup>4</sup> No relapse occurred.

### **Chemotherapy**

Historically, pharmacologic therapy for *M chelonae* has met with only moderate success. Treatment

options were limited, and antimicrobial therapy was made difficult by this highly drug-resistant organism.<sup>17,18</sup> Both subspecies *M chelonae* and *M abscessus* required long-term therapy, which often-times ultimately proved unsuccessful.<sup>19</sup> Until recently, parenteral therapy with amikacin and cefoxitin for 2 to 6 weeks remained the mainstay.<sup>2,3</sup>

Clarithromycin is a new macrolide antibiotic that has excellent absorption after oral dosing.<sup>17</sup> It is actively concentrated by tissue phagocytes and produces tissue drug levels several times higher than those in serum.<sup>17</sup> Several recent studies<sup>7,17,20</sup> have reported oral clarithromycin 500 mg twice a day to be extremely effective against *M chelonae*. In one in vitro study, the lowest drug concentration that completely inhibits bacterial growth was shown to be 1 µg/mL or less for 100 percent of species tested. Serum and tissue concentrations of this level are easily obtained after oral dosing.<sup>17</sup> Excellent clinical results, with no abnormal blood cell counts or liver function tests, have been achieved using this drug.<sup>20</sup> Patients taking clarithromycin showed appreciable tolerance, experienced fewer side effects, and had excellent clinical results.<sup>18,20</sup> It should be noted, however, that rare cases of *M chelonae* resistance to clarithromycin have been documented in the literature.<sup>21-23</sup> Thus clear documentation of sensitivity should be obtained before using this antibiotic as the sole course of therapy.

Using this drug regimen, debridement of areas already cleared of devitalized tissue might be unnecessary. In our patient's case, further debridement of the ulcers was unnecessary. Currently, local excision of *M chelonae* ulcers may be reserved for cases in which drug treatment with clarithromycin has failed.

A nonhealing, apparently sterile cutaneous ulcer should suggest the diagnosis of *M chelonae* infection. Culture for mycobacteria should be performed. If *M chelonae* is discovered in the wound and is judged a likely pathogen, clarithromycin therapy is indicated.

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