Chronic Multifocal *Mycobacterium fortuitum* Osteomyelitis Following Penetrating Plantar Trauma

Andrea T. Cruz, MD, MPH, and Shannon B. Antekeier, MD

Abstract

We present the case of a 10-year-old girl with *Mycobacterium fortuitum* osteomyelitis following a plantar puncture wound with vegetative material. Nontuberculous mycobacterial (NTM) skin and soft tissue infections are well described in immunocompromised populations. However, NTM infection can also be seen in healthy hosts following direct inoculation. Magnetic resonance imaging examination demonstrated multifocal midfoot and metatarsal osteomyelitis. Surgical exploration revealed caseation necrosis and a chronic draining sinus tract. Combined surgical debridement and medical therapy resulted in clinical cure. A high index of suspicion and adequate collection and handling of surgical specimens facilitate the diagnosis and treatment of NTM skin and soft tissue infections.

Nontuberculous mycobacteria (NTM) are environmentally ubiquitous organisms present in soil and water; there is no human-to-human transmission of NTM. In areas with low prevalence for tuberculosis, it is estimated that 90-95% of acid-fast bacilli (AFB)-positive cultures are NTM.[1] NTM can cause localized or disseminated disease in immunocompromised individuals and in otherwise healthy young children. Risk factors for NTM disease include human immunodeficiency virus infection,[2] deficiencies in macrophage activation,[3] and cystic fibrosis.[4] Cutaneous infection with NTM species can result from external inoculation, contiguous spread from a deeper infection, or hematogenous dissemination in patients with disseminated disease. In the otherwise healthy child, direct inoculation into tissues following puncture wounds or skin abrasions is the most common transmission route.

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Perhaps the best-described NTM skin/soft tissue infection (SSTI) is the "fish tank" granuloma caused by *Mycobacterium marinum*.[5,6] However, a variety of NTM species with widely differing drug susceptibility profiles can cause SSTIs. These include *M fortuitum, Mycobacterium abscessus, Mycobacterium chelonae, Mycobacterium avium* complex, and *Mycobacterium ulcerans*.[5-10] While NTM infections in other locations (eg, lymphadenopathy) can be managed with surgical therapy alone,[11] NTM SSTIs are treated with a combination of surgical and medical therapy.[12] Consequently, obtaining a microbiologic diagnosis and drug susceptibility testing optimizes management. The patient's guardian provided written informed consent for print and electronic publication of this case report.

Case Report

A 10-year-old, previously healthy, girl presented to the emergency department (ED) with a 3-month history of progressively worsening right foot pain and swelling. She was in her usual state of health until she was walking barefoot in her yard after a hurricane and stepped on vegetative material, sustaining a puncture to the plantar surface of her foot. Since then, she had intermittent purulent drainage refractory to multiple courses of antistaphylococcal and antistreptococcal antibiotics. Multiple prior routine bacterial cultures were negative. At ED presentation, physical examination showed purplish discoloration, swelling, and fluctuance of the plantar medial aspect of her foot; the remainder of her examination was normal.

Laboratory evaluation revealed a white blood cell count of 9,420 cells/μL (differential: 43% neutrophils, 46% lymphocytes, 10% monocytes, 1% eosinophils), hemoglobin of 14.4 gdL, and platelet count of 320,000/μL. Erythrocyte sedimentation rate (ESR) was 7 mm/hr and C-reactive protein (CRP) was less than 0.3 mg/dL. Magnetic resonance imaging demonstrated extensive soft tissue inflammatory changes and increased bone marrow signal intensity involving the cuboid, navicular, lateral cuneiform, and all the metatarsals, consistent with multifocal osteomyelitis (Figure). A draining sinus tract was seen between the first and second metatarsals. Orthopedic consultation was obtained, and the child underwent drainage and debridement of the lesion. Operative findings included a 3x3 cm cavity plantar to the flexor tendons filled with caseous material. The area

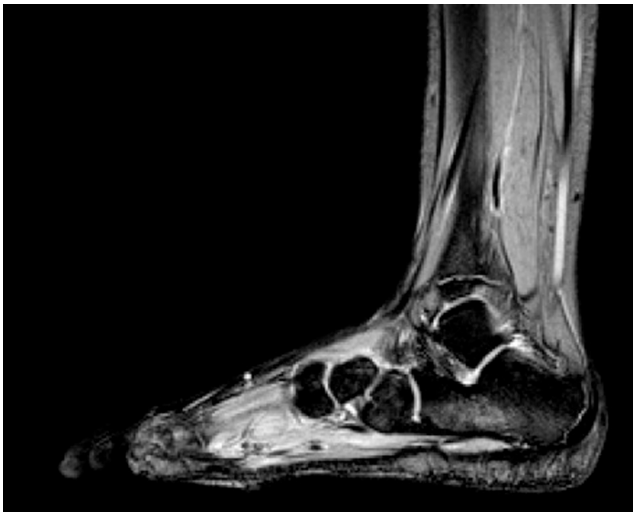

Figure. MRI of the right foot showing inflammatory change within the plantar soft tissues of the right midfoot with increased bone marrow signal in the cuboid, navicular, lateral cuneiform, and metatarsals. A draining sinus tract between first and second metatarsals was seen after gadolinium administration.

was curetted, and aerobic, anaerobic, fungal, and AFB cultures were obtained in addition to histopathology. The latter 3 culture types were ordered given the indolent nature and chronicity of the infection; the wound was closed after irrigation.

Histopathology demonstrated suppurative granulomatous inflammation with rare acid-fast organisms. Acid-fast culture grew *M fortuitum* within 2 weeks; the isolate was susceptible to amikacin, cefoxitin, ciprofloxacin, and sulfamethoxazole. The remaining cultures were negative. Postoperatively, amikacin, ethambutol, rifampin, and azithromycin were started empirically. After susceptibility results became available, the child's regimen was changed to azithromycin, ciprofloxacin, and trimethoprim-sulfamethoxazole to complete 6 months of therapy. She did well, with full return of function at 1-year follow-up, and did not experience adverse effects of medications.

Discussion

The microbiologic differential diagnosis of chronic infections after puncture wounds is extensive, including skin flora pushed into the wound (eg, *Staphylococcus*), bacteria living in shoe lining (eg, *Pseudomonas aeruginosa*), or soil flora (eg, *Pantoea agglomerans*).[13-15] Children with subacute or chronic osteomyelitis often have been treated with multiple courses of broad-spectrum antibiotics, and their lack of response to these drugs should prompt consideration of NTM disease and/or the possibility of undrained fluid collections. Aside from *M marinum*, the NTM species most associated with SSTIs is *M fortuitum*.[7,9,10] In one of the few pediatric case series, over 50% of all NTM SSTIs were due to *M fortuitum*, and most were associated with penetrating trauma.[7]

M fortuitum is 1 of 3 NTM species termed rapidly-growing mycobacteria, with culture-positivity often seen within 1 week.[12] *M fortuitum* is one of the few mycobacterial species that can grow on routine (non–AFB) culture media. Infection of a number of superficial and deep structures has been reported, with increasing reports of infections of foreign bodies and prosthetic devices ranging from central venous catheters to valvular prostheses to ventriculoperitoneal shunts reported.[5-10]

M fortuitum is associated with cutaneous ulcers, subcutaneous nodules, sinus tracts, and abscesses; violaceous discoloration often is noted. When compared with other NTM species, *M fortuitum* was more commonly associated with single lesions due to direct inoculation and, in adult patients, was more likely to be found on the torso than on extremities.[10] Immunocompetent hosts had single lesions and antecedent trauma, compared with immunocompromised persons.[10] In contrast to *M marinum*,[6] lymphocutaneous patterns and sporotrichoid lesions are less common with *M fortuitum*. Deeper infections are less common with NTM species and more common with *M tuberculosis*. There are case reports of *M fortuitum* tenosynovitis, osteomyelitis, and septic arthritis from presumably hematogenous spread,[9] from open fractures[16] and following direct inoculation after penetrating trauma.[17-19] Systemic signs and symptoms of inflammation often are lacking and ESR and CRP usually are normal, compared with routine bacterial causes of osteomyelitis.

Microbiologic diagnosis optimizes therapy. The first step, AFB smear, is estimated to have a sensitivity of 22%-78%.[16] The next step, AFB culture, may be hampered by the fastidious growth requirements of different species. Some of the geographic variation seen in NTM species may be more reflective of laboratory protocols than biological distribution. Given these limitations, it is all the more important to increase the yield of surgically-obtained specimens. This can be done in several ways. First, an adequate volume of tissue and/or fluid should be sent for AFB culture. In a child with subacute or chronic osteomyelitis, routine studies should include aerobic, anaerobic, fungal, and AFB cultures and stains, in addition to histopathology. Second, the fluid sent down should never be on a swab. Most mycobacterial species—despite living in an aquatic milieu—are hydrophobic; the moment the laboratory uses saline or fluid to wash off the swab and inoculate it onto a plate, many organisms will die. The best way to send fluid down for AFB and anaerobic cultures is by placing the liquid into a syringe and sending it to the laboratory for processing. Third, the specimen should be received by the laboratory and processing initiated within 2 hours to maximize culture yield. This may have implications for procedures performed overnight or during off-hours. Finally, if soft tissue or bone is available, this should also be sent to the microbiology laboratory. For many mycobacte-

rial species, the purulent material has few AFB and a predominantly inflammatory response. Culture yield is maximized by also culturing the tissue. This also offers the possibility of earlier clues to diagnosis, as the AFB stains used in tissue are more sensitive than the ones used in the microbiology laboratory. Additionally, findings of granulomas on histopathology may be the first clue to a mycobacterial etiology.

Conclusion

Definitive treatment for NTM infections often is delayed by the indolent growth of the organisms, the stepwise approach of speciating the organism, and the time required for drug-susceptibility testing. Given the wide variation in drug susceptibility patterns, choice of empiric antibiotic therapy is dependent on knowledge of local NTM epidemiology. This strategy is hampered by NTM infections not being reportable infections to health departments. Another approach is to base empiric therapy upon the most likely species to cause disease at certain sites. M fortuitum isolates are almost uniformly susceptible to aminoglycosides and fluoroquinolones, and the majority were susceptible to trimethoprim-sulfamethoxazole and imipenem; macrolide susceptibility was low.[7,12] The American Thoracic Society has published guidelines on empiric and definitive management of NTM infections.[12] The optimal duration of therapy is unknown, but courses of 6 to 12 months have been recommended.[12] Of note, medical monotherapy without surgical debridement is not recommended and has resulted in treatment failures.[12,16] Optimal therapy includes combined surgical and medical management.

Authors' Disclosure Statement

The authors report no actual or potential conflicts of interest in relation to this article.

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