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M. chelonae Soft Tissue Infection Spreading to Osteomyelitis

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A previously healthy, 54-year-old woman presented with Mycobacterium chelonae soft tissue infection and osteomyelitis of her left lower leg. The infection had started from soft tissue emerging at the medial aspect of the distal femur and had spread through the bone because of delayed diagnosis. The largely indolent, 8-month course to diagnosis was attributable to unremarkable clinical manifestations combined with a low index of suspicion such as immunocompetent patient and/or inadequate finding of acid-fast bacilli in a lesion smear, characteristic histopathological features, and culture techniques. Soft tissue infection and osteomyelitis were successfully treated without surgical intervention and with a 6-month course of chemotherapy.

Key Words: Localized cutaneous infection, osteomyelitis, mycobacterium chelonae infections, atypical mycobacterium

INTRODUCTION

Nontuberculous mycobacteria (NTM) have been an uncommon cause of illness in humans until the last decade despite their potential for causing diseases.[1,2] Although the recent rise in the incidence of NTM infection is directly attributable to AIDS and other immunosuppressive diseases, Mycobacterium chelonae does appear to be responsible for rare episodes of NTM. We describe a case of a woman with Mycobacterium chelonae infection that was started from soft tissue emerging at the medial aspect of the distal femur and had spread through the bone.

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CASE REPORT

A previously healthy, 54-year-old woman presented with a history of largely indolent, 8-month course to diagnosis on NTM soft tissue infection and osteomyelitis of her left lower leg. Initially she noticed that the medial aspect of the knee was associated with lesion-like insect bites and she suffered from intermittent pain. She was treated at local clinics, referred to our hospital and then returned to another clinic again.

Upon her referral to our department, we obtained pertinent medical records, x-rays and slides from two of the previous clinics that had cared for her.

Four weeks after the initial onset of symptoms, she visited a local clinic due to progressive pain and an indurated, inflamed lesion with discharge present. There was no fever or constitutional symptom. The provisional diagnosis at the clinic based on symptom manifestation was low-grade infection of bursitis or cellulitis. The patient underwent a 2-week course of cephalexin to recover from low-grade infection but the lesion was not improved. When she was referred to our hospital for further evaluation and treatment, she denied any history of antecedent trauma to her legs, or treatment with systemic steroids or other immunosuppressive agents. There were no risk factors for human immunodeficiency virus infection. All of the initial laboratory studies, including tests for VDRL and HIV, were normal except the erythrocyte sedimentation rate. Physical examination was unremarkable except for tenderness in the medial aspect of the distal femur and the persistent erythema with serous discharge. Knee X-rays were normal (Fig. 1). At this time, a chronic infectious process with abscess was suspected in

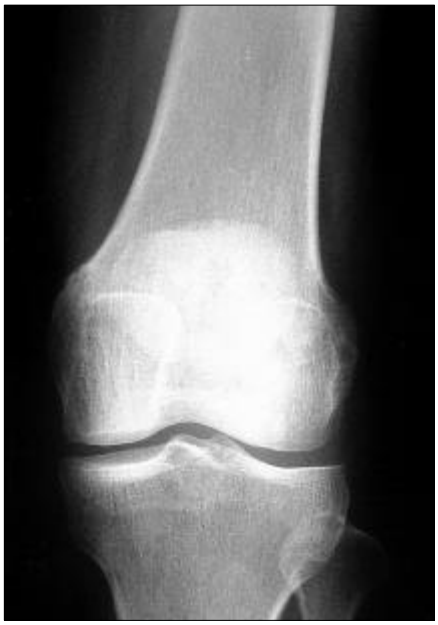

Fig. 1. Six weeks after the initial symptoms, the knee AP view shows no abnormal finding.

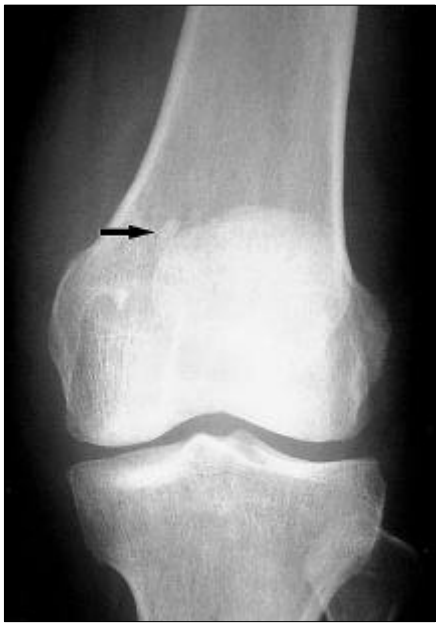

Fig. 2. Twelve weeks after the initial symptoms, the knee AP view demonstrates calcifications of the soft tissue.

the medial aspect of the distal femur. After the abscess was confirmed in the medial aspect of the distal femur with ultrasonogram, she underwent therapeutic intervention, a debridement of the drained sinus. Biopsy and discharge samples drained from the sinus were sent for Gram stain, acid-fast bacteria smears and cultures, routine bacterial cultures and histologic tests. All of these were negative except the histologic tests which revealed chronic inflammation. She began receiving cephalosporin for 14 days. Subjectively, this regimen did not improve the symptoms or discharge. Discharge samples from the drained sinus were sent for acid-fast bacteria cultures and routine bacteria cultures. The culture was positive for staphylococci with resistance except to vancomycin. She consequently began receiving vancomycin (500 mg iv every 6 hours), but the therapy was discontinued after four weeks because of undesirable side effects and the absence of any clinical benefit. Radiographs of the left knee demonstrated calcification in the medial aspect of the distal femur (Fig. 2). We were concerned with the unusual behavior of the clinical manifestation and lack of any response to chemotherapy. At this time, we suspected that the chronic infectious process was a tuberculosis infection. She refused extensive debridement and transferred herself for further evaluation and treatment to another clinic, 2 weeks after being discharged from our hospital, this being 14 weeks after the initial symptoms.

At the new clinic, routine bacterial cultures, and acid-fast bacteria cultures, and acid-fast bacilli smear, but not pathologic tests, were done. Radiological examination of the left knee revealed an apparent periosteal reaction and permeative osteoporotic changes on the distal femur (Fig. 3). MRI examination revealed an intramedullary infection after 20 weeks' initial symptoms (Fig. 4). Empirically she was given rifampicin, ethambutol, isoniazid, and pyrazinamide to combat M tuberculosis for 16 weeks, following the identification of the acid-fast organism at the species level as *M. chelonae*. *In vitro* sensitivity tests had shown sensitivity to clarithromycin, amikacin, cefoxitin, imipenem, tobramycin, doxycycline, ciprofloxacin, and sulfonamide.

Two weeks after therapy with clarithromycin (500 mg twice daily) and amikacin (400 mg im twice daily) was initiated, the patient's condition was improved. The drained sinus was healed completely within three weeks. Although the patient tolerated both drugs, amikacin was stopped dafter 3 weeks due to concerns regarding

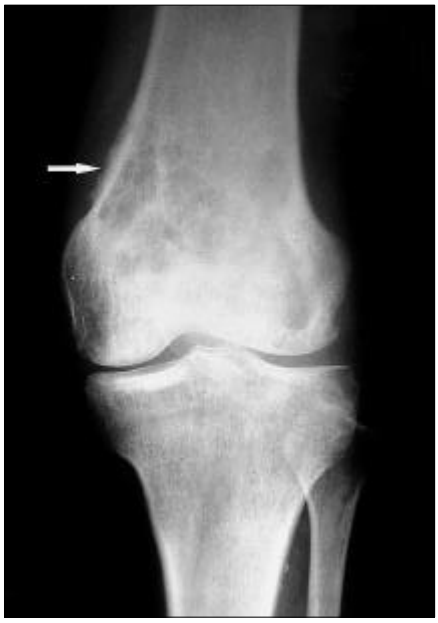

Fig. 3. Twenty weeks after the initial symptoms, the knee AP view demonstrates apparent periosteal reaction on the medial aspect of the distal femur.

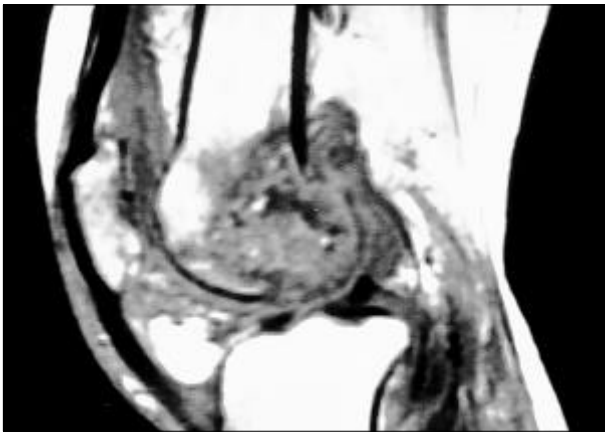

Fig. 4. Twenty weeks after the initial symptoms, Sagittal T1 weighted image demonstrates a low signal intensity area in the posterior knee and in bone marrow of the femoral condyle.

it adverse effects. Therapy with clarithromycin was continued for 6 months, during which time there was no recurrence, nor during the following two years of follow-up.

DISCUSSION

Although all species of NTM have been incriminated in cutaneous NTM disease,[3,4] Mycobacterium chelonae is probably the most common NTM involved in cases of community-acquired infections of skin and soft tissue.[5] The most common infection events are localized traumatic injury, such as accidental penetrating trauma or a medical procedure injury. However, some patients had less serious injury, such as superficial abrasion[6] or no history of trauma.[7,8]

The present patient developed the disease without any wound or medical procedure. We believe that it was unlikely that this infection entered through an unnoticed break in the skin since the incubation period only lasts from 1 to 2 weeks and the clinical manifestations are generally evident within 4 - 6 weeks.[9,10] The exact source of infection was not confirmed in this patient.

A high index of suspicion in an immunocompromised host, the finding of acid-fast bacilli in a smear from the lesion and characteristic histopathological features, with or without organisms, are helpful for making relative diagnosis. A definite diagnosis is confirmed through isolation and identification of the organism.[3,11] Although the incidence of NTM identification has increased since the advent of the acquired immunodeficiency syndrome epidemic and immunosuppressed treatment, it remains low. The incidence of Mycobacterium chelonae, though less than 1 percent, is being reported with increasing frequency in patients who are immunocompromised.[12]

Previous studies reported that granulomatous inflammation was a prominent feature,[11,13-15] but this patient's histological findings of non-specific chronic inflammation were different from those described in other reports. The lack of granulomas in this patient was not surprising, as it has been previously documented that pulmonary and disseminated NTM infection may not have this histological feature.[16-19] Although the diagnosis of NTM disease is based initially on the presence of acid-fast bacilli in smears, NTM species were not isolated from several specimens from this patient. Although previous reports have indicated a low yield of positive smear, repeated smears of pus and tissue are necessary in order to establish the diagnosis.[20]

The largely indolent, 8-month course to diagnosis was attributable to the unremarkable clinical manifestations combined with a low index of suspicion such as immunocompetent patient and/or inadequate finding of acid-fast bacilli in a lesion smear, characteristic histopathological features, and culture techniques.[21,22]

The infection is usually localized in the skin and soft tissue, and most commonly presents to a pyogenic abscess. Occasionally, one progresses slowly with chronic inflammation, ulceration, and sinus tract formation. We supposed that the calcification was evidence of the soft tissue infection as the basic lesion, and was subsequently spread to osteomyelitis because of delayed diagnosis.

In general the most efficacious treatment for infections due to rapidly growing mycobacteria is a combination of adjunctive chemotherapy and surgical resection for abscess or limited bone involvement.[7,22-25] Antimicrobial chemotherapy may be necessary for widespread, or disseminated distribution, and a combination of agents is preferred.[7,23,26] Rapidly growing mycobacteria, including *M. chelonae*, are characteristically very resistant to standard antituberculous drugs and often to antimicrobial agents as well. Sensitivity tests for susceptible drugs are necessary to identify recalcitrant organisms.

Clarithromycin is generally the drug of choice, with its long serum half-life and best tissue penetration, while amikacin is commonly used for *M. chelonae* infections.[3,8] The recommended duration of therapy is usually 4 to 6 months[27] or an extension for 4 - 6 weeks after complete resolution of clinical signs,[28-31] but the optimal duration of treatment remains to be elucidated.

In conclusion, there has been, as far as we know, no previously reported case of soft tissue infection spreading to osteomyelitis in the distal femur due to *M. chelonae* in a non-immunocompromised host. Soft tissue infection and osteomyelitis were successfully treated without surgical intervention and with a 6-month course of chemotherapy. However, our patient demonstrated that atypical mycobacterial infections must also be considered in immunocompetent patients who have a prolonged clinical course.

REFERENCES

1. Grange JM, Yates. Infections caused by opportunist mycobacteria: A review. J R Soc Med 1986;79:226-9.
2. Grange JM. Mycobacterial infections following heart valve replacement. J Heart Valve Dis 1992;1:102-9.
3. The American Thoracic Society. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. American Thoracic Society Statement. Am J Respir Crit Care Med 1997;156 Suppl:S1-S25.
4. Wolinsky E. Nontuberculous mycobacteria and associated diseases. Am Rev Respir Dis 1979;119:107-59.
5. Wallace RJJ, Swenson JM, Silcox VA, Good RC, Tschen JA, Stone MS. Spectrum of disease due to rapidly growing mycobacteria. Rev Infect Dis 1983;5:657-79.
6. Levin RH, Bolinger AM. Treatment of nontuberculous mycobacterial infections in pediatric patients. Clin Pharm 1988;7:545-51.
7. Wallace RJ Jr, Tanner D, Brennan PJ, Brown BA. Clinical trial of clarithromycin for cutaneous (disseminated) infection due to Mycobacterium chelonae. Ann Intern Med 1993;119:482-6.
8. Wallace RJ Jr, Brown BA, Onyi GO. Skin, soft tissue, and bone infections due to Mycobacterium chelonae chelonae: importance of prior corticosteroid therapy, frequency of disseminated infections, and resistance to oral antimicrobials other than clarithromycin. J Infect Dis 1992;166:405-12.
9. Hautmann G, Lotti T. Atypical mycobacterial infections of the skin. Dermatol Clin 1994;12:657-68.
10. Lotti T, Hautmann G. Atypical mycobacterial infections: a difficult and emerging group of infectious dermatoses. Int J Dermatol 1993;32:499-501.
11. Grange JM. Tuberculosis and environmental (atypical) mycobacteriosis bacterial, pathological and immunological aspects. Mycobacterial skin diseases. Dordrecht: Kluwer Academic Publishers; 1989.
12. Horsburgh CR Jr. Epidemiology of disease caused by nontuberculous mycobacteria. Semin Respir Infect 1996; 11:244-51.
13. Gunther SF, Elliott RC, Brand RL, Adams JP. Experience with atypical mycobacterial infection in the deep structures of the hand. J Hand Surg [Am] 1977;2:90-6.
14. Hoffman PC, Fraser DW, Hinson PL. Delayed hypersensitivity reactions in patients with Mycobacterium chelonei and Mycobacterium fortuitum infections. Am Rev Respir Dis 1978;117:527-31.
15. Jenkins PA. Nontuberculous mycobacteria and disease. Eur J Respir Dis 1981;62:69-71.
16. Marchevsky A, Damsker B, Gribetz A, Tepper S, Geller SA. The spectrum of pathology of nontuberculous mycobacterial infections in open-lung biopsy specimens. Am J Clin Pathol 1982;78:695-700.
17. Marchevsky A, Damsker B, Green S, Tepper S. Nontuberculous mycobacterial osteoarticular infections. J Bone Joint Surg 1985;67-A:925-9.
18. Damsker B, Bottone EJ. Nontuberculous mycobacteria

as unsuspected agents of dermatological infections: diagnosis through microbiological parameters. J Clin Microbiol 1980;11:569-72.
19. Marchevsky A, Rosen MJ, Chrystal G, Kleinerman J. Pulmonary complications of the acquired immunodeficiency syndrome: a clinicopathologic study of 70 cases. Hum Pathol 1985;16:659-70.
20. Zeligman I. Mycobacterium marinum granuloma. A disease acquired in the tributaries of Chesapeake Bay. Arch Dermatol 1972;106:26-31.
21. Raffi F, Moinard D, Drugeon HB. Non-tuberculous mycobacterial tenosynovitis. Lancet 1990;335:613.
22. Gunther SF, Levy CS. Mycobacterial infections. Hand Clin 1989;5:591-8.
23. Brown BA, Wallace RJ Jr, Onyi GO, De Rosas V, Wallace RJ 3rd. Activities of four macrolides, including clarithromycin, against Mycobacterium fortuitum, Mycobacterium chelonae, and *M. chelonae*-like organisms. Antimicrob Agents Chemother 1992;36:180-4.
24. Kozin SH, Bishop AT. Atypical Mycobacterium infections of the upper extremity. J Hand Surg [Am] 1994; 19:480-7.
25. Hellinger WC, Smilack JD, Greider JL Jr, Alvarez S, Trigg SD, Brewer NS, et al. Localized soft-tissue infections with Mycobacterium avium/Mycobacterium intracellular complex in immunocompetent patients: granulomatous tenosynovitis of the hand or wrist. Clin Infect Dis 1995;21:65-9.
26. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. Am Rev Respir Dis 1990;142: 940-53.
27. Brown BA, Wallace RJJ. Bacterial Disease. Principles and Practice of Infectious Diseases volume 2: 5th Edition. Phildelphia: Churchill Livingstone; 2000.
28. Pring M, Eckhoff DG. Mycobacterium chelonae infection following a total knee arthroplasty. J Arthroplasty 1996;11:115-6.
29. Woods GL, Washington JA, 2nd. Mycobacteria other than Mycobacterium tuberculosis: review of microbiologic and clinical aspects. Rev Infect Dis 1987;9:275-94.
30. Westmoreland D, Woodwards RT, Holden PE, James PA. Soft tissue abscess caused by Mycobacterium fortuitum. J Infect 1990;20:223-5.
31. Kelley LC, Deering KC, Kaye ET. Cutaneous Mycobacterium chelonei presenting in an immunocompetent host: case report and review of the literature. Cutis 1995;56:293-5.