M. cheloneae Soft Tissue Infection Spreading to Osteomyelitis

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INTRODUCTION

Nontuberculous mycobacteria (NTM) have been an uncommon cause of illness in humans until the last decade despite their potential for causing diseases.⁹¹² Although the recent rise in the incidence of NTM infection is directly attributable to AIDS and other immunosuppressive diseases, Mycobacterium cheloneae does appear to be responsible for rare episodes of NTM. We describe a case of a woman with Mycobacterium cheloneae infection that was started from soft tissue emerging at the medial aspect of the distal femur and had spread through the bone.

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 cephalaxin 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
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 after 3 weeks due to concerns regarding
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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. Microbacterium chelonae is probably the most common NTM involved in cases of community-acquired infections of skin and soft tissue. 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 or no history of trauma.

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. 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. Although the incidence of NTM identification has increased since the advent of the acquired immunodeficiency syndrome epidemic and immuno suppressed 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.

Previous studies reported that granulomatous inflammation was a prominent feature, 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. 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.
The largely indolent, 8-month course to diagnosis was attributable to the remarkable 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.20,22

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. chelonei, 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. chelonei infections.35 The recommended duration of therapy is usually 4 to 6 months27 or an extension for 4–6 weeks after complete resolution of clinical signs,26,31 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. chelonei 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

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