Disseminated Cutaneous Infection with *Mycobacterium chelonae* in a Renal Transplant Recipient

Paraskevi Chatzikokkinou, MD; Roberto Luzzati, MD; Konstantinos Sotiropoulos, MD; Andreas Katsambas, MD; Giusto Trevisan, MD

PRACTICE **POINTS**

- Nontuberculous mycobacteria (NTM) are environmental saprophytes that can cause infection in immunosuppressed individuals as well as immunocompetent individuals with certain predisposing factors.
- It is important for clinicians to consider NTM in the differential diagnosis for patients who present with chronic skin or soft tissue infections.
- Histologic examination and culture of a biopsy specimen followed by polymerase chain reaction assay for genotyping of the specimen are recommended to determine the responsible *Mycobacterium* species.
- New molecular genetic strip tests can differentiate NTM species more quickly.

Mycobacterium chelonae *belongs to a rapidly growing group of nontuberculous mycobacteria (NTM). These organisms are environmental saprophytes that can cause infection in humans. Nontuberculous mycobacteria infections have been described in immunosuppressed patients (eg, in the setting of AIDS or immunotherapy following solid organ transplantation) as well as in immunocompetent patients with certain predisposing factors (eg, recent history of a traumatic wound, recent drug injections, impaired cell-mediated immunity). Due to the increasing prevalence of immune deficiency disorders as well as the rising number of cosmetic procedures performed on healthy individuals, NTM may become a frequent cause of serious morbidity, causing chronic infections of the skin, soft tissue, and lungs. We report a case of* M chelonae *infection in a 61-year-old woman who was receiving immunosuppressive therapy following renal transplantation 6 years prior to presentation. It is important for clinicians to consider NTM in the differential diagnosis for patients who present with chronic skin or soft tissue infections.*

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Drs. Chatzikokkinou, Luzzati, and Trevisan are from the University Hospital of Trieste, Ospedale Maggiore, Italy. Drs. Chatzikokkinou and Trevisan are from the Department of Dermatology and Venereology and Dr. Luzzati is from the Infectious Diseases Unit. Dr. Sotiropoulos is from the Second Department of Internal Medicine–Propaedeutic, Athens University Medical School, Attikon University Hospital, Greece. Dr. Katsambas is from the Department of Dermatology and Venereology, School of Medicine, National and Kapodistrian University of Athens, Andreas Syggros Hospital.
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Correspondence: Paraskevi Chatzikokkinou, Department of Dermatology and Venereology, University Hospital of Trieste, Ospedale Maggiore, Via Stuparich 1, I-34100 Trieste, Italy (chatzikokkinouparaskevi@hotmail.com).

Mycobacterium chelonae, along with *Mycobacterium fortuitum* and *Mycobacterium abscessus*, belongs to a rapidly growing group of nontuberculous mycobacteria (NTM), which are classified as environmental saprophytes found in soil, water, and dust. Under certain circumstances, NTM

can cause infection in humans. Nontuberculous mycobacteria are known to cause infection in immunosuppressed patients (such as in the setting of AIDS or immunotherapy following solid organ transplantation); however, they can also cause serious morbidity in immunocompetent patients with certain predisposing factors (eg, recent history of a traumatic wound, recent drug injections, impaired cell-mediated immunity).[1-4]

We present the case of a patient who presented with multiple reddish blue, nodular, suppurative lesions on the bilateral legs of 1 month's duration. The patient had a history of renal transplantation 6 years prior followed by immunosuppressive therapy. A punch biopsy of a sample nodule was performed, followed by histologic examination and culture of the biopsy specimen, but polymerase chain reaction (PCR) assay for genotyping of the specimen was necessary to determine the responsible *Mycobacterium* species.

Case Report

A 61-year-old woman was admitted to our hospital for evaluation and treatment of multiple subcutaneous nodules on the bilateral legs. The patient had undergone successful cadaveric renal transplantation 6 years prior due to polycystic kidney disease and was undergoing maintenance immunosuppressive combination therapy with tacrolimus 4 mg and methylprednisolone 4 mg daily. No other medications or concomitant diseases were reported.

Physical examination revealed multiple slightly tender, brown to purple papules and nodules on the lower legs ranging in size from 2 mm to 1 cm in diameter (Figure 1), some of which exhibited central necrosis (Figure 2). The patient did not recall any previous trauma to the lower legs. Her body temperature was measured at 37.9°C and no regional lymphadenopathy or any other physical abnormalities were observed. Multiple blood culture samples were negative for bacteria, fungi, and mycobacteria.

During her 2 weeks in the hospital, the patient's tacrolimus and methylprednisolone dosages were decreased to 2 mg daily. Routine laboratory tests and serum chemistry were normal with the exception of elevated creatinine levels (1.88 mg/dL [reference range, 0.6 to 1.2 mg/dL]). Chest radiography and interferon-γ release assay were negative. A punch biopsy from a sample nodule was performed and revealed granulomatous inflammation surrounded by giant cells on histopathology. Microscopic examination of the specimen revealed alcohol- and acid-resistant bacilli on Ziehl-Neelsen staining. A biopsy specimen was cultured on Löwenstein-Jensen medium at 25°C, 37°C, and 42°C according to NTM detection protocol[5] and showed growth of NTM at 37°C. On the basis of the positive culture, genetic analysis of the specimen was performed using a strip test that permits identification of 13 common species of NTM. The organism was identified as *M chelonae*.

While awaiting species identification and results of drug susceptibility testing, treatment with oral clarithromycin 250 mg twice daily was initiated and continued for 10 days until the patient developed gastrointestinal adverse effects, at which point oral ciprofloxacin 250 mg twice daily was substituted. In laboratory testing, the isolated *M chelonae* strain showed sensitivity to ciprofloxacin, clarithromycin, tobramycin, and amikacin at minimum inhibitory concentrations of less than 1, 2, 4, and 16, respectively. Treatment with ciprofloxacin 250 mg twice daily was continued for 6 months, which resulted in

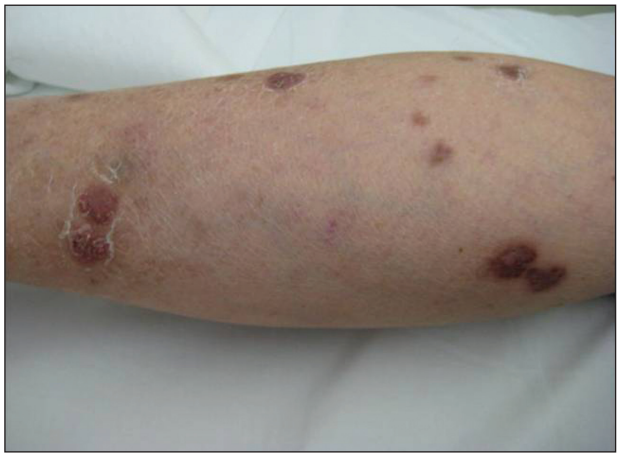

Figure 1. Multiple slightly tender, brown to purple papules and nodules on the lower left leg.

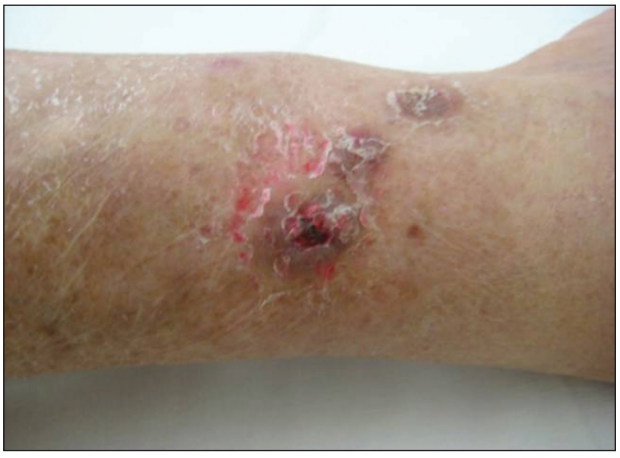

Figure 2. A nodule on the lower right leg exhibited central necrosis.

slow resolution of the lesions until the end of treatment (Figure 3). No recurrence of the lesions was noted at 24-month follow-up, but areas of hyperpigmentation were noted at the lesion sites (Figure 4).

Comment

Mycobacterium chelonae, a member of the NTM group, grows rapidly on Löwenstein-Jensen medium, usually following incubation for 5 to 7 days at temperatures of 28°C to 32°C, and is characterized by its lack of pigmentation. Nontuberculous mycobacteria, which are resistant to standard disinfectants such as chlorine, organomercurials, and alkaline glutaraldehydes, may cause nosocomial outbreaks, infecting otherwise healthy individuals receiving any type of injection (eg, in cosmetic procedures), as well as those with suppressed immunity.[6]

In addition to cutaneous manifestations, NTM may cause various extracutaneous diseases, such as osteomyelitis, infective bronchiectasis, endocarditis, pericarditis, lymphadenopathy, and ocular infections.[1-4] The species M *chelonae* may cause localized skin infections, soft tissue lesions (eg, granulomatous nodules, ulcers, abscesses, sporotrichoid lesions), and cutaneous disseminated infections.

Immunosuppression associated with treatment following renal transplantation was the primary cause of M *chelonae* infection in our patient, as has previously been reported in the literature.[3-4] This was further supported by the lack of prior trauma or invasive procedure (eg, mesotherapy) in the affected areas. Specifically, our patient had more than 5 lesions on the lower legs; in accordance with a previous comprehensive study,[1] the presence of more than 5 lesions indicates a disseminated cutaneous infection, which usually is correlated with immunosuppression (such as in our patient). Localized infections generally are observed in immunocompetent hosts.[1]

The exact pathogenetic mechanism of M *chelonae* infection in our patient is not clear. In patients with suppressed immunity, the variable clinical presentation of infection with NTM often impedes diagnosis. Cutaneous M *chelonae* lesions may be mistakenly diagnosed as Kaposi sarcoma or rarely as pyoderma gangrenosum. The differential diagnosis of subcutaneous nodules includes histoplasmosis, cryptococcosis, blastomycosis, coccidioidomycosis, nocardiosis, mycetoma, sporotrichosis, actinomycosis, and tuberculosis. In our patient, approximately 2 months elapsed between presentation of symptoms and definitive diagnosis, which was less than that reported in previously published cases.[2,7-9]

Histology and tissue culture followed by proper genetic analysis remains the gold standard for diagnosing NTM infection.[10,11] In the interest of patients, time-consuming biochemical analyses should be replaced by molecular genetic diagnostic strip tests, which are fast, exact, and available in commercial kits for both common mycobacteria and additional species.[12]

Once the diagnosis of NTM infection has been established, sensitivity testing is mandatory to guide targeted therapy; however, clinicians should bear in mind that susceptibility testing does not guarantee clinical success, as correlations of susceptibility testing and clinical response have not been assessed.[8] Standard antituberculous drugs (eg, isoniazid, rifampin, pyrazinamide) have no role in the treatment of M *chelonae* infection. The first-line antibiotics are clarithromycin, tobramycin, and linezolid,

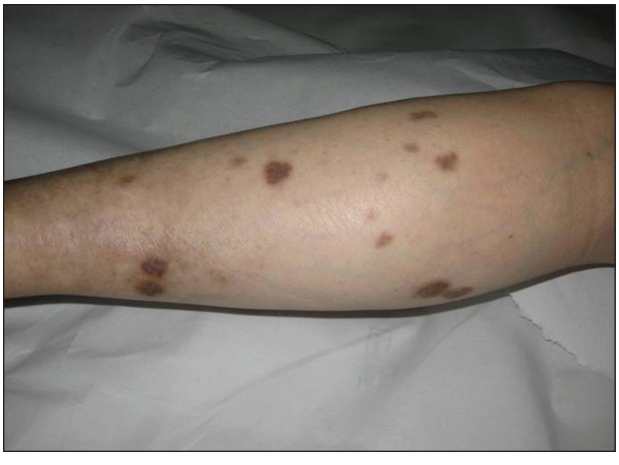

Figure 3. Following 6 months of treatment with oral ciprofloxacin 250 mg twice daily, nodules on the left leg had resolved and papules had decreased in size.

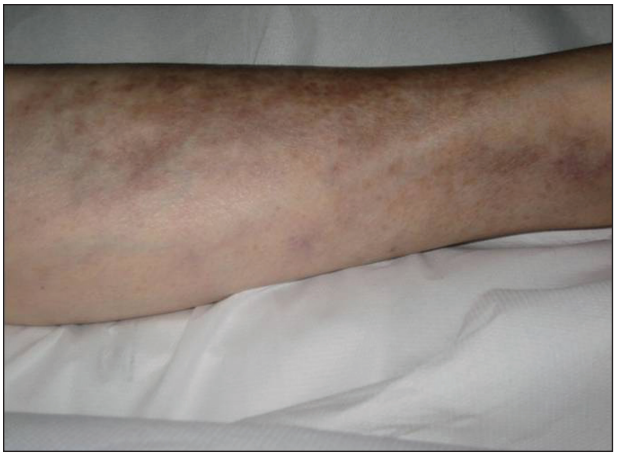

Figure 4. Skin lesions had resolved without recurrence at 24-month follow-up, although hyperpigmented areas remained.

followed by imipenem, amikacin, clofazimine, doxycycline, and ciprofloxacin.[10] Optimal outcomes have been reported in patients treated both with antibiotics and with surgical debridement. Although monotherapy with quinolones is not recommended for treatment of infection with NTM due to the high risk of mutational resistance, our patient received long-term antibiotic treatment with ciprofloxacin over a 6-month period and showed no recurrence at 24-month follow-up.

Conclusion

Clinicians who treat patients with chronic skin or soft tissue infections should consider infection with NTM in the differential diagnosis, particularly in patients with suppressed immunity, but also in immunocompetent patients following any invasive procedure. Detailed medical history and skin biopsy followed by histology and culture are recommended for the diagnosis. Infection with NTM requires rapid action. Sensitivity testing is necessary in choosing an effective treatment. New molecular genetic diagnostic strip tests can differentiate species of NTM sooner than biochemical analyses, thereby helping clinicians initiate appropriate antimicrobial treatment in a timely fashion.

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