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Mycobacterium chelonae infection in an immunocompromised patient presenting as multiple papulonodules on the leg

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Abstract

Mycobacterium chelonae is a rapidly growing nontuberculous mycobacteria that is a rare cause of cutaneous infections in both immunocompromised and immunocompetent patients. The clinical presentation is heterogeneous and non-specific, and therefore, despite an increasing incidence of these infections, patients are often misdiagnosed. Here we present the case of an immunocompromised 73-year-old female patient that developed tender, erythematous, violaceous to brownish papules and nodules on both the anterior and posterior aspects of her left lower leg. A histopathological examination revealed acid-fast bacilli, and a tissue culture identified *M. chelonae*. Disease resolution was achieved with long-term targeted antibiotic therapy based on susceptibility testing.

Keywords: *Mycobacterium chelonae*, immunosuppression, infection, nontuberculous mycobacteria

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Introduction

More than 170 species of nontuberculous mycobacteria (NTM) have been identified, not all of which have been documented to cause disease in humans (1). The most commonly reported cutaneous infections with NTM are caused by *Mycobacterium marinum* (2). *M. chelonae* is classified as an acid-fast, rapidly growing NTM that usually grows in subcultures within 1 week (3) and is most commonly associated with human skin and soft tissue infections (4, 5). Infections with *M. chelonae* may affect both immunocompromised and immunocompetent patients (6). The pathogen is an environmental saprophyte and has been found in soil, water, and aquatic animals and plants (7–10).

Case presentation

A 73-year-old immunocompromised female with a previous diagnosis of erythema nodosum presented with a 4-month history of erythematous, violaceous to brown papules and nodules on her left lower leg. She reported that the papules and nodules remained stable; however, she observed that new ones were appearing. They were tender to palpation, non-pruritic, and never ulcerated. The skin lesions were tender, erythematous, violaceous to brownish nodules and papules approximately 0.5 to 3 cm diameter, with a fine overlying scale and no ulcerations or exudation. The lesions were located on the anterior and posterior aspects of her left lower leg (Fig. 1). Regional lymph nodes were not enlarged. However, the left lower leg was swollen. The patient denied any fever, night sweats, or other constitutional symptoms. She denied having an infectious disease in the previous year, abdominal pain, arthralgia, myalgia, prior exposure to tuberculosis, recent travel abroad, or any changes in her urine or feces. She denied any recent exposure to swimming pools. However, she said she does some gardening and does have a pond with waterlilies and goldfish in her garden. She sometimes had a productive cough in the previous few years. The skin changes were previously treated with moderate to potent topical steroids and an increased dose of systemic steroids that was slowly tapered. The patient denied any trauma to the area. She underwent a kidney transplantation 8 years previously, for which she was receiving three-track immunosuppressive therapy with tacrolimus, prednisolone, and mycophenolate mofetil. Her concomitant diseases were diabetes mellitus, arterial hypertension, osteoporosis, and atrial fibrillation, which were adequately treated with no recent changes in therapy.

Due to the atypical clinical picture, extensive laboratory examinations were performed (complete blood count, C-reactive protein, erythrocyte sedimentation rate, liver function tests, tumor markers, ACE, ANCA antibodies, QuantiFERON Gold Plus, and serology for hepatitis B and C), which revealed no clinically relevant alterations for her skin manifestations.

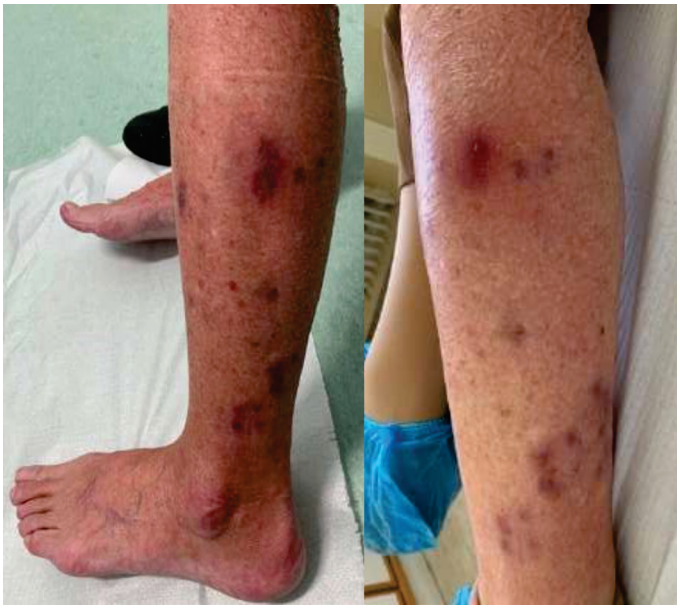

Figure 1 | Violaceous to brownish nodules and papules, with a fine overlying scale on the anterior and posterior aspects of the left lower leg.

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A biopsy of the nodular lesion was performed, and the sample was sent for histopathological diagnosis. The biopsy of the sample (Fig. 2) showed suppurative and granulomatous dermatitis. A Ziehl–Neelsen stain, performed on a direct sample of the biopsy, was positive for acid-fast bacilli (Fig. 3). Another punch biopsy of the lesion was cultured, and *M. chelonae* was identified as the causative organism. Due to the possibility of pulmonary infection, a sputum test and a chest X-ray were conducted; the former was negative and the latter revealed no pathologic lesions in the lungs.

Based on the results of antibiotic susceptibility testing, systemic treatment with oral clarithromycin and parenteral tobramycin was started. Tobramycin was initiated due to three-track immunosuppressive therapy and possible drug interactions. Due to drug interactions, the dose of tacrolimus was adjusted and frequently monitored. Tobramycin was discontinued after 4 months due to decreased kidney function and improper excretion of tobramycin. Clarithromycin was continued for the 6-month period. Slow but steady improvement after 6 months of antibiotic therapy was observed, and only post-inflammatory hyperpigmentation remained with no new lesions.

Discussion

We report a case of an immunocompromised patient with a confirmed diagnosis of *M. chelonae*, who presented with nodules and papules on her leg mimicking erythema induratum. We suspect that the infection might have been caused by gardening or contact with pond water.

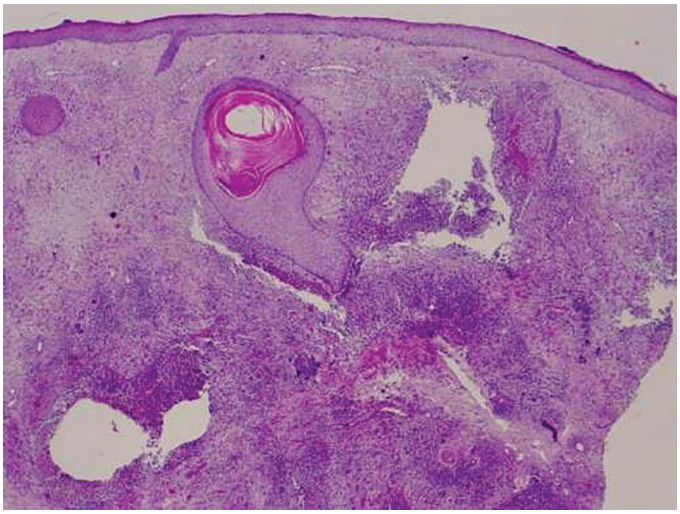

Figure 2 | Histopathological examination, H&E, suppurative and granulomatous dermatitis.

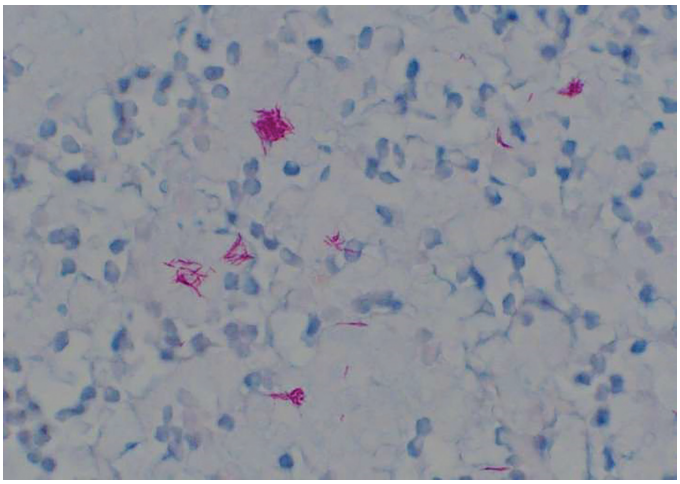

Figure 3 | Ziehl–Neelsen stain, positive for acid-fast bacilli.

M. chelonae was first isolated in 1903 from a sea turtle (*Chelonia corticata*) (11) and is a rapidly growing NTM (RGM). No specific seasonal trends or geographical distribution is currently known because cases have been reported worldwide; furthermore, no affinity with age, sex, or race has been documented (5). The incubation period usually lasts from 4 to 6 weeks, and the infection can affect the skin, soft tissues, eyes, lungs, lymph nodes—as lymphadenitis, especially in children (12)—and osteoarticular system, and it can also cause disseminated disease (3). *M. chelonae* is a low-virulence bacterium and is rarely found as a cause of skin infections in immunocompetent and immunocompromised patients. When immunocompetent patients are affected, it is usually following trauma to the skin, which includes both invasive and minimal procedures, intradermal and subcutaneous injections, and minor skin trauma, such as laparoscopic surgery (13), blepharoplasty (14), tattoos (15), mesotherapy (16), pedicures (17), liposuction and lipofilling (18), acupuncture (19), sclerotherapy (20), and contact lens wear (21). *M. chelonae* infections can also affect immunocompromised patients; for example, cancer patients (22), HIV patients (23), patients with hematological malignancies (24), patients on corticosteroid therapy (25–27) and biologic therapy, especially on tumor necrosis factor alpha inhibitors (28, 29), patients with autoimmune disorders (30), and patients following organ transplantation (31), as was the case in the patient presented (6, 32). Infections with RGM have been increasing over time, possibly due to greater use of immunosuppressive medications, more numerous surgical procedures, and enhanced detection, as well as increasing age of the population, which may contribute to risk factors for the disease (33). The cutaneous clinical manifestations of *M. chelonae* are extremely variable and can present as painful or asymptomatic erythematous or livedoid papules, plaques or nodules, pustules, drainage fistulas, recurrent abscesses, folliculitis, scrofuloderma, sporotrichoid lesions, hard-to-heal ulcers, or panniculitis, mainly on the limbs (3, 5, 6, 25, 34). Immunocompetence status may alter the clinical presentation. Compared to other RGMs, *M. chelonae* is more likely to cause multiple lesions; moreover, patients with multiple lesions are more likely to be immunosuppressed, as was the case in our patient (32, 35). Furthermore, patients presenting with cutaneous nodules are more likely to have a disseminated disease (32). Disseminated and pulmonary disease should be excluded in all immunocompromised patients, using sputum samples for acid-fast bacilli and a chest X-ray to exclude other disorders, such as malignancy and tuberculosis (36, 37). Our patient presented with violaceus to erythematous nodules and papules, which presented in a sporotrichoid pattern. The differential diagnosis included an atypical presentation of erythema induratum, traumatic panniculitis, erythema nodosum, and cutaneous polyarteritis nodosa. Based on her immunocompromised status, several infectious etiologies were included in the differential diagnosis: sporotrichosis, tuberculosis, bartonellosis, tularemia, nocardiosis, histoplasmosis, cryptococcosis, blastomycosis, coccidioidomycosis, actinomycosis, and other types of atypical mycobacteria (especially *M. marinum*).

In order to acquire the correct diagnosis, it is mandatory to perform a detailed patient history and physical examination, followed by a biopsy, which includes both histological analysis and tissue culture (3, 5, 6, 34). Histological features are nonspecific and do not have pathognomonic features; they include acute and chronic inflammation, microabscesses, and granulomas (38–41). Therefore,

acid-fast staining is required to identify the organism, followed by culture in appropriate mediums, to determine the correct mycobacterial species. Upon diagnosis of the species, antibiotic susceptibility testing is essential to guide effective and targeted therapy of the infection (3, 5, 6, 34, 36). RGMs are resistant to standard antituberculosis agents. Clarithromycin has long been the basis of therapy for RGM; however, the antibiotic alone should no longer be used as a monotherapy due to resistance and can be used in *M. chelonae* infection as empiric therapy when awaiting susceptibility results. Concurrent therapy with two antibiotic agents for 4 to 6 months is recommended (36, 42, 43). Adjuvant surgical procedures, such as excision, debridement, incision, and drainage, may also be performed. Furthermore, regular follow-up is recommended to monitor clinical response and adverse reactions.

Conclusions

Because RGM infections include a wide array of nonspecific and subtle clinical presentations, a high index of suspicion is necessary for the correct diagnosis. Furthermore, with the rise of RGM, NTM should be considered in the differential diagnosis of both immunocompromised patients and immunocompetent patients, especially after surgical procedures and trauma. Due to the reasons mentioned above, the diagnosis is often delayed, even though the disease calls for rapid action. We stress the importance of a multidisciplinary approach in such patients, as well as susceptibility testing and targeted prolonged antibiotic treatment.

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