# Primary Cutaneous Infection by *Mycobacterium avium*: A Case Report and Literature Review

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*Nontuberculous mycobacteria (NTM) are becoming increasingly important cutaneous pathogens as the number of susceptible patients increases. Nevertheless, primary cutaneous infection by one particular species,* Mycobacterium avium complex *(MAC), remains relatively unusual, particularly in immunocompetent patients. We review the English-language literature on primary cutaneous MAC in patients who were neither immunocompromised nor pharmacologically immunosuppressed. We offer an additional report of a healthy patient who presented to our clinic with primary cutaneous MAC following seemingly innocuous trauma to the leg.*

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The term *nontuberculous mycobacteria* (NTM) defines a heterogeneous group of nonmotile, acid-fast bacilli that are ubiquitous in the environment. The ever-rising importance of these organisms mirrors their increased prevalence, which comes from mounting numbers of immunosuppressed patients and a rise in surgical procedures. Affected individuals may present with pulmonary infection, lymphadenitis, disseminated disease, skin infection, or hard and soft tissue disease.[1]

Regarding cutaneous disease, nearly all species of NTM have been implicated, including *Mycobacterium avium complex* (MAC). In human immunodeficiency virus (HIV)–negative patients, MAC is primarily a pulmonary pathogen. In patients with HIV, it is more commonly disseminated or can present as gastrointestinal tract disease. *Mycobacterium avium complex* rarely produces cutaneous manifestations in any patient population. In those exceptional instances of cutaneous expression, skin findings usually are secondary to disseminated disease[2] and are seen almost exclusively in immunocompromised hosts.[2,3] We present a case of a primary cutaneous infection with MAC following presumed traumatic inoculation in a healthy patient.

## Case Report

A 57-year-old woman presented with an erythematous scaly plaque on her right shin. The lesion initially was diagnosed as allergic contact dermatitis and treated with desoximetasone ointment 0.25%. When it failed to improve in 2 months, a biopsy was performed, which showed stasis dermatitis with superficial and deep eosinophils and pseudoepitheliomatous hyperplasia. Accordingly, the patient was treated with halobetasol ointment and advised to utilize compression stockings. When the lesion persisted, she was treated with econazole cream and referred to our clinic for patch testing.

On physical examination, she had an erythematous plaque with hyperkeratotic scale on the right shin (Figure) and xerotic erythematous patches affecting the right lower leg, left shin, and left foot. Examination was unremarkable for any lymphadenopathy. The patient denied explicit knowledge of trauma but reported exposure to an organic fertilizer on her legs while gardening prior to the onset of the lesion. Patch testing showed an allergy to a fragrance ingredient, and a repeat open application test by the patient confirmed allergy to econazole cream. However, these allergic reactions were felt to be secondary, and the differential diagnosis included

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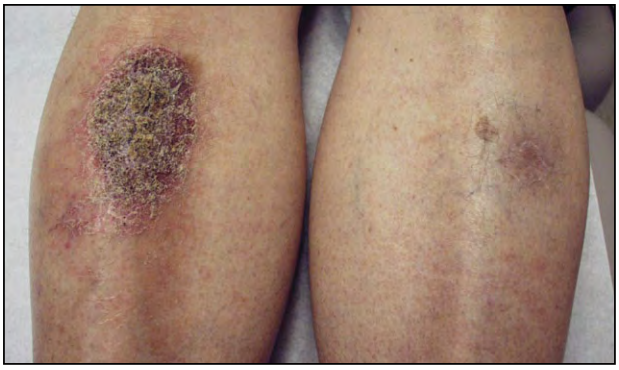

Erythematous scaling plaque on the right shin.

Majocchi granuloma, deep fungal infection, mycobacterial infection, and staphylococcal infection, along with superimposed irritant and allergic contact dermatitis. The patient was started on doxycycline hyclate 100 mg orally twice daily, along with desoximetasone ointment applied to the left shin and petroleum jelly to the right shin. Although the lesions resolved elsewhere, the plaque on the right shin progressed to a red plaque with several deep pustules. A second biopsy of the right shin showed pseudoepitheliomatous hyperplasia with intraepidermal and dermal neutrophils as well as increased vasculature. Periodic acid–Schiff and Fite stains were negative for fungi and mycobacteria, respectively. Treatment was initiated for suspected mycobacterial infection with minocycline hydrochloride 100 mg twice daily and hyperthermia therapy in the form of warm compresses. Chest radiograph did not reveal any abnormalities. Laboratory investigations (ie, complete blood cell count, thyroid function tests, urinalysis, electrolytes) were all within reference range, with the exception of the hematocrit, which was slightly low at 34.3% (reference range, 35%–45%). Cultures returned positive for MAC after 1 month's duration.

The infectious disease service was consulted and treatment with clarithromycin, ethambutol, and rifampin was initiated. After 3 weeks of therapy, the patient's lesions mildly improved.

## Comment

*Mycobacterium avium complex* collectively refers to *M avium*, *Mycobacterium intracellulare*, and other unnamed species. Although it is the most common atypical *Mycobacterium* causing disseminated disease, MAC rarely is implicated in primary cutaneous lesions. Because its preferred means of contagion is the respiratory tract, MAC is commonly associated with pulmonary infection in individuals with underlying lung disease.[1]

Additionally, MAC may gain entry through traumatic inoculation or result in gastrointestinal tract disease. As with other NTM, immunocompromised patients are particularly susceptible to infection and may exhibit subsequent hematogenous dissemination to the skin, central nervous system, and the reticuloendothelial system.[3] Dissemination typically follows gut infection. Skin infection may be a product of direct inoculation, cervical lymphadenitis with overlying abscess formation, or disseminated disease.[1,4]

*Mycobacterium avium complex* may be isolated from any number of environmental sources including soil, freshwater, seawater, dairy products, animal tissues, and house dust.[5] Despite its omnipresence and its ability to infect nearly any organ system, MAC tends to be underdiagnosed due to a low index of suspicion. Its nonspecific and polymorphous presentation lends itself to misdiagnosis. The differential diagnosis of cutaneous MAC may include other infectious and granulomatous diseases such as *Mycobacterium marinum* infection (fish tank granuloma)[3]; lepromatous leprosy[6]; lupus vulgaris[7]; sarcoidosis[8-10]; prurigo nodularis[11]; and, as in the present report, dermatitis. There has even been a case report of a particularly uncommon presentation appearing as rosacea.[12]

Clinically, cutaneous disease may present as diversely as scaling papules,[6] ulcerated or subcutaneous nodules,[4,13] abscesses,[14] painless ulcers,[9] panniculitis, ecthymalike lesions, draining sinuses,[13] or granulomatous plaques.[7] Distribution also may vary, with most cases of primary cutaneous disease presenting with localized skin involvement affecting the extremities, face, neck, back, and groin, usually sparing the palms and soles.[15] Disseminated skin involvement has been reported less frequently. Cox and Strausbaugh[16] reported a case of long-term untreated *M intracellulare* in an immunosuppressed patient that progressed to involve large portions of the head and trunk. Similarly, Epps et al[8] reported 2 patients misdiagnosed with sarcoidosis who progressed to develop widespread cutaneous infection. Lugo-Janer et al[13] reported a case of disseminated cutaneous MAC associated with osteomyelitis in a healthy 11-year-old patient following trauma to the foot. Regarding the clinical pattern, lesions may be solitary or multiple localized cutaneous lesions (nonlymphocutaneous lesions at the site of trauma or lesions having a sporotrichoid distribution[3,15,17]) or disseminated cutaneous lesions. Bartralot et al[3] reported that 7 of 29 patients (24%) without immunologic deficiencies had more than 1 type of presenting lesion; overall, healthy patients had fewer lesions and more localized disease in comparison to immunosuppressed patients.

Disseminated MAC has been well-described in immunosuppressed patients. However, primary

**Immunocompetent[a] Patients With Primary Cutaneous[b] *Mycobacterium avium Complex* Infection Reported in the Literature[c]**

| Reference | Case No. | Age, y | Sex | Distribution | Clinical Appearance | Underlying Condition | Treatment |
|---|---|---|---|---|---|---|---|
| Schmidt et al[19] | 1 | 28 | M | Dorsal right foot | Ulcer with erythematous borders and yellow shaggy base with sinus tract formation | History of minor abrasion to the affected area | Isoniazid, cycloserine, streptomycin |
| Lugo-Janer et al[13] | 2 | 11 | F | Lateral right foot with later dissemination to all extremities and infraorbital area | Ulcerated plaques, draining sinuses, erythematous subcutaneous plaque and nodules | History of trauma to the right foot with fracture of metatarsal bones and subsequent osteomyelitis | Unknown |
| Ichiki et al[4] | 3 | 9 | F | Abdomen, hips, thighs | 10 subcutaneous nodules, 2 ulcers | Suspected exogenous inoculation | Isoniazid, cycloserine, clarithromycin, excision |
| Escalonilla et al[20] | 4 | 57 | M | Wrist | Nodule | None | Excision |
| Nassar et al[10] | 5 | 43 | F | Right earlobe, progression to entire ear and cheek | Infiltrating plaque progressing to a nodular infiltrating lesion | None initially, but treated with oral steroids, thalidomide, methotrexate, and infliximab for suspected sarcoidosis | Clarithromycin, ethambutol, rifabutin |

Abbreviations: M, male; F, female.

[a]Patients without conditions associated with impaired immunity (eg, human immunodeficiency virus/AIDS, diabetes mellitus) or conditions requiring treatment with systemic immunosuppressive therapy.

[b]*Mycobacterium avium complex* could not be isolated from a visceral, deep (hard or soft tissue), or hematogenous source.

[c]Not included in this table are 3 reported cases of primary cutaneous *Mycobacterium avium complex* noted by Street et al[21]; nothing is known regarding these patients' immune status. Furthermore, Nedorost et al[12] reported a case of primary cutaneous infection in an immunocompetent host; however, the authors later found the patient to have bone involvement.

cutaneous involvement without bacteremia remains relatively uncommon, even in immunocompromised patients, and is exceedingly rare in healthy individuals.[18] Schmidt et al[19] presented the first case of primary inoculation mycobacteriosis in an apparently healthy individual. However, due to chest radiograph abnormalities, the authors could not conclusively rule out hematogenous spread from a primary pulmonary focus.[19] In the ensuing 38 years, according to a PubMed search of articles indexed for MEDLINE using the terms *Mycobacterium avium complex* and *Mycobacterium avium-intracellulare*, the English-language literature contains only 5 reports of primary cutaneous MAC in nonimmunosuppressed patients (Table). Nassar et al[10] reviewed a case in which an initially immunocompetent individual presented with a nodular infiltrating lesion on the right cheek and ear. When immunosuppressive therapy was initiated for suspected sarcoidosis, the lesion extended to more extensive areas of the cheek and the entire external ear,[10] which may attest to the predilection for disseminated disease in immunocompromised patients.

Of note, the Japanese literature has produced a large subset of pediatric cases in which healthy children have presented with multiple subcutaneous or ulcerating nodules. Prior to their own reported case, Ichiki et al[4] noted 9 cases of primary cutaneous MAC in Japanese literature.

The treatment of MAC includes monotherapy or combination therapy with a variety of antibiotics, along with possible excision. Although susceptibility testing may be advantageous in cases of prior drug exposure, clinical recurrence, or resistant disease, it has been suggested that MAC may be treated based on established sensitivity patterns. This same study recommended that in vitro sensitivity studies are in fact only necessary for clarithromycin in patients previously exposed to macrolides.[22] In their earlier review of the literature, Kakinuma and Suzuki[5] concluded that clarithromycin, minocycline, ciprofloxacin, and ansamycins individually or in various combinations are the best forms of antibiotic treatment; however, surgical excision is advocated when possible. In the same report, the authors presented a case of primary cutaneous MAC treated efficaciously with a more simplified regimen consisting of minocycline in combination with hyperthermia therapy.[5] More recently, successful treatment has been demonstrated with a combination of clarithromycin, ethambutol, and rifabutin.[10] An earlier case presented by Kayal and McCall[15] made use of a similar regimen, substituting levofloxacin for rifabutin; considerable improvement was reported in an HIV-positive patient with a sporotrichoid cutaneous MAC infection. Excisional therapy for localized disease or for solitary lesions refractory to treatment has proven favorable, if not definitive, in a few reported cases.[4,5,14]

Despite the extensive literature on MAC, there is a paucity of reports on primary cutaneous *M avium* in healthy individuals. Primary cutaneous MAC, as with other cutaneous NTM infections, typically is secondary to trauma in immunocompetent hosts. The literature on cutaneous mycobacteriosis secondary to NTM other than MAC is extensive. Similar to our patient, there has been a report of cutaneous MAC infection in a patient with a preceding history of gardening and no explicit recollection of trauma to the affected area.[15] Another patient was a farmer, implicating soil and vegetation as a possible reservoir.[7] However, both of these patients were immunodeficient. Of the remaining cases of healthy patients presented in the Table, an uncertain history or suspicion of trauma is thought to be implicated in the cause of disease. Our case highlights how a seemingly innocuous substance, even within the context of full immunocompetence, can be implicated in cutaneous disease.

Accordingly, as more cases of cutaneous MAC in healthy individuals are reported, a certain degree of suspicion must be maintained, particularly in patients who present with unresponsive lesions and a history of possible trauma with environmental exposure.

As corroborated by prior cases, a misdiagnosis can indeed progress to more extensive skin involvement and added morbidity for the patient.

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