Title
Mycobacteria infection in an immunocompetent patient with no risk factors: evaluation and management of non-healing majocchi granuloma-type nodule

Journal
Dermatology Online Journal, 19(8)

Authors
Siamas, Katherine
Khachemoune, Amor

Publication Date
2013

DOI
10.5070/D3198019260

Volume 19 Number 8
August 2013

Case report

Mycobacteria infection in an immunocompetent patient with no risk factors: evaluation and management of non-healing majocchi granuloma-type nodule

Katherine Siamas MD, Amor Khachemoune, MD

Dermatology Online Journal 19 (8): 3

SUNY Downstate, Brooklyn, New York

Correspondence:

Amor Khachemoune MD
SUNY Downstate
Brooklyn, New York
amorkh@gmail.com

Abstract

Atypical mycobacterial infections are more commonly described among immunocompromised patients, although there has been an increasing incidence in recent years of infections in immunocompetent hosts. Normally preceding trauma is a risk factor for infection. We describe a case of *Mycobacteria chelonae* infection in a healthy individual with no risk factors.

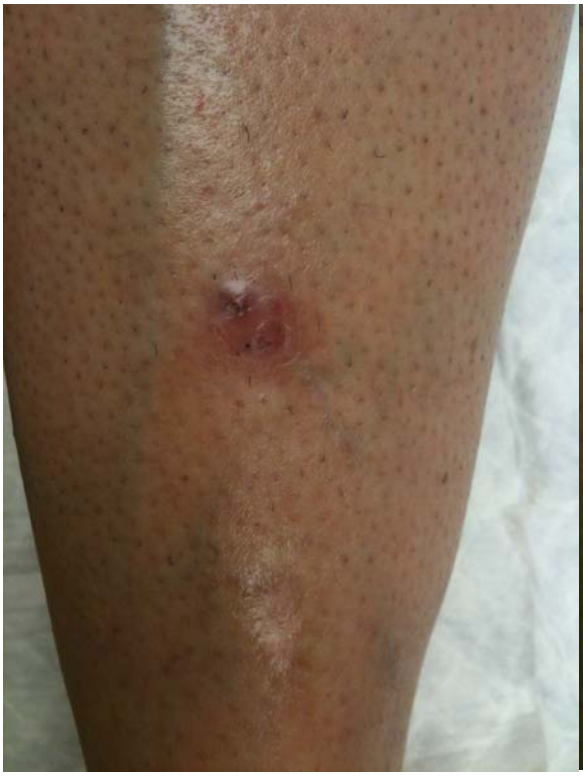
Introduction

The atypical mycobacteria are a group of organisms that can cause a variety of clinical diseases. Reported non-tuberculoid mycobacteria (NTM) causing cutaneous infections exceed a dozen species. These organisms are found in the natural environment such as in water, soil, and dust. They are also found on animals and even as commensals on humans [1]. Immunosuppression and preceding trauma, either incidental or iatrogenic, are risk factors for infection. The clinical presentation is varied and can consist of pustules, keratotic plaques, nodules, and ulcers with draining sinuses. Although immunocompromised patients are usually more susceptible to infection with atypical mycobateria, there has been an increasing incidence of infections caused by NTM in recent years in both immunocompromised and normal hosts [2]. We report a case of *Mycobacteria chelonae* infection in an immunocompetent woman with no preceding history of trauma or iatrogenic procedures. Although *M. chelonae* infection is more common in immunocompromised hosts, there are few case reports in the literature of infection occurring in healthy individuals with no risk factors [3,4].

Case synopsis

A 48 year-old woman presented for evaluation of a persistent nodule on the right shin for approximately a two-month duration. The lesion was asymptomatic and she did not report any trauma. The patient is otherwise healthy, she works as a housekeeper, and she has no history of an abnormal immune status. She does not take any immunosuppressive medications. She denied any recent travel or cosmetic and medical procedures. She had been initially seen by her primary care physician and treated with a course of cephalexin for 7 days for presumed cellulitis. At this time a bacterial culture was performed and results were negative, but she was started on trimethoprim and sulfamethoxazole (Bactrim Double strength) , twice daily, for one week. She then presented to the dermatology department because of lack of improvement and the bactrim was continued for four more weeks. The presumed diagnosis based on history and physical examination included atypical mycobacterial infection.

On skin examination was there was a solitary irregularly shaped nodule on the right shin measuring approximately 1.2cm x 1.2 cm with surface ulcerations and superficial crusting with surrounding erythema (Figure 1). Prior to her dermatology visit the patient had a complete physical examination performed by her primary care physician with no significant findings other than the persistent nodule on the right shin and a negative review of symptoms.



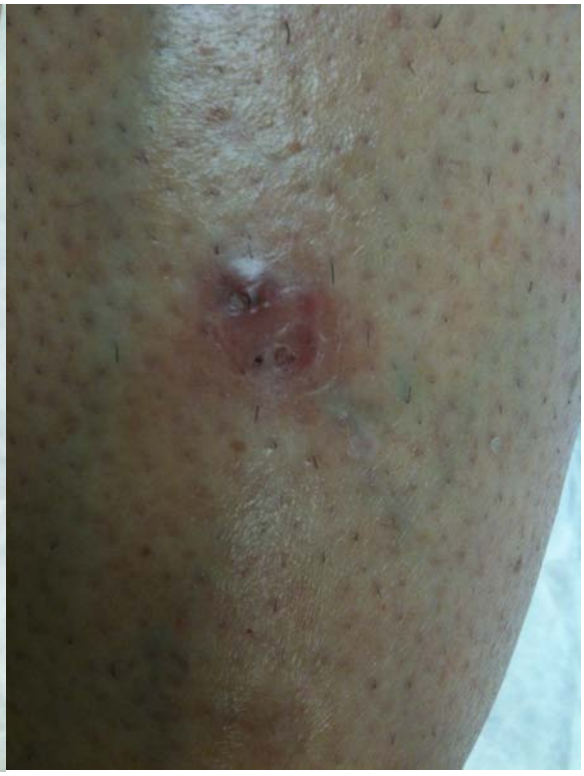
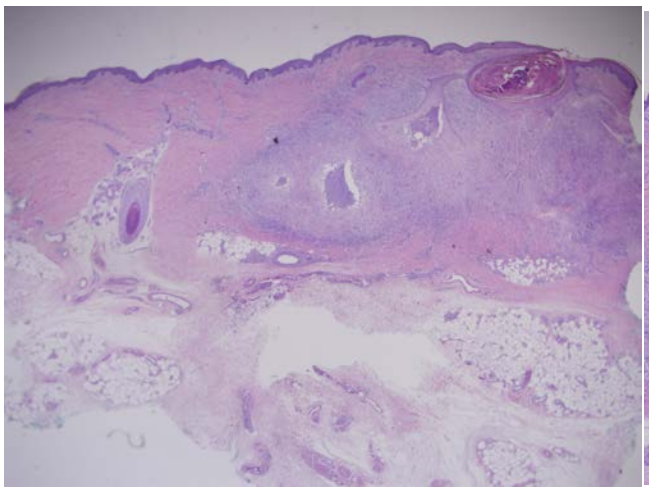


Figure 1 **Figure 2**

Figures 1 and 2. Erythematous solitary nodule on the shin with surface ulcerations and superficial crusting.

An excisional biopsy was performed after a course of five weeks of the trimethoprim and sulfamethoxazole course given the lack of improvement and at the patient's request for a definitive diagnosis and culture. The specimen was sent in formalin for H&E (hematoxylin and eosin) and normal saline for tissue culture. Histopathologic examination revealed a suppurative granulomatous dermatitis with a dense inflammatory infiltrate consisting of numerous neutrophils, histiocytes, lymphocytes, and eosinophils within the dermis. The gomori methenamine silver (GMS), periodic acid-Schiff (PAS), and acid-fast bacillus (AFB) stains were negative for microorganisms. Mycobacterial cultures were grown at a reference laboratory and after approximately two weeks, acid-fast bacilli were seen in broth culture, and a subculture was performed isolating Mycobacteria chelonae-abscessus. The patient was treated with clarithromycin for four weeks at a dose of 500mg twice daily. At follow up after four weeks of clarithromycin, the physical examination revealed a well healing scar, although there was persistent crust and erythema. Thus, clarithromycin was continued; the literature suggests a lengthy treatment course anywhere from 4-6 months.



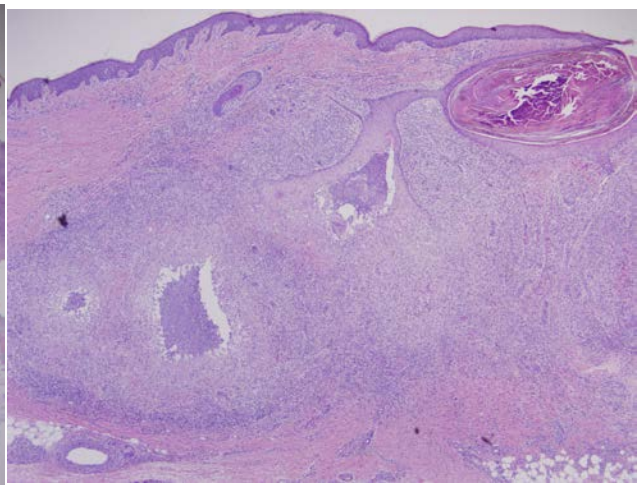


Figure 3(20x) **Figure 4 (40x)**

Figures 3 and 4. Biopsy showing a dense, diffuse inflammatory cell infiltrate that contains numerous neutrophils, histiocytes, lymphocytes, and eosinophils within the dermis. There are a proliferation of fibroblasts, small blood vessels, and thickened collagen bundles. The GMS, PAS, and AFB stains failed to reveal microorganisms (20x and x40).

Discussion

The NTM are a group of acid-fast bacteria that cause a wide variety of clinical diseases. These organisms were not identified as human pathogens until the 1950s [2]. Runyon originally classified the NTM into four broad categories based on colony pigmentation, optimal growth temperature, and growth rate [2]. These organisms were typically regarded as non-pathogenic because of their low virulence, but they are now recognized as true pathogens and important causes of human disease [5].

NTM are ubiquitous in the environment and important reservoirs include water, soil, and animals. They can also be found as colonizers of medical equipment [5]. More than 125 species have been identified and about 60 are known to cause clinically significant disease [5]. There is a wide spectrum of clinical diseases caused by NTM, which can be divided into chronic pulmonary infections, superficial lymphadenitis, skin and skeletal infections, and disseminated disease [2,5]. The most common species causing skin disease are the rapid growing mycobacteria (RGM), including *M. chelonae, abscessus, and fortuitum*. In addition *M. marinum* and *M. ulcerans* are also specifically responsible for cutaneous diseases [2].

The incidence of NTM infection has increased in recent years [2,7]. The increasing incidence of infection is likely secondary to increased recognition of NTM clinical syndromes, the greater number of skin medical procedures, and the overall greater prevalence of immunosuppression in the general population, particularly patients with HIV/AIDs [2,5].

The most common skin presentations of NTM infection are non-healing wounds or skin ulcers, or in cases of deeper involvement, chronically draining subcutaneous nodules or fistulas. Progression to tenosynovitis or osteomyelitis is also possible. Usually in immunocompetent patients the infection presents as a localized form, whereas in immunocompromised patients the clinical picture is more commonly that of disseminated skin lesions or a sporotrichoid pattern [2,8]. Cutaneous infections with these organisms usually occur secondary to traumatic inoculation most commonly from the environment or from contaminated surgical instruments [1,8]. It is frequently associated with contaminated water sources, although contaminated methylene blue and gentian violet used for skin marking have also been implicated [8]. In addition to the above, there are reports in the literature of NTM infection associated with tattoos, acupuncture, subcutaneous insulin therapy, whirlpool footbaths, and nail salons [7,9]. In immunocompromised patients, however, there is usually no history of preceding trauma.

Diagnosis: Infection is easily misdiagnosed because of its clinically subtle or non-specific presentation. In addition, a low index of suspicion, inadequate culture and/or biopsy samples, and negative results of conventional microbiologic studies can lead to misdiagnosis or late diagnosis. The gold standard in diagnosis is the identification of mycobacterium species in culture [7]. Given that cultures can take weeks, properly performed smears can aid in the diagnosis and are sensitive in about 50%. The preferred method of smear examination is with auramine-rhodamine fluorescently stained smear [5]. Specimen collection can be accomplished using a liquid sample directly inoculated onto the appropriate medium or sterile tissue in a saline-based homgenate [5]. It should be noted that special conditions are needed for the growth of these microorganisms in culture [10]. Cultivation requires long term incubation in rich media and inactivation of rapidly growing microorganisms whose growth impedes observation of mycobacterial colonies [11]. Although routine culture media such as blood or chocolate agar will support the growth of some NTM, the preferable medium is Lowenstein-Jensen with contaminant- inhibiting antimicrobials with the addition of 2% ferric ammonium citrate added if M. *haemophilum* is suspected [7]. The cultures should also be saved under refrigeration for sensitivity testing and biochemical identification by a reference laboratory [7]. NTM growth is affected by temperature, as proposed by the Runyon classification, and this parameter can be useful for colony survival and differentiation among various species of NTM [7]. Although most mycobacteria grow optimally between 35 and 37°C in 5% to 10% CO2 atmosphere, a subset including M. *marinum*, M. *ulcerans*, M. *chelonae*, and M. *haemophilum* thrive better between 25 and 33°C [5]. It can take anywhere from 6-8 weeks for cultures to confirm mycobacterial infections [11]. Detection of mycobacterial DNA by amplification of ribosomal RNA has emerged as a vastly used modality in recent literature [12]. Polymerase chain reaction should be used for rapid initial detection of infection in order to initiate prompt therapy and then confirmation achieved through culture [12]. Thus, clinical suspicion and appropriate microbiologic diagnostic tools are important for the diagnosis of NTM [2].

Treatment: It is important for the distinction to be made between different species of mycobacteria because this directly impacts therapeutic decisions. Culture and in vitro sensitivity tests are advisable prior to treatment of these infections because of the variable sensitivity of different antimicrobials against these strains [13]. These organisms are usually resistant to typical anti-tuberculosis medications. There is no firmly established standardized treatment regimen for NTM infections [12]. For most NTM infections macrolide-based drug regimens are an effective option [5]. Based on reported NTM sensitivities, to date nearly all *M. Chelonae* are sensitive to clarithromycin [1,4]. If clarithromycin is not an option, other agents with activity against NTM such as linezolid, rifampin, amikacin, sulfas, and clofazamine are available, although toxicities can be limiting [5, 13]. If there is ulceration, an excisional approach and/or debridement may be necessary and is usually curative [1]. A combination of the above may be needed. The literature does support the use of multidrug therapy because there have been cases of drug resistance to single agents [4]. Of note, a prolonged course of antibiotics is usually necessary to eradicate the infection even with early clearing of lesions [4,12]. Tailoring of the treatment is necessary based on immunologic status, depth of infection, and response to treatment

[14]. A minimum of 3 months of antibiotic therapy, or continuing treatment for at least 3-6 weeks after wound healing is recommended to prevent recurrence [12]. Appropriate imaging should be performed to exclude the presence of bone infection; this will increase the duration of treatment to a minimum of 6 months [5]. In addition, removal of prosthetic material involved is essential to treatment because resolution of NTM infection is unlikely with antibiotics alone [5]. Although the optimal length of antibiotic therapy has not been established, recent studies suggest that antibiotic therapy should be continued for 3-6 months [12]. The development of newer antibiotics with a better side effect profile, such as tigecycline, is promising for the treatment of rapidly growing mycobacteria [5]. The recommended antibiotics and treatment are listed in Table 1.

Table 1: Classification and treatment of most common atypical mycobacteria causing cutaneous disease [1,5,6]

Runyon Classification and characteristics	Mycobacteria species	Treatment	Schedule
Class I Photochromogens Slow Growing Yellow-orange pigment when exposed to light	M. kansasii (primarily a pulmonary pathogen)	Isoniazid + rifampin + ethembutol (plus either streptomycin or clarithromycin)	9-18 months
	M. marinum	Minocycline>doxycycline; Clarithromycin+rifampin; rifampin + ethambutol; TMP-SMX; ciprofloxacin	Two agent therapy for 3-6 months, including 1-2 months after symptoms resolve
Class II Scotochromogens Slow Growing Yellow-orange pigment production with or without light	M. scrofulaceum (primarily causes local lymphadenitis)	Cutaneous involvement occurs rarely Treatment of choice is surgery	
Class III Nonchromogens Slow growing No pigment production	M. avium complex (cutaneous involvement occurs primarily in the case of disseminated disease)	Ethambutol + clarithromycin or azithromycin + rifampin or rifabutin	Multidrug regimen with a macrolide base for 6-12 months
	M. ulcerans	Rifampin + streptomycin(early lesions); nitrogen oxide releasing topical creams, hyperbaric oxygen Surgical excision	1-2 months (early lesions)
	M. haemophilum	Rifampin + clarithromycin +/- amikacin Surgical excision	6-9months (longer in immunocompromised patients)
Class IV Rapid Growers No pigment production Production of mature colonies	M. fortuitum	Ciprofloxacin, levofloxacin, clarithromycin, azithromycin, TMP-SMX, minocycline, doxycycline, amikacin Surgical excision	Minimum 4 months

in ≤ 7 days	M. chelonae-abscessus*	Clarithromycin+ doxycycline or ciprofloxacin Surgical excision	Minimum 4-6 months**

* M. chelonae and abscessus are often grouped together as M. chelonae-abscessus complex, and treatment is the same, although they are considered separate species.
**bone infection minimum of 6 months

Conclusion

In summary, NTM infections should be suspected if there is a persistent non-healing lesion, especially in an immunocompromised patient or if there is a history of preceding trauma or surgical intervention. In addition, this case and others in the literature demonstrate that there may not necessarily be any such history. If there is a high clinical suspicion, mycobacterial cultures should be performed early on because the bacilli of M. Chelonae are not easily identified on H&E and Ziehl-Neelson staining, making an accurate diagnosis difficult [3].

References

1. Ramos-e-Silva Marcia and MC Ribeiro de Castro. Mycobacterial Infections. In: Bolognia Textbook of Dermatology. 2nd Edition. Spain: Mosby Elsevier publishing; 2008. p. 1107-1125.
2. Lee WJ, Kang SM, Sung H, Won CH, Chang SE, Lee MW, Kim MN, Choi JH, Moon KC. Non-tuberculous mycobacterial infections of the skin: a retrospective study of 29 cases. J Dermatol. 2010 Nov;37(11):965-72. [PMID: 21039785]
3. Chung WK, Kim MS, Kim CH, Lee MW, Choi JH, Moon KC, Koh JK. Cutaneous Mycobacterium chelonae infection presenting as symmetrical plaques on both shins in an immunocompetent patient. Acta Derm Venereol. 2009 Nov;89(6):663- [PMID: 19997711]
4. Halpern J, Biswas A, Cadwgan A, Tan BB. Disseminated cutaneous Mycobacterium chelonae infection in an immunocompetent host. Clin Exp Dermatol. 2010 Apr;35(3):269-71. [PMID: 20500199]
5. Jarzembowski JA, Young MB. Nontuberculous mycobacterial infections. Arch Pathol Lab Med. 2008 Aug;132(8):1333-41. Review. [PMID: 18684037]
6. Jogi R, Tyring SK. Therapy of nontuberculous mycobacterial infections. Dermatol Ther. 2004;17(6):491-8. Review. PubMed [PMID: 15571497]
7. Khan FA, Khakoo R. Nontuberculous mycobacterial cutaneous infections: an updated review. Cutis. 2011 Oct;88(4):194-200. Review. [PMID: 22106729]
8. Shim TN, Lew TT, Preston PW. Disseminated cutaneous Mycobacterium chelonae. Lancet Infect Dis. 2012 Mar;12(3):254. [PMID: 22361431]
9. Kennedy BS, Bedard B, Younge M, Tuttle D, Ammerman E, Ricci J, Doniger AS, Escuyer VE, Mitchell K, Noble-Wang JA, O'Connell HA, Lanier WA, Katz LM, Betts RF, Mercurio MG, Scott GA, Lewis MA, Goldgeier MH. Outbreak of Mycobacterium chelonae infection associated with tattoo ink. N Engl J Med. 2012 Sep 13;367(11):1020-4. Epub 2012 Aug 22. PubMed [PMID: 22913660]
10. Bamias G, Daikos GL, Siakavellas SI, Kaltsa G, Smilakou S, Katsogridakis I, Vafiadis-Zouboulis I, Ladas SD. Atypical mycobacterial infection presenting as persistent skin lesion in a patient with ulcerative colitis. Case Report Med. 2011;2011:480987. Epub 2011 Oct 5. [PMID: 22007233]
11. Radomski N, Cambau E, Moulin L, Haenn S, Moilleron R, Lucas FS. Comparison of culture methods for isolation of nontuberculous mycobacteria from surface waters. Appl Environ Microbiol. 2010 Jun;76(11):3514-20. Epub 2010 Apr 2. PubMed [PMID: 20363776]; PubMed Central [PMCID: PMC2876437].
12. Lim JM, Kim JH, Yang HJ. Management of infections with rapidly growing mycobacteria after unexpected complications of skin and subcutaneous surgical procedures. Arch Plast Surg. 2012 Jan;39(1):18-24. Epub 2012 Jan 15. [PMID: 22783486]
13. Esteban J, Martín-de-Hijas NZ, Fernandez AI, Fernandez-Roblas R, Gadea I; Madrid Study Group of Mycobacteria. Epidemiology of infections due to nonpigmented rapidly growing mycobacteria diagnosed in an urban area. Eur J Clin Microbiol Infect Dis. 2008 Oct;27(10):951-7. Epub 2008 May 6. [PMID: 18458972]
14. Dodiuk-Gad R, Dyachenko P, Ziv M, Shani-Adir A, Oren Y, Mendelovici S, Shafer J, Chazan B, Raz R, Keness Y, Rozenman D. Nontuberculous mycobacterial infections of the skin: A retrospective study of 25 cases. J Am Acad Dermatol. 2007 Sep;57(3):413-20. Epub 2007 Mar 26. [PMID: 17368631]