

Cutaneous infection due to *Mycobacterium immunogenum*: an European case report and review of the literature

Elena Garcia-Zamora, Henar Sanz-Robles, Marta Elosua-Gonzalez, Ximena Rodriguez-Vasquez, Jose Luis Lopez-Estebarez.

Affiliations: Department of Dermatology, Hospital Universitario Fundacion Alcorcon, Madrid, Spain.

Corresponding Author: Elena Garcia-Zamora, Calle Budapest 28922, Alcorcón, Madrid, Spain, Tel: 34-916219504, Email: garciazamoraelena@gmail.com

Abstract

In the last few years, the incidence of cutaneous infections caused by nontuberculous mycobacteria is increasing. Since *Mycobacterium immunogenum* was first described in 2001, few case reports have been described, all of them in the American continent. We report a case with cutaneous infection caused by this newly discovered NTB in Europe.

A 65-year-old woman presented with a 3-months history of pruritic lesions on abdomen. Examination revealed erythematous inflammatory papules, pustules, and crusts. Three weeks later, mycobacteria were cultured from the biopsy specimen. *Mycobacterium immunogenum* was identified based on susceptibility test results and polymerase chain reaction (PCR) restriction enzyme analysis. Treatment with clarithromycin was started. *M. immunogenum* is a nontuberculous mycobacterium that was first described by Wilson et al. in 2001 as a rapidly growing variety and new species in the *Mycobacterium chelonae-Mycobacterium abscessus* group. PCR-restriction analysis of a 439-bp segment of the hsp65 gene and/or sequencing the species-specific region of the 16S rDNA can confirm this new species. Since the description of *M. immunogenum*, 8 clinical case reports have been published, most involving cutaneous infections and all of them in the American continent. We present a case of cutaneous infection caused by *M. immunogenum* in a Spanish woman.

Keywords: *Mycobacterium immunogenum*, nontuberculous mycobacteria, cutaneous infection

Introduction

In the last few years, the incidence of cutaneous infections caused by nontuberculous mycobacteria (NTB) is increasing owing to a high prevalence of immunosuppressed patients and invasive procedures common in the general population (mesotherapy, tattoo, manicure, surgery, injections, and insulin pumps). Since *Mycobacterium immunogenum* was described in 2001, few case reports have been reported, all of them in the American continent. We present a case of cutaneous infection caused by this newly discovered NTB in Europe.

Case Synopsis

A 65-year-old healthy Spanish woman presented with a 3-month history of pruritic lesions on abdomen. She was allergic to penicillin, procaine, tetracyclines, and streptomycin. She suffered from depression, hypertension, and hypercholesterolemia and was currently under therapy with lexapro, trankimazin,



Figure 1. Erythematous inflammatory papules, pustules and crust in different stages of evolution involving abdomen.

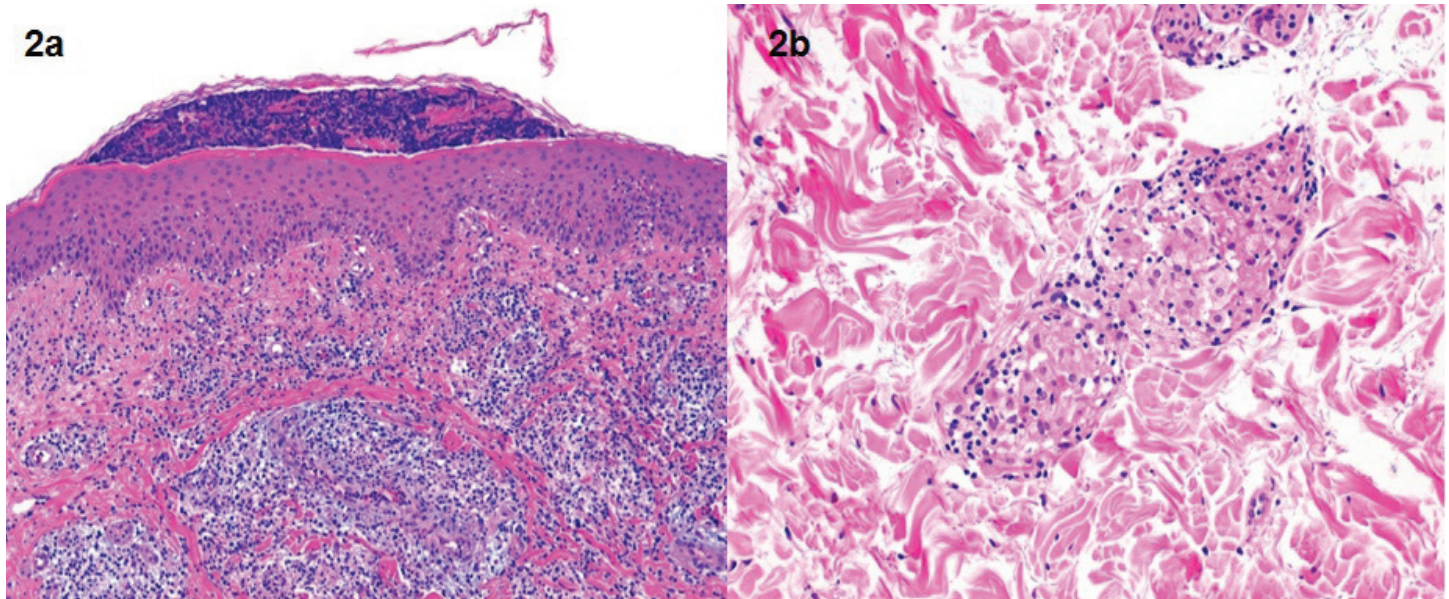


Figure 2. A) Subcorneal sterile pustule and lymphoplasmacytic inflammatory infiltrate, H&E, 40x. B) A non-necrotizing granuloma, H&E, 40x.

atorvastatin, and antihypertensive drugs. Examination revealed erythematous inflammatory papules, pustules, and crusts in different stages of evolution distributed on her abdomen and lateral trunk (**Figure 1**). We performed three skin biopsies, which demonstrated a subcorneal sterile pustule and lymphoplasmacytic inflammatory infiltrate (**Figure 2a**) with non-necrotizing granulomas (**Figure 2b**). A bacterial and fungal culture from a pustule showed normal skin flora. A general blood test, chest radiography, and an abdominal ultrasound showed no abnormalities. Our patient was first treated with topical betamethasone and fusidic acid with a 10-day period of systemic corticosteroids without improvement. After incubation for 3 weeks, mycobacteria were cultured in the biopsy specimen. *M. immunogenum* was identified based on susceptibility test results and polymerase chain reaction (PCR) restriction enzyme analysis. Treatment with clarithromycin was started based on antibiotic susceptibility. Our patient has finished her sixth month of clarithromycin and all the lesions have resolved without adverse effects.

Case Discussion

Nontuberculous mycobacteria, especially rapidly growing mycobacteria (RGM), are environmental organisms found in water, soil, dust, and aerosols, which can form biofilms and are resistant to standard disinfectants. In most cases, cutaneous infections result from dermatological or plastic surgery

procedures, abscesses at injection sites, or contact with contaminated water [1]. *M. immunogenum* is an NTB that was first described by Wilson et al. in 2001 as RGM and a new species in the *Mycobacterium chelonae-Mycobacterium abscessus* group [2]. It has been frequently recovered from metal-working fluids and implicated in cases of hypersensitivity pneumonitis among metal workers [3]. Owing to the lack of molecular identification methods before 2001, probably *M. immunogenum* had previously been identified phenotypically as *M. chelonae* or *M. abscessus*. PCR-restriction analysis of a 439-bp segment of the *hsp65* gene and/or sequencing the species-specific region of the 16S rDNA can now confirm this new species [3].

Since the initial description of *M. immunogenum*, 8 clinical case reports have been published describing infection with this organism, most describing cutaneous infections (**Table 1**). To date, 25 patients with *M. immunogenum* confirmed infection have been described. The first 11 patients correspond to the discovery of the mycobacterium species. In these cases, the clinical isolation was performed in urine and corneal samples, skin biopsies, joint fluid, or bronchoalveolar lavage fluid. No other data from these isolations are known. After that, 14 new patients have been reported with *M. immunogenum* infection. Most of them are young people with neither comorbidities nor immunosuppression. However, Shedd et al. described 2 cases of skin lesions identified

Table 1. Characteristic of patients with *Mycobacterium immunogenum* infection.

	Year	N° cases	Country	Clinical specimen	Clinical presentation	IS	Enviromental source
Wilson et al. [1]	2001	11	USA	Clinical specimen and fluids	Skin, cornea, urine, blood, joint fluid	Yes/No	Metal-working /fluids
Loots et al. [4]	2005	1	Guatemala	Skin biopsy	Leg ulcer	No	Contaminated water
Sampaio et al.	2006	5	Brazil	Corneal scraping	Keratitis post LASIK	Unknown	Contaminated material (Surgical material)
Del-Castillo et al. [5]	2009	3	Argentina	Skin biopsy	Mesotherapy site injections	Unknown	Contaminated material (Injectable mesotherapy solutions)
Shedd et al. [6]	2010	2	USA	Skin biopsy/ drainage	Surgical wound/ leg plaque	No/ multiple myeloma	Contaminated material (Razor blade/Surgical material)
Mitchel et al. [7]	2011	1	USA	Skin biopsy	Infected tattoo	No	Contaminated material (Tatto reservoir)
Biggs et al. [3]	2012	1	USA	Blood	Leg ulcers, fever, hypotension	Renal transplant	Unknown
Greninger et al. [10]	2015	1	USA	Cerebral abscess	Headache, fever, visual impairment	No	Contaminated water
García-Zamora et al.	2016	1	Spain	Skin biopsy	Abdominal papules and pustules	No	Unknown

IS: immunosuppression

by 16S rRNA gene sequencing, one of which involved an elderly man with multiple myeloma treated with dexamethasone and IL-6 inhibitor [6].

More than 50% of patients presented with 1-3 months history of persistent cutaneous papules, nodules, or plaques with evolution despite treatment with topical corticosteroids and several antibiotic systemic cycles. Neither fever nor chills nor general discomfort was noted with the exception of the first case of disseminated *M. immunogenum* infection reported by Biggs et al., which involved a 59-year-old man with renal transplant presenting with septic shock and skin lesions [1, 7]. In most cases, some invasive procedure of the skin had been performed in the previous weeks or months. Del-Castillo et al. described 28 cases of skin lesions after mesotherapy [5]; PCR-restriction analysis of hsp65 gene identified *M. immunogenum* in three of ten biopsy samples, and Mitchell et al. described cutaneous lesions at the site of a recent tattoo [7].

Once the diagnosis was made, all patients described

received antibiotic treatment based on antibiotic susceptibilities. Most were treated with clarithromycin plus other antibiotic (levofloxacin or ciprofloxacin) or amikacin over approximately 6 months without complications and with complete resolution of the lesions.

Optimal treatment for *M. immunogenum* remains unknown. Retrospective studies of cutaneous NTM infections recommended the use of clarithromycin because of excellent in vitro susceptibility as well as clinical response [8]. Treatment of disseminated cutaneous infection with an organism in the *M. chelonae*-*M. abscessus* group should last at least 6 months and consist of clarithromycin plus additional agents, given the risk of clarithromycin resistance with monotherapy (estimated 10-20%), [9].

Conclusion

We present a new case of cutaneous infection caused by *M. immunogenum* in Europe in an immunocompetent Spanish woman with erythematous inflammatory papules and pustules

on the abdomen. No invasive or esthetic procedures were performed in our patient and we could not discover any possible source of infection.

References

1. Biggs HM, Chudgar SM, Pfeiffer CD, Rice KR et al. Disseminated Mycobacterium immunogenum infection presenting with septic shock and skin lesions in a renal transplant recipient. *Transpl Infect Dis* 2012; 14: 415-421. [PMID: 22548769].
2. Wilson RW, Steingrube VA, Bottger EC, et al. Mycobacterium immunogenum sp. nov., a novel species related to Mycobacterium abscessus and associated with clinical disease, pseudo-outbreaks and contaminated metalworking fluids: an international cooperative study on mycobacterial taxonomy. *Int J Syst Evol Microbiol* 2001; 51 (Pt 5): 1751-1764. [PMID: 11594606].
3. Wallace RJ Jr, Zhang Y, Wilson RW, Mann L et al. Presence of a single genotype of the newly described specie Mycobacterium immunogenum in industrial metalworking fluids associated with hypersensitivity pneumonitis. *Appl Environ Microbiol.* 2002 Nov;68(11):5580-4. [PMID: 129929].
4. Loots MA, de Jong MD, van Soolingen D, Wetsteyn JC, Faber WR. Chronic leg ulcer caused by Mycobacterium immunogenum. *J Travel Med* 2005;12 (6): 347-349. [PMID: 16343388].
5. Del-Castillo M, Palmero D, Lopez B, et al. Mesotherapy-associated outbreak caused by Mycobacterium immunogenum. *Emerg Infect Dis* 2009; 15 (2): 357-359. [PMID: 19193300].
6. Shedd AD, Edhegard KD 2nd, Lugo-Somolinos A. Mycobacterium immunogenum skin infections: two different presentations. *Int J Dermatol* 2010; 49 (8): 941-944. [PMID: 21128921].
7. Mitchell CB, Isenstein A, Burkhart CN, Groben P, Morrell DS. Infection with Mycobacterium immunogenum following a tattoo. *J Am Acad Dermatol* 2011; 64 (5): e70-e71. [PMID: 21496684].
8. Dodiuk-Gad R, Dyachenko P, Ziv M, et al. Nontuberculous mycobacterial infections of the skin: a retrospective study of 25 cases. *J Am Acad Dermatol* 2007; 57: 413-420. [PMID: 17368631].
9. Brown-Elliott BA, Wallace RJ Jr. Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. *Clin Microbiol Rev* 2002; 15 (4): 716-746. [PMID: 12634376].
10. Greninger AL, Langelier C, Cunningham G, Keh C et al. Two rapidly growing mycobacterial species isolated from a brain abscess: first whole-genome sequences of Mycobacterium immunogenum and Mycobacterium Ilatzerense. *J Clin Microbiol* 2015; 53 (7): 2374-2377. [PMID: 25926490].