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Journal
Dermatology Online Journal, 23(10)

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Publication Date
2017

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

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Abstract
In the last few years, the incidence of cutaneous infections caused by nontuberculous mycobacteria is increasing. Since Mycobacterium immunogenenum 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 immunogenenum was identified based on susceptibility test results and polymerase chain reaction (PCR) restriction enzyme analysis. Treatment with clarithromycin was started. M. immunogenenum 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. immunogenenum, 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. immunogenenum in a Spanish woman.

Keywords: Mycobacterium immunogenenum, 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 immunogenenum 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.

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

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,
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. immunogenenum 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. immunogenenum 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. immunogenenum 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. immunogenenum, 8 clinical case reports have been published describing infection with this organism, most describing cutaneous infections (Table 1). To date, 25 patients with M. immunogenenum 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. immunogenenum 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.

<table>
<thead>
<tr>
<th>Year</th>
<th>No cases</th>
<th>Country</th>
<th>Clinical specimen</th>
<th>Clinical presentation</th>
<th>IS</th>
<th>Enviromental source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson et al. [1]</td>
<td>2001</td>
<td>11</td>
<td>USA</td>
<td>Clinical specimen and fluids</td>
<td>Skin, cornea, urine, blood, joint fluid</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Loots et al. [4]</td>
<td>2005</td>
<td>1</td>
<td>Guatemala</td>
<td>Skin biopsy</td>
<td>Leg ulcer</td>
<td>No</td>
</tr>
<tr>
<td>Sampaio et al.</td>
<td>2006</td>
<td>5</td>
<td>Brazil</td>
<td>Corneal scraping</td>
<td>Keratitis post LASIK</td>
<td>Unknown</td>
</tr>
<tr>
<td>Del-Castillo et al. [5]</td>
<td>2009</td>
<td>3</td>
<td>Argentina</td>
<td>Skin biopsy</td>
<td>Mesotherapy site infections</td>
<td>Unknown</td>
</tr>
<tr>
<td>Shedd et al. [6]</td>
<td>2010</td>
<td>2</td>
<td>USA</td>
<td>Skin biopsy/drainage</td>
<td>Surgical wound/leg plaque</td>
<td>No/ multiple myeloma</td>
</tr>
<tr>
<td>Mitchell et al. [7]</td>
<td>2011</td>
<td>1</td>
<td>USA</td>
<td>Skin biopsy</td>
<td>Infected tattoo</td>
<td>No</td>
</tr>
<tr>
<td>Biggs et al. [3]</td>
<td>2012</td>
<td>1</td>
<td>USA</td>
<td>Blood</td>
<td>Leg ulcers, fever, hypotension</td>
<td>Renal transplant</td>
</tr>
<tr>
<td>Greninger et al. [10]</td>
<td>2015</td>
<td>1</td>
<td>USA</td>
<td>Cerebral abscess</td>
<td>Headache, fever, visual impairment</td>
<td>No</td>
</tr>
<tr>
<td>García-Zamora et al.</td>
<td>2016</td>
<td>1</td>
<td>Spain</td>
<td>Skin biopsy</td>
<td>Abdominal papules and pustules</td>
<td>No</td>
</tr>
</tbody>
</table>

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 at 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


