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ORIGINAL RESEARCH

# Cutaneous Nontuberculous Mycobacteria Infections Following Cosmetic Procedures: A Retrospective Study

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**Background:** Reports of skin infections associated with nontuberculous mycobacteria (NTM) following cosmetic procedures are increasing. The diagnosis and treatment of these infections remain a significant challenge for clinicians.

**Objective:** We examined the clinical characteristics, microbiology, histopathology, and treatment strategies of NTM infections following cosmetic procedures, including botulinum toxin injection, lipolysis injection, hyaluronic acid injection, mesotherapy, autologous fat grafting, and other related procedures.

**Methods:** This retrospective study of cosmetology-related cutaneous NTM infections diagnosed based on culture or molecular identification was conducted at a tertiary dermatology hospital in China. Demographic, clinical, microbiological, pathological biopsy, management, and outcome data were also collected.

**Results:** The series enrolled 28 patients, four diagnosed by molecular identification and histology, and 24 by positive culture. All 24 NTM cultures were rapid-growing mycobacteria, mainly *Mycobacterium abscessus* complex (75%), with a mean time to positive culture of 11.8 days. The mean incubation period for the lesions was three weeks, while the mean time to diagnosis was 9.8 weeks. Treatment typically requires long-term, multi-drug therapy. Surgical intervention may shorten the disease course.

**Conclusion:** Cosmetology-related cutaneous NTM infections are frequently underrecognized and challenging to diagnose, leading to delayed treatment. We aimed to enhance clinician awareness of NTM infections to facilitate early detection and prompt treatment. Empirical therapy with clarithromycin and moxifloxacin may be considered in the absence of susceptibility results, but treatment decisions should be carefully guided by susceptibility testing results. Surgical intervention may be beneficial, and tigecycline is a viable option when resistant to clarithromycin.

**Keywords:** nontuberculous mycobacteria, rapidly growing mycobacteria, skin, infections, cosmetic procedures, treatment

## Introduction

Nontuberculous mycobacteria (NTM) refer to mycobacteria other than *Mycobacterium tuberculosis* complex and *Mycobacterium leprae*.[1] These acid-fast bacilli are widely distributed in environmental reservoirs, including water and soil.[2]

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In recent years, the occurrence of skin and soft tissue infections related to NTM has become more prevalent, particularly those caused by RGM.[3,4] Cutaneous NTM infections often arise following traumatic injuries and have also been linked to exposure to NTM-contaminated solutions used during invasive procedures or to insufficiently sterilized medical equipment.[5,6] Some invasive aesthetic procedures, such as liposuction, botulinum toxin injections, and silicone injections into breast implants, can increase the risk of NTM infection by compromising the skin barrier, exposing underlying tissues and organs, or the presence of implanted devices.[7]

NTM has increasingly been recognized as a cause of infections associated with cosmetic procedures in many countries, including the United States, France, Colombia, Venezuela, South Korea, and others, with the number of reported cases gradually rising.[8–14] However, due to a lack of awareness of NTM infections, along with limited laboratory facilities and diagnostic tests, the diagnosis is often challenging, leading to misdiagnosis initially, such as foreign body granulomas or staphylococcal infections[15] and prolonged suffering for patients.[16] To raise clinicians' awareness of NTM infections for prompt diagnosis and intervention, we retrospectively analyzed the clinical, microbiological, and pathological findings, as well as treatment outcomes, of 28 cases of cutaneous NTM infections following cosmetic procedures. This study aimed to contribute future epidemiological data, clinical insights, and management strategies for cutaneous NTM infections resulting from cosmetic procedures.

# Methods

We conducted a retrospective study of a series of cutaneous NTM infections acquired through cosmetic procedures at The Hospital for Skin Diseases, Institute of Dermatology, Chinese Academy of Medical Sciences. The Ethics Committee of the hospital reviewed and approved the study (approval number: 2021-KY-013) and the study was conducted in accordance with the Declaration of Helsinki.

Clinical records of patients diagnosed with cutaneous NTM infections, identified from the hospital's electronic medical record system between January 2018 and December 2023, were reviewed by 2 independent investigators. The inclusion criteria consisted of positive cultures or PCR results for NTM infections, along with a history of cosmetic procedures prior to the onset of disease. A standardized data extraction form was used to collect patient information, including demographic, clinical, microbiological, pathological biopsy, and treatment data. Detailed patient histories, as well as information on outcomes and prognosis, were obtained through telephone interviews. Discrepancies were resolved through consensus discussion with a third senior investigator.

All tissue samples were processed as previously described and cultured on Lowenstein Jensen slopes for solid medium enrichment at 32°C and 37°C.[17] An initial examination for acid-fast bacilli (AFB) was conducted using Ziehl-Neelsen staining. Genomic DNA of mycobacteria was isolated from the remaining tissue homogenates directly or from NTM isolates. The hsp65, 16S ribosomal RNA, and rpoB genes, as well as the 16S-23S rRNA internal transcribed spacers (ITS), were amplified by PCR, sequenced, and the sequences were processed and analyzed using BLAST (https://blast.ncbi.nlm.nih.gov/Blast.cgi) to identify NTM. The turnaround time for complete genetic testing was approximately 3 working days, including DNA extraction, amplification, and sequence analysis. The broth microdilution method, as recommended by the Clinical and Laboratory Standards Institute, was used to conduct antimicrobial susceptibility testing for RGM.[18]

Histopathological examination was performed using routine hematoxylin and eosin staining, and a subset of the patients underwent Ziehl-Neelsen staining. Statistical analysis was performed using SPSS version 24.0, with continuous variables described as means, medians, minimums, and maximums, and categorical variables are shown as frequencies and percentages.

# Results

## Demographic and Clinical Profiles of the Patients

We included 28 patients, all of whom were women, with a mean age of 37.4 years (median 33, range 23–57). Twenty-four (85.7%) cases were diagnosed through positive culture results, and four (14.3%) through tissue homogenate PCR testing and pathological examination. All the patients developed infections following cosmetic procedures at various private plastic surgery institutions. As detailed in Table 1, the distribution of procedures among the 28 cases showed that

**Table 1** Patients' Clinical, Histological, and Microbiological Features

| Case | Age (Years)/ Sex | Exposure/Incubation Period (Weeks) | Clinical Appearance | Site | Culture/Time (Days)/Temperature (°C) | Tissue PCR | Treatment Agent/Duration (Months) | SI | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 23/F | BoNT injection/5 | Nodules, abscesses | Face | *M. abscessus*/15/37 | ND | CLA, MXF/7 | Yes | Healed |
| 2 | 27/F | BoNT injection/ 4 | Nodules | Face | *M.massiliense*/26/32 | ND | CLA, MXF, RIF/9 | No | Healed |
| 3 | 56/F | BoNT injection/1 | Nodules, erythema | Face | *M.chelonae*/10/32 | ND | CLA, MXF/11 | No | Healed |
| 4 | 56/F | Injection lipolysis/3 | Nodules | Neck | *M.chelonae*/17/32 | ND | CLA, MXF/9 | No | Healed |
| 5[#] | 31/F | Injection lipolysis/2 | Nodules, abscesses | Face | *M. abscessus*/6/37 | ND | CLA,MXF/1, TGC,FOX,MIN/ND | Yes | Lost to follow-up |
| 6 | 32/F | BoNT injection/4 | Nodules | Face | *M.massiliense*/8/37 | ND | CLA,MXF/5 | Yes | Healed |
| 7 | 37/F | Injection lipolysis/1.5 | Nodules, abscesses | Neck | *M.massiliense*/7/37 | ND | CLA,MXF/7 | Yes | Healed |
| 8 | 38/F | Tattoo/3 | Nodules | Breast | Negative | *M. abscessus* | CLA,MXF/6 | Yes | Healed |
| 9* | 32/F | Hyaluronic acid injection/8 | Nodules, abscesses | Face | *M.massiliense*/14/37 | ND | CLA,MXF,RIF/8 | Yes | Healed |
| 10 | 32/F | Injection lipolysis/2 | Nodules, abscesses, draining sinus tracts | Upper arms | *M.massiliense*/8/32 | ND | AZM,MXF/11 | Yes | Healed |
| 11 | 56/F | BoNT injection/3 | Nodules, erythema | Face | *M.bolletii*/17/37 | ND | CLA,MXF/6 | Yes | Healed |
| 12 | 31/F | Mesotherapy/1 | Nodules, abscesses | Face | *M.massiliense*/11/32,37 | ND | CLA,MXF/4 | Yes | Healed |
| 13 | 41/F | Thread embedding at acupuncture points for weight loss/3 | Nodules, abscesses | Abdomen, thighs | *M.massiliense*/11/32 | ND | CLA,MXF/1, CLA,TGC,AMK/6, CLA,MXF,RFB/5 | Yes | Healed |
| 14 | 48/F | BoNT injection/2 | Nodules | Face | *M.bolletii*/21/32 | ND | CLA,MXF/4 | Yes | Healed |
| 15 | 37/F | Injection lipolysis/1 | Nodules, abscesses | Face | *M. abscessus*/13/37 | ND | CLA,MXF/ND | Yes | Lost to follow-up |
| 16 | 54/F | Autologous fat grafting/4 | Nodules, abscesses | Face | *M.Wolinskyi*/7/32,37 | ND | CLA,MXF,RIF/9 | Yes | Healed |
| 17[#] | 24/F | Injection lipolysis/4 | Nodules, crusts | Thighs | *M.fortuitum*/11/32,37 | ND | CLA,MXF,RIF/12 | No | Healed |
| 18[+] | 46/F | Injection lipolysis/2 | Plaques, abscesses, ulcers | Upper arms | *M.immunogenum*/14/32 | ND | CLA,MXF,RIF/11 | Yes | Healed |
| 19 | 24/F | BoNT injection/1 | Nodules, abscesses | Face | *M. abscessus*/11/37 | ND | CLA,MXF/10 | Yes | Healed |
| 20 | 34/F | Thread embedding at acupuncture points for weight loss/4 | Plaque, nodules, ulcer | Abdomen, thighs | *M. abscessus*/8/32 | ND | CLA,MXF/9 | No | Healed |
| 21 | 47/F | BoNT injection/2 | Nodules, abscesses | Face | *M.chelonae*/7/32 | ND | CLA+MXF/8 | Yes | Healed |
| 22 | 57/F | Injection lipolysis/1 | Nodules, crusts | Abdomen | Negative | *M.immunogenum* | CLA,MXF/11 | No | Healed |
| 23 | 32/F | Thread embedding at acupuncture points for weight loss/3 | Plaque, abscesses, ulcers | Abdomen, thighs | *M.massiliense*/8/32 | ND | CLA,MXF,RIF/12 | Yes | Healed |
| 24 | 26/F | Mesotherapy/4 | Nodules, abscesses | Face | *M.massiliense*/14/32 | ND | CLA,MXF,RIF/8 | Yes | Healed |
| 25 | 31/F | Injection lipolysis/4 | Nodules, crusts | Thighs, lower legs | Negative | *M. abscessus* | CLA,MXF/11 | No | Healed |
| 26 | 31/F | Injection lipolysis/3 | Nodules, crusts | Thighs, lower legs | Negative | *M. abscessus* | CLA,MXF/13 | No | Healed |
| 27[#] | 34/F | BoNT injection/4 | Nodules, abscesses | Face | *M.massiliense*/10/32 | ND | CLA,MXF/9 | Yes | Healed |
| 28 | 31/F | BoNT injection/4 | Nodules, abscesses | Face | *M.massiliense*/10/32 | ND | CLA,MXF/8 | Yes | Healed |

**Notes**: * History of Sjögren syndrome. [+]Ziehl-Neelsen stain showing positivity in biopsy samples. [#]Granulomas were not identified in the biopsy specimens.

**Abbreviations**: AMK, amikacin; AZM, azithromycin; BoNT, Botulinum toxin; CLA, clarithromycin; F, female; FOX, cefoxitin; MIN, minocycline; MXF, moxifloxacin; *M. abscessus, Mycobacterium abscessus; M. bolletii, Mycobacterium bolletii; M. chelonae, Mycobacterium chelonae; M. fortuitum, Mycobacterium fortuitum; M. immunogenum, Mycobacterium immunogenum; M. massiliense, Mycobacterium massiliense; M. Wolinskyi, Mycobacterium Wolinskyi*; ND, no data; PCR, polymerase chain reaction; RFB, Rifabutin; RIF, rifampicin; SI, surgical intervention; TGC, tigecycline.

botulinum toxin injections (n=10, 35.7%) and injection lipolysis (n=10, 35.7%) were the most common interventions. Other identified procedures, in descending order of frequency, included: thread embedding at acupuncture points for weight loss (n=3, 10.7%), mesotherapy (n=2, 7.1%), hyaluronic acid injection (n=1, 3.6%), autologous fat grafting (n=1, 3.6%), and tattooing (n=1, 3.6%).

The clinical presentation of skin lesions includes nodules, abscesses, plaques, crusts, draining sinus tracts, and erythema. The lesions were primarily found at locations where cosmetic procedures were performed. Approximately 28.6% of the patients exhibited infections involving multiple sites, and all patients had local multifocal infections (Supplementary Figure 1). The mean incubation period for the lesions was 3 weeks (median 3, range 1–12) while the mean time to diagnosis was 9.8 weeks (median 8, range 4–20). Except for one patient with a 1-year history of Sjogren's syndrome, all other patients were healthy before undergoing the procedures.

## Identification of Mycobacterial Isolates

Based on growth rates, specifically the time required for the formation of mature colonies on solid media, nontuberculous mycobacteria are grouped into two categories: slowly growing mycobacteria (SGM) and rapidly growing mycobacteria (RGM). The former requires a period of over 7 days to develop mature colonies, whereas the latter can form mature colonies within 7 days.[1] All 24 NTM cultured from skin lesions were rapid-growing mycobacteria. The most frequently identified species were *Mycobacterium abscessus* complex, *M. massiliense* (45.8%), *M. abscessus* (20.8%), and *M. bolletii* (8.3%), together comprising 75% of the isolates. Additional species identified included *M. chelonae* (12.5%), *M. fortuitum* (4.2%), *M. immunogenum* (4.2%), and *M. wolinskyi* (4.2%). The *M. abscessus* complex demonstrates resistance to multiple antibiotics, and its in vitro antimicrobial susceptibility profile is summarized in Table 2.

## Histopathological Characteristics of Skin Biopsy Samples

Granulomas were observed in 89.3% of the cases (Supplementary Figure 2); two (7.1%) cases had suppurative inflammation instead of granulomas, and one case presented with nonspecific chronic inflammation. Consistent with previous studies, granulomatous inflammation is a hallmark feature of NTM infections, and the observed variability in histopathological presentation highlights the diverse nature of the condition.[19,20] Ziehl–Neelsen staining was performed on 14 samples to identify acid-fast bacilli, with 1 (7.1%) yielding a positive result, which is lower than the 27% reported in previous studies.[20] Epidermal changes include hyperkeratosis, parakeratosis, acanthosis, intercellular edema, and ulceration.

**Table 2** In vitro Antimicrobial Susceptibility Profile of the Mycobacterium Abscessus Complex

| Antimicrobial Agents | *M. abscessus* (n=5) | | | *M. massiliense* (n=11) | | | *M. bolletii* (n=2) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Sensitive | Intermediate | Resistant | Sensitive | Intermediate | Resistant | Sensitive | Intermediate | Resistant |
| Amikacin | 4 | 1 | 0 | 10 | 1 | 0 | 1 | 1 | 0 |
| Cefoxitin | 3 | 2 | 0 | 11 | 0 | 0 | 1 | 1 | 0 |
| Ciprofloxacin | 0 | 0 | 5 | 0 | 0 | 11 | 0 | 0 | 2 |
| Clarithromycin | 2 | 0 | 3 | 11 | 0 | 0 | 1 | 1 | 0 |
| Doxycycline | 0 | 0 | 5 | 0 | 0 | 11 | 0 | 0 | 2 |
| Imipenem | 0 | 5 | 0 | 0 | 7 | 4 | 0 | 1 | 1 |
| Linezolid | 2 | 1 | 2 | 0 | 8 | 3 | 0 | 1 | 1 |
| Meropenem | 0 | 1 | 4 | 0 | 0 | 11 | 1 | 1 | 0 |
| Moxifloxacin | 0 | 0 | 5 | 0 | 0 | 11 | 0 | 0 | 2 |
| Minocycline | 0 | 1 | 4 | 0 | 3 | 8 | 1 | 1 | 0 |
| Tigecycline | ≤0.25–0.5 μg/mL | | | ≤0.25–1 μg/mL | | | 0.5μg/mL | | |
| Tobramycin | 0 | 2 | 3 | 0 | 0 | 11 | 0 | 0 | 2 |
| Trimethoprim-sulfamethoxazole | 3 | 0 | 2 | 2 | 0 | 9 | 0 | 0 | 2 |

## Management and Outcome

Antibiotic treatment was administered to all patients, with 20 (71.4%) patients receiving a combined treatment approach that included both antibiotics and surgical intervention, including incision and drainage or excision (Table 1). Antibiotics used were clarithromycin, azithromycin, amikacin, moxifloxacin, minocycline, cefoxitin, tigecycline, and rifampicin. The mean treatment duration was 8.8 months (median 9, range 4–13), with two patients lost to follow-up prior to treatment completion excluded from outcome analysis.

Among the 21 patients infected with *M. abscessus* complex, two were administered oral clarithromycin and moxifloxacin for treatment, two received a three-drug regimen, while fourteen patients received a combination of oral antibiotic agents and surgical intervention. One patient (case 10) who was allergic to clarithromycin underwent treatment with a combination of azithromycin and moxifloxacin. Two individuals (case 5, 13) who were treated with oral clarithromycin and moxifloxacin for one month showed poor clinical responses. According to the antimicrobial susceptibility pattern, one patient (case 5) was treated with tigecycline, cefoxitin, and minocycline, whereas the other patient (case 13) was treated with clarithromycin, amikacin, and tigecycline. Both patients showed improvement after one month of therapy. Except for two patients lost to follow-up, the other 19 individuals demonstrated favorable clinical responses with minimal side effects, apart from one patient who initially experienced gastrointestinal discomfort. The average treatment duration in the combined surgical treatment group (7.8 months) was shorter than that in the oral medication only group (10.5 months). Three patients with *M. chelonae* infection were successfully treated with a combination of clarithromycin and moxifloxacin. One patient infected with *M. fortuitum*, another with *M. wolinskyi*, and two with *M. immunogenum* infections responded well to a treatment regimen that included rifampicin, clarithromycin, and moxifloxacin. All patients who completed follow-up achieved treatment success, precluding analysis of factors affecting outcomes. Two patients were lost to follow-up and excluded from outcome analysis.

# Discussion

This study provides a comprehensive analysis of patients with NTM infections following aesthetic procedures, focusing on the clinical characteristics, microbiological results, antimicrobial susceptibility, diagnostic challenges, and treatment outcomes. Through a retrospective analysis of patients from a tertiary dermatology hospital in China, this study offers valuable insights into the management of NTM infections in post-aesthetic surgery patients and provides important guidance for clinicians.

Initially, the increase in NTM infections was believed to reflect a growing immunosuppressed population. However, numerous reports have documented these infections in otherwise healthy individuals.[16] Particularly in recent decades, the global demand for cosmetic procedures has increased substantially,[21] highlighting the need for vigilance regarding the NTM infections associated with these interventions. Their ability to withstand conventional disinfectants, including organomercurials, chlorine, and glutaraldehyde, allows their persistence in processed water, increasing the likelihood of contamination of medical devices, instruments, and reagents, thereby posing a risk for human infection.[22] Rapidly growing mycobacteria are increasingly being identified as significant contributors to skin infections, especially those associated with cosmetic surgery and aesthetic treatments.[23]

We reviewed 28 cases of cutaneous NTM infection associated with cosmetic procedures. All NTM strains isolated from these patients had RGM. Among them, *M. abscessus* complex (75%) was the predominant species, which can be further divided into *M. bolletii, M. abscessus*, and *M. massiliense*.[24] In our study, *M. massiliense* (39.3%) was identified as the predominant strain, aligning with prior study that found *M. massiliense* was more likely linked to the infections involving cutaneous and soft tissue.[25] Before the onset of infection, all patients had undergone various invasive cosmetic procedures (Table 1), which may have facilitated the invasion of mycobacteria.

Skin and soft tissue NTM infections present with diverse clinical symptoms.[23] Immunocompromised patients may develop disseminated infections. Patients sometimes present with systemic symptoms.[26] In our patients, the clinical presentation primarily consisted of localized nodules and abscesses at the cosmetic procedure sites, with some cases being accompanied by swelling, pain, or tenderness. These infections typically manifest with a delayed appearance of

symptoms.[19] In our patients, the mean time for the appearance of clinical symptoms was 3 weeks after the procedure. Systemic symptoms such as fever or chills were absent in our case series.

Owing to the diverse and nonspecific clinical manifestations and challenges in diagnostic testing, diagnosis of skin infections induced by NTM is often delayed. The patients we reported required an average of 9.8 weeks from the onset of clinical symptoms to a definitive diagnosis. Initial misdiagnosis led to prolonged suffering. Some of our patients initially received conventional antibiotics, such as cephalosporins and levofloxacin, because of the common isolation of Staphylococcus aureus after plastic surgery,[16] or were misdiagnosed with foreign body granulomas and treated with corticosteroids, but none of these treatments were effective. We suggest that clinicians maintain a high index of suspicion for mycobacterial infections in cases of postoperative or post-procedural infections that are unresponsive to standard antimicrobial therapies. A timely and comprehensive diagnostic workup, including histopathological examination, microbiological culture, and molecular testing, should be performed promptly to confirm the diagnosis and guide appropriate treatment.

The isolation and cultivation of NTM presents a significant challenge. Routine cultures in many healthcare settings often fail to identify these infections effectively. Moreover, for cases suspected of Mycobacterium infections, media such as Lowenstein–Jensen medium are typically used for culturing, requiring extended incubation periods, often for at least 7 days.[7,19] In our cases, the mean time to obtain a positive culture result was 11.8 days (range: 6–26 days). We recommend incubating the cultures at different temperatures. In our study, 54.2% of the cultures yielded positive results at 32°C, 33.3% at 37°C, and 12.5% at 32°C and 37°C simultaneously (Table 1).

Molecular techniques facilitate quicker and more precise identification of NTM. For extract identification of NTM, sequencing of the 16S rRNA subunit and the hsp65 and rpoB genes is recommended.[27] This approach can accelerate the diagnostic process and offer valuable insights. Different NTM require different treatment regimens, and identifying specific NTM species is key to determining appropriate management.

Cutaneous infections due to NTM demonstrate diverse histopathological patterns, often described as nonspecific granulomatous dermatitis.[28] In immunocompetent patients, the most common pattern is suppurative granulomatous inflammation, with acid-fast bacilli either undetectable or present in minimal amounts on special stains.[29] The histological findings in our study revealed granuloma formation in 89.3% of cases, with 57.1% showing varying degrees of neutrophil infiltration. In three cases, abscess formation was observed without granulomas. The acid-fast staining positivity rate was lower than previous study.[20] This discrepancy may be attributed to the fact that our patients were immunocompetent.

Currently, there are no standardized guidelines for the treatment of cutaneous infections caused by RGM. The Clinical and Laboratory Standards Institute (CLSI) recommends the testing of certain antimicrobials for RGM. These include amikacin, cefoxitin, ciprofloxacin, clarithromycin, doxycycline (or minocycline), imipenem, linezolid, meropenem, moxifloxacin, tigecycline, trimethoprim-sulfamethoxazole, and tobramycin (specifically for *M. chelonae*).[18,30]

In our cases, the predominant causative agent was the *M. abscessus* complex. *M. abscessus* complex exhibits inherent resistance to standard anti-tuberculosis agents and multi-drug resistance, presenting significant challenges for its treatment.[26]

Given the limited number of cases and clinical studies, treatment options for *M. abscessus* complex skin and soft tissue infections largely follow those for pulmonary infections.[26] A variety of antibiotics are available for clinical use, including amikacin, clarithromycin, azithromycin, cefoxitin, imipenem, linezolid, and tigecycline.[26,31] *M. massiliense*, Unlike *M. abscessus, M. massiliense* is thought to have a nonfunctional erythromycin resistance methylase gene *erm*(41), leading to macrolide susceptibility.[27] Our antimicrobial susceptibility testing revealed that all tested *M. massiliense* strains were susceptible to clarithromycin (Table 2). Therefore, infections caused by *M. massiliense* may respond favorably to treatment. In this study, the majority of patients showed a positive response to combination therapy involving at least two drugs, including clarithromycin. Oral clarithromycin, combined with moxifloxacin, is the most commonly used antibiotic. A study investigating the management of skin infections caused by *M. abscessus* has demonstrated the efficacy of a combination of moxifloxacin and clarithromycin.[32] In vitro drug susceptibility testing indicated a synergistic effect when these two agents were used in combination.[33]

Two patients failed to respond to one month of treatment with clarithromycin and moxifloxacin. Based on antimicrobial susceptibility testing, both were switched to three-antibiotic regimens, including tigecycline, resulting in significant clinical improvement after one month of therapy. Tigecycline effectively inhibited the growth of RGM

in vitro at very low minimum inhibitory concentrations (MICs).[34] In our study, all tested *M. abscessus* complex strains demonstrated strong susceptibility to tigecycline, with MICs of ≤1 μg/mL (Table 2). Thus, tigecycline may be a valuable treatment option for diseases induced by *M. abscessus* complex.

*M. chelonae* is consistently resistant to cefoxitin, but remains susceptible to various antibiotics, including clarithromycin, amikacin, tobramycin, linezolid, imipenem, and tigecycline.[21,26,34,35] *M. fortuitum* is considered susceptible to a variety of antimicrobials, making it more treatable than other RGM. Many antibiotics exhibit antimicrobial activity against this species, including amikacin, ciprofloxacin, clarithromycin, tigecycline, moxifloxacin, linezolid, cefoxitin, doxycycline, and imipenem.[26,34] Macrolide resistance in *M. fortuitum* may be induced by the *erm*(39) gene.[36] Thus, the use of clarithromycin monotherapy is not recommended. In vitro susceptibility results should serve as a guiding factor for selecting an appropriate treatment regimen. In our study, all patients required long-term combination therapy with multiple antimicrobial agents, which may be attributed to the delayed diagnosis and the presence of multifocal infections in the patient population. The observed treatment duration was shorter in patients receiving combined surgical intervention and antimicrobial therapy compared to those receiving antibiotic therapy alone. However, this observation should be interpreted with caution, as it is based on uncontrolled data without statistical support. Further studies with a more robust design are needed to draw definitive conclusions.

Inevitably, this study has several limitations. First, due to the limited sample size and absence of control group, this study lacks sufficient statistical power to perform meaningful comparisons and draw definitive conclusions. As such, the findings should be interpreted with caution, and further research with larger, controlled cohorts is needed to validate these observations. Additionally, the retrospective design introduces the possibility of information bias due to reliance on potentially incomplete or inaccurate medical records, as well as the potential for selection bias, since the study sample is drawn from a tertiary center and may not be representative of the broader population. Meanwhile, all of our patients were immunocompetent, and our experience in managing immunocompromised patients is limited. While we established a strong association between cosmetic procedures and NTM infections through patient history, clinical, and microbiological evidence, we acknowledge that the absence of environmental sampling from cosmetic facilities limits our ability to definitively confirm the infection source.

## Conclusion

There has been an increase in NTM skin infections associated with cosmetic procedures, primarily involving RGM. Clinicians should maintain a high index of suspicion for RGM infection in patients presenting with persistent skin infections following cosmetic procedures, particularly when conventional antibiotic therapy proves ineffective. An accurate diagnosis relies on histopathological analysis and pathogen identification. In our clinical experience, a combination of clarithromycin and moxifloxacin has been used as an empirical treatment regimen, though treatment decisions should be individualized based on clinical presentation and, when available, susceptibility testing results. Tigecycline may be considered in select cases based on susceptibility patterns. Surgical interventions including debridement or abscess drainage, are important adjunctive treatments. While combined surgical intervention may shorten the disease course, current evidence remains limited due to the observational nature of available studies. Well-designed prospective studies with standardized treatment protocols and control groups are needed to establish its potential benefits.

## IRB Approval Status

This study was reviewed and approved by the Ethics Committee of the Hospital for Skin Diseases, Institute of Dermatology, Chinese Academy of Medical Sciences (approval number 2021-KY-013) and was conducted in accordance with the Declaration of Helsinki.

## Patient Consent

Consent was obtained for publication of recognizable patient photographs or other identifiable materials. All patients provided consent with an understanding that this information may be publicly available. All patients consented to participate in this study and signed a written consent form.

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## Disclosure

The authors report no conflicts of interest in this work.

## References

1. Gonzalez-Santiago TM, Drage LA. Nontuberculous mycobacteria: skin and soft tissue infections. *Dermatol Clin*. 2015;33(3):563–577. doi:10.1016/j.det.2015.03.017
2. Chung J, Ince D, Ford BA, et al. Cutaneous infections due to nontuberculosis mycobacterium: recognition and management. *Am J Clin Dermatol*. 2018;19(6):867–878. doi:10.1007/s40257-018-0382-5
3. Mei Y, Zhang W, Shi Y, et al. Cutaneous tuberculosis and nontuberculous mycobacterial infections at a national specialized hospital in China. *Acta Derm Venereol*. 2019;99(11):997–1003. doi:10.2340/00015555-3283
4. Yeo PM, Lee SX, Tan YE, et al. Epidemiology, risk factors, and outcomes of adult cutaneous non-tuberculous mycobacterial infection over a 10-year period in Singapore. *Int J Dermatol*. 2019;58(6):679–687. doi:10.1111/ijd.14356
5. van Ingen J, Blaak H, de Beer J, et al. Rapidly growing nontuberculous mycobacteria cultured from home tap and shower water. *Appl Environ Microbiol*. 2010;76(17):6017–6019. doi:10.1128/AEM.00843-10
6. Takajo I, Iwao C, Aratake M, et al. Pseudo-outbreak of Mycobacterium paragordonae in a hospital: possible role of the aerator/rectifier connected to the faucet of the water supply system. *J Hosp Infect*. 2020;104(4):545–551. doi:10.1016/j.jhin.2019.11.014
7. Carbonell RCC, Oliveira LLF, Galan LEB, et al. Beauty's betrayal: mycobacterium abscessus case series following aesthetic procedures in the Brazilian Amazon. *Infect Dis Rep*. 2024;16(4):724–734. doi:10.3390/idr16040055
8. Liu Y, Chen Y. Surgical treatment for Cutaneous Mycobacterium abscessus infection caused by injections of hyaluronic acid. *Clin Cosmet Invest Dermatol*. 2023;16:687–692. doi:10.2147/CCID.S394594
9. Jiang Y, Lei X, Lu W. Outbreak of cosmetology-acquired Mycobacterium abscessus skin infection. *JAMA Dermatol*. 2023;159(7):780–781. doi:10.1001/jamadermatol.2022.6385
10. Xing Y, Li M, Jiang Y, Zhong Q. Three cases of non-tuberculosis mycobacterium skin infection outbreak in beauty institutions. *Clin Lab*. 2024;70(6). doi:10.7754/Clin.Lab.2024.240101
11. Fang RY, Sun QN. Mycobacterium abscessus infections following injection of botulinum toxin. *J Cosmet Dermatol*. 2020;19(4):817–819. doi:10.1111/jocd.13094
12. Wang CJ, Song Y, Li T, et al. Mycobacterium smegmatis skin infection following cosmetic procedures: report of two cases. *Clin Cosmet Invest Dermatol*. 2022;15:535–540. doi:10.2147/CCID.S359010
13. Jabbour SF, Malek AE, Kechichian EG, et al. Nontuberculous Mycobacterial Infections after cosmetic procedures: a systematic review and management algorithm. *Dermatol Surg*. 2020;46(1):116–121. doi:10.1097/DSS.0000000000001929
14. Ma X, Li XY, Liu JW. Demographic and clinical features of nontuberculous mycobacteria infection resulting from cosmetic procedures: a systematic review. *Int J Infect Dis*. 2024;149:107259. doi:10.1016/j.ijid.2024.107259
15. Sañudo A, Vallejo F, Sierra M, et al. Nontuberculous mycobacteria infection after mesotherapy: preliminary report of 15 cases. *Int J Dermatol*. 2007;46(6):649–653. doi:10.1111/j.1365-4632.2007.02976.x
16. Moreno-Izquierdo C, Zurita J, Contreras-Yametti FI, et al. Mycobacterium abscessus subspecies abscessus infection associated with cosmetic surgical procedures: cases series. *IDCases*. 2020;22:e00992. doi:10.1016/j.idcr.2020.e00992
17. Feng Y, Wang M, Jiang H, et al. Comparative evaluation of LAMP and nested PCR for the rapid diagnosis of Mycobacterium marinum infection. *Infect Drug Resist*. 2023;16:1601–1609. doi:10.2147/IDR.S404929
18. Woods GL, Brown-Elliott BA, Conville PS, et al. CLSI standards: guidelines for health care excellence. In: *Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes; Approved Standard—Second Edition*. 2011.
19. Rodríguez-Cerdeira C, Hernández-Castro R, Sánchez-Cárdenas CD, et al. Atypical Mycobacteriosis due to Mycobacterium abscessus subsp. massiliense: our experience. *Pathogens*. 2022;11(12):1399. doi:10.3390/pathogens11121399
20. Rodríguez G, Ortegón M, Camargo D, et al. Iatrogenic Mycobacterium abscessus infection: histopathology of 71 patients. *Br J Dermatol*. 1997;137(2):214–218. doi:10.1046/j.1365-2133.1997.18081891.x
21. Hypolite T, Grant-Kels JM, Chirch LM. Nontuberculous mycobacterial infections: a potential complication of cosmetic procedures. *Int J Womens Dermatol*. 2015;1(1):51–54. doi:10.1016/j.ijwd.2014.12.007
22. van Ingen J, Boeree MJ, Dekhuijzen PN, et al. Environmental sources of rapid growing nontuberculous mycobacteria causing disease in humans. *Clin Microbiol Infect*. 2009;15(10):888–893. doi:10.1111/j.1469-0691.2009.03013.x
23. Franco-Paredes C, Marcos LA, Henao-Martínez AF, et al. Cutaneous mycobacterial infections. *Clin Microbiol Rev*. 2018;32(1). doi:10.1128/CMR.00069-18
24. Johansen MD, Herrmann JL, Kremer L. Non-tuberculous mycobacteria and the rise of Mycobacterium abscessus. *Nat Rev Microbiol*. 2020;18(7):392–407. doi:10.1038/s41579-020-0331-1
25. Hsu JY, Cheng A, Ku CC, et al. Mycobacterium abscessus and Mycobacterium massiliense exhibit distinct host and organ specificity: a cross-sectional study. *Int J Infect Dis*. 2022;116:21–26. doi:10.1016/j.ijid.2021.12.348
26. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med*. 2007;175(4):367–416. doi:10.1164/rccm.200604-571ST

27. Lee MR, Sheng WH, Hung CC, et al. Mycobacterium abscessus Complex Infections in Humans. *Emerg Infect Dis*. 2015;21(9):1638–1646. doi:10.3201/2109.141634
28. Santa Cruz DJ, Strayer DS. The histologic spectrum of the cutaneous mycobacterioses. *Hum Pathol*. 1982;13(5):485–495. doi:10.1016/S0046-8177(82)80032-4
29. Li JJ, Beresford R, Fyfe J, Henderson C. Clinical and histopathological features of cutaneous nontuberculous mycobacterial infection: a review of 13 cases. *J Cutan Pathol*. 2017;44(5):433–443. doi:10.1111/cup.12903
30. CLSI. *Performance Standards for Susceptibility Testing of Mycobacteria, Nocardia Spp. and Other Aerobic Actinomycetes*. 2nd ed. CLSI supplement M24S; 2023.
31. Daley CL, Iaccarino JM, Lange C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. *Eur Respir J*. 2020;56(1):2000535. doi:10.1183/13993003.00535-2020
32. Choi WS, Kim MJ, Park DW, et al. Clarithromycin and amikacin vs. clarithromycin and moxifloxacin for the treatment of post-acupuncture cutaneous infections due to Mycobacterium abscessus: a prospective observational study. *Clin Microbiol Infect*. 2011;17(7):1084–1090. doi:10.1111/j.1469-0691.2010.03395.x
33. Zhang Z, Lu J, Liu M, et al. In vitro activity of clarithromycin in combination with other antimicrobial agents against Mycobacterium abscessus and Mycobacterium massiliense. *Int J Antimicrob Agents*. 2017;49(3):383–386. doi:10.1016/j.ijantimicag.2016.12.003
34. Hatakeyama S, Ohama Y, Okazaki M, Nukui Y, Moriya K. Antimicrobial susceptibility testing of rapidly growing mycobacteria isolated in Japan. *BMC Infect Dis*. 2017;17(1):197. doi:10.1186/s12879-017-2298-8
35. Da Mata-Jardín O, Angulo A, Rodríguez M, et al. Drug susceptibility patterns of rapidly growing mycobacteria isolated from skin and soft tissue infections in Venezuela. *Eur J Clin Microbiol Infect Dis*. 2020;39(3):433–441.
36. Nash KA, Zhang Y, Brown-Elliott BA, et al. Molecular basis of intrinsic macrolide resistance in clinical isolates of Mycobacterium fortuitum. *J Antimicrob Chemother*. 2005;55(2):170–177. doi:10.1093/jac/dkh523