

# Rapid-Growing Mycobacteria Infections in Medical Tourists: Our Experience and Literature Review

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## Abstract

**Background:** “Medical tourism” has gained popularity over the past few decades. This is particularly common with patients seeking elective cosmetic surgery in the developing world. However, the risk of severe and unusual infectious complications appears to be higher than for patients undergoing similar procedures in the United States.

**Objectives:** The authors describe their experience with atypical mycobacterial infections in cosmetic surgical patients returning to the United States post-operatively.

**Methods:** A review of patient medical records presenting with infectious complications after cosmetic surgery between January 2010 and July 2015 was performed. Patients presenting with mycobacterial infections following cosmetic surgery were reviewed in detail. An extensive literature review was performed for rapid-growing mycobacteria (RGM) related to cosmetic procedures.

**Results:** Between January 2010 and July 2015, three patients presented to our institution with culture-proven *Mycobacterium abscessus* at the sites of recent cosmetic surgery. All had surgery performed in the developing world. The mean age of these patients was 36 years (range, 29–44 years). There was a delay of up to 16 weeks between the initial presentation and correct diagnosis. All patients were treated with surgical drainage and combination antibiotics with complete resolution.

**Conclusions:** We present series of patients with mycobacterial infections after cosmetic surgery in the developing world. This may be related to the endemic nature of these bacteria and/or inadequate sterilization or sterile technique. Due to low domestic incidence of these infections, diagnosis may be difficult and/or delayed. Consulting physicians should have a low threshold to consider atypical etiologies in such scenarios.

## Level of Evidence: 5



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“Medical tourism” – traveling for the purpose of seeking healthcare – has become an increasingly common practice over past few decades. Patients may be seeking care that is perceived to be better, cheaper, or more discreet; with the most important motivating factors for such practice being decreased cost and shorter waiting times.<sup>1–3</sup> Data suggest that approximately 4 million patients from the United States seek overseas medical care annually.<sup>4</sup> Those undergoing cosmetic procedures have been referred to as “lipotourists.”<sup>5,6</sup>

The effects of medical tourism on the healthcare system of the home country and the individual patient are highly debated. The risks of infectious complications in patients

seeking healthcare in the developing world may be significantly higher compared with similar procedures performed in Europe and the United States.<sup>7,8</sup> The cost of dealing with such complications when “tourists” return home may be

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significant and is often borne by domestic and government insurers.

Patient care is frequently compromised by “lipotourism”. First, a lack of recordkeeping and communication makes it hard for domestic physicians to obtain an accurate history. Second, foreign physicians are often reluctant to discuss their treatment. Third, medical equipment and products may be sub-standard or not approved for human surgical use, with little regulation or oversight. Fourth, patients frequently leave their destination to return home before sufficient follow up is completed. Finally, endemic diagnoses are often not seen in routine practice in the United States and a lack of familiarity may delay diagnosis when patients return home.

In April 2004, Centers for Disease Control (CDC) received reports of twelve patients infected with rapid-growing mycobacteria (RGM) after cosmetic surgery procedures in Santo Domingo, Dominican Republic.<sup>9</sup> Definitive testing at CDC determined that all the cases resulted from infection with *Mycobacterium abscessus*.

Given that other institutions have also noticed mycobacterial infections in patients returning from the developing world,<sup>6,9-17</sup> the goal of this study was to evaluate our experience with mycobacterial infections in patients undergoing cosmetic surgery outside of the United States.

## METHODS

The study was approved by the Institutional Review Board (IRB Protocol #2015P001933) at Brigham & Women’s Hospital (Boston, MA). Medical records of patients who presented to our institution between January 2010 and July 2015 with infectious complications from cosmetic surgery procedures were reviewed. All patients with positive cultures for mycobacteria were included in the present study

and underwent a detailed chart review and examination of microbiology and pathology.

## Literature Review

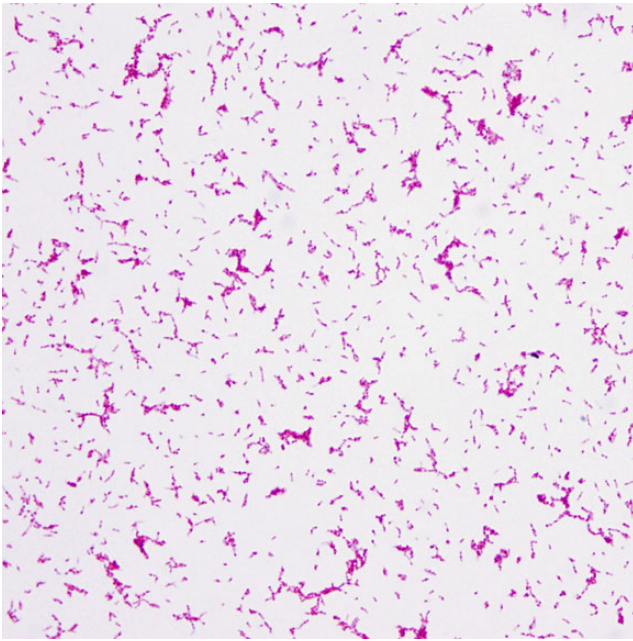
An extensive literature review was also performed. A PubMed search was conducted using the keywords “atypical mycobacteria” and “cosmetic surgery” in November 2015. Studies published in language other than English were excluded. Among remaining studies, only those reporting RGM in medical tourists undergoing cosmetic surgical procedures from a developed country that underwent cosmetic surgical procedures in a developing region were included.

## RESULTS

During the period studied, three patients presented to our center with postoperative cosmetic surgery complications due to mycobacterial infections – all related to foreign cosmetic procedures. By comparison, no domestic cosmetic surgical patients presented to our institution with mycobacterial infections from over 1200 cosmetic cases. All grew *M. abscessus* from deep tissue cultures. The mean age of the patients was 36 years (range, 29-44 years) and all were female. Two patients had surgery in Dominican Republic while the third patient underwent their procedures in Mexico. The surgical procedures included silicone implant breast augmentation, mastopexy, liposuction, and abdominoplasty. The demographics and the disease characteristics of all three patients are described in Table 1. Cultures from all three patients were positive for *M. abscessus* while tissue acid-fast bacilli stains were positive in two patients. A representative image of *M. abscessus* from an isolate is

**Table 1.** Demographics and Disease Characteristics of the Patients Diagnosed With RGM Wound Infections Following Cosmetic Surgery Procedures in Developing Countries

Patient Age (yrs), Gender	Date and Country of Procedure	Surgical Procedure(s)	Initial Presentation (weeks from surgical procedure)	Predominant Clinical Manifestation	Time to Diagnosis (weeks from initial procedure)	Microbiologic Findings Culture (+/–) AFB Stain (+/–)	Treatment	Follow-up (months)
36, female	July 2013, Dominican Republic	Bilateral silicone implant breast augmentation, liposuction, bilateral buttock fat injection	4	Bilateral breast abscesses Right buttock abscess	16	<i>Mycobacterium abscessus</i> Culture + AFB Stain +	Abscess drainage, implant removal amikacin, cefoxitin	30
29, female	August 2014, Mexico	Bilateral silicone implant breast augmentation	3	Left breast abscess	5	<i>Mycobacterium abscessus</i> Culture + AFB Stain +	Abscess drainage, implant removal amikacin, cefoxitin	17
44, female	April 2015, Dominican Republic	Bilateral mastopexy, abdominoplasty	4	Bilateral breast abscesses	14	<i>Mycobacterium abscessus</i> Culture + AFB Stain –	Abscess drainage, amikacin, imipenem, linezolid, azithromycin	6



**Figure 1.** Acid-fast stain (Kinyoun method) of *M. abscessus* colonies highlights numerous acid-fast bacilli (100 × objective with oil immersion).

shown in Figure 1. The mycobacteria were resistant to most of the commonly used antibiotics (Table 2). Two of the three patients developed inducible clarithromycin resistance due to erythromycin ribosomal methyltransferase (*erm*) gene expression. A representative photograph of an infected breast wound at the time of presentation is included in Figure 2A. Prosthetic implants in all infected patients were removed and a 6 to 14 week course of culture-directed antibiotic therapy was provided. The mean time between cosmetic surgery and initial symptoms was 3.7 weeks (range, 3-4 weeks). The mean time between initial symptoms and correct diagnosis of the atypical bacterial infection was 11.7 weeks (range, 5-16 weeks). The delayed diagnosis was generally due to a combination of delayed presentation for medical care, failure to obtain wound cultures, misdiagnosis including the initiation of treatment for *typical* infections at initial presentation, and time to obtain culture results for atypical bacteria. All infections completely resolved within 12 weeks from diagnosis after the combination of surgical drainage and completion of an appropriate antibiotic regimen. (Figure 2B). No recurrent infections have occurred within a mean follow up of 17.66 months (range, 6-30 months).

## Literature Review

Seventy studies were selected using the keywords “atypical mycobacteria” and “cosmetic surgery.” Only 59 studies

**Table 2.** *Mycobacterium Abscessus* Susceptibility Test Report in the Reported Patients

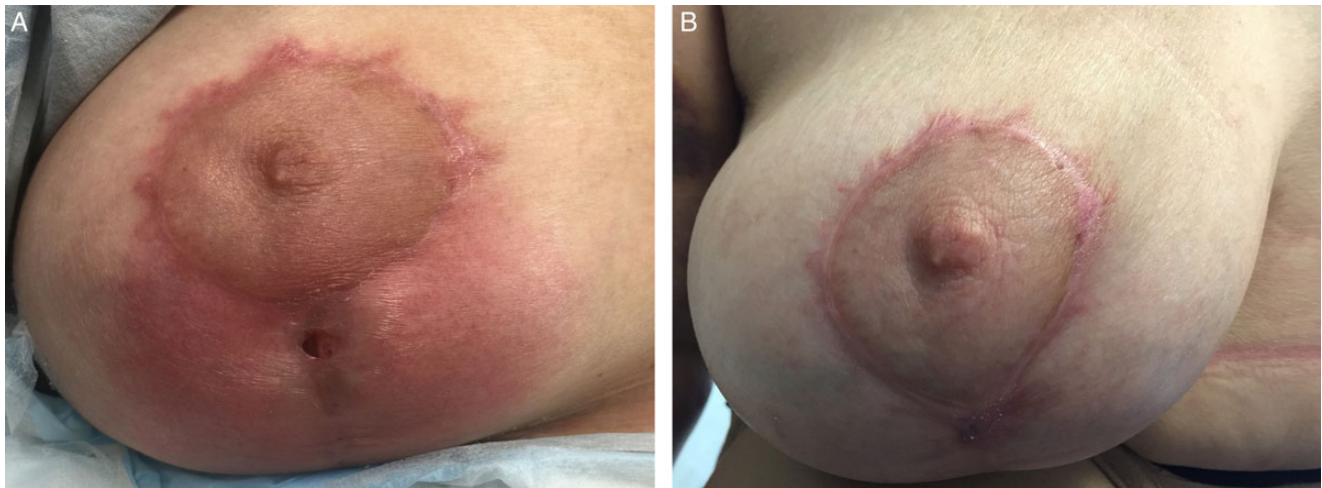
	Patient 1 (36-year-old female)	Patient 2 (29-year-old female)	Patient 3 (44-year-old female)
TMP-SMX	R	R	R
Linezolid	R	I	I
Ciprofloxacin	R	R	R
Imipenem	R	I	I
Moxifloxacin	R	R	R
Cefoxitin	I	I	I
Amikacin	S	S	S
Doxycycline	R	R	R
Minocycline	R	R	R
Clarithromycin*	Inducible Resistance	S	Inducible Resistance
Ertapenem	R	R	R
Meropenem	R	R	R
Levofloxacin	R	R	R
Kanamycin	N/R	S	S

I, indeterminate; N/R, not reported, R, resistant; S, susceptible. \*Clarithromycin resistance in 2 out of 3 patients was due to inducible erythromycin ribosomal methyltransferase (*erm*) gene. The broth Minimum Inhibitory Concentration (MIC) methods as well as clinical definition of susceptible and resistant breakpoints as it applies to these organisms have been approved by Clinical and Laboratory Standards Institute (CLSI).

were reported in English. Out of those 59 studies, only 10 studies reported RGM in medical tourists from a developed country that underwent cosmetic surgical procedures in a developing region and were included for further review.

## DISCUSSION

Medical tourism is a rapidly expanding industry with a projected annual revenue of about \$21 billion per year.<sup>18</sup> Cosmetic surgical procedures account for a significant portion of this industry, primarily because these procedures are not covered either by the state-sponsored or typical private health insurance plans.<sup>19</sup> A recent study of the general public in the United Kingdom reported that 97% of 197 respondents would consider going abroad for cosmetic surgery procedures with Eastern Europe and South America being favored destinations.<sup>19</sup> Decreased cost of surgical procedures in developing countries, shorter wait list time, and patients' perceptions of similar outcomes compared to local providers are most critical reasons driving medical tourism.<sup>20</sup> In one study, 60% of the surveyed plastic surgeons reported seeing complications from cosmetic tourists.<sup>21</sup> Of these, 53% of complications were seen as an emergency and two-thirds of these patients required inpatient admission which further increases healthcare costs.<sup>21</sup> Furthermore, only 26% of these cosmetic tourists had an opportunity to follow up with their



**Figure 2.** (A) A representative patient with *M. abscessus* infection at initial presentation. The patient is a 44-year-old woman who underwent bilateral mastopexy and abdominoplasty in April 2015 in Dominican Republic. She presented 4 weeks after her surgical procedure. (B) Resolution of the infection after surgical drainage and appropriate antibiotic treatment 14 weeks after diagnosis with RGM wound infection.

operating surgeon. Another study reported an additional cost of £6360 per patient to manage the complications of cosmetic tourism.<sup>22</sup>

The goal of this manuscript was to review all the reported case series and case reports of the cosmetic tourists diagnosed with RGM, in addition to reporting the experience at our center. A comprehensive overview of the available literature could provide a better insight vis-à-vis the demographics of the affected patient population, prevalence of the disease with regional specificity, and clinical outcomes of the affected patients. The reported studies comprise of case reports and small case series which highlight the rarity of this disease and are summarized in Table 3.<sup>6,9-17</sup> All the patients described in the literature are young and middle-aged females. Abdominoplasty, liposuction, and cosmetic breast surgeries were the most commonly performed procedures. The reported interval between the procedure and the initial presentation was 4 to 7 weeks for majority of the patients. Most of the involved procedures have been reported from the Dominican Republic and other Latin American countries. However, there are also reports of the procedures being performed in Asian countries for patients who are residents in Europe and Australia.<sup>16,17</sup> Molecular typing using pulsed-field gel electrophoresis and randomly amplified polymorphic DNA polymerase chain reaction confirmed that *M. abscessus* isolates from 7 out of 12 reported cases by CDC in 2004 were indistinguishable.<sup>9</sup> This suggested that the mycobacteria outbreak stemmed from the same source in all 7 cases. Also, out of 19 cases identified by the Maryland Department of Health and Mental Hygiene, 12 reported undergoing surgery at the same clinic in Dominican Republic.<sup>13</sup> Furuya et al reported that 9 out of the 19 patients in their study underwent surgery at the

same clinic and 8 of these 9 patients were related by molecular typing.<sup>6</sup> These data support the belief that these infections often stem from the same initial source.

*M. abscessus* belongs to the group of RGM which also includes *M. fortuitum* and *M. chelonae*.<sup>23</sup> They grow within one week, compared with other species of mycobacteria which take up to 6 weeks to grow in culture. *M. abscessus* is ubiquitous in the environment and has been isolated from municipal and well water, soil, and dust.<sup>23</sup> It has been associated with a variety of nosocomial outbreaks following cosmetic procedures and non-cosmetic procedures such as podiatric surgery, hemodialysis, and myringotomy.<sup>6,9-17,24-26</sup> In the largest published series of 63 patients with skin and soft tissue infection due to RGM over 17 years, most of the patients with single lesion had a history of trauma or a medical procedure at the subsequent site of infection.<sup>27</sup> The median time between symptom onset and microbiological diagnosis was 86 days. Forty-five patients were treated with total of 102 courses of antimicrobial agents, with combination therapy prescribed in 80% of these cases. The median duration of parenteral antimicrobial agents was 25 days while the median duration of oral antimicrobial agents was 127 days. Specific information about sequential usage of parenteral antibiotics followed by oral antibiotics was not available in this study. Surgery was performed in 37 (59%) patients out of whom 9 patients were treated with surgery alone.<sup>27</sup>

There has only been a single study describing the outbreak of RGM infection following liposuction in the United States<sup>28</sup> as compared to multiple studies described in the developing world.<sup>6,9-17,29,30</sup> A review of microbiology reports from 2000 to 2005 at New York–Presbyterian Hospital–Columbia University Medical Center established

**Table 3.** An Extensive Literature Review Describing the Demographics and Disease Characteristics of the Patients Diagnosed With RGM Wound Infection Following Cosmetic Surgery Procedures in Developing Countries

Study	Patients with Culture Proven RGM	Mean Age (Years)/Gender	Country of Residence	Country of Procedure	Procedure(s)	Interval between Procedure and Presentation	Treatment
Furuya et al <sup>6</sup>	19	33, all female	United States	Dominican Republic	Abdominoplasty, liposuction, cosmetic breast surgery	7 weeks	Surgical drainage. Clarithromycin alone or on combination for 6 months
CDC <sup>9</sup>	12	32, all female	United States	Dominican Republic	Abdominoplasty, liposuction, breast lift, breast reduction, breast implant	5 weeks	Surgical drainage, and antibiotic therapy
Newman et al <sup>10</sup>	2	53, all female	United States	Dominican Republic	Abdominoplasty, liposuction	7 weeks	Surgical drainage/ macrolides alone or in combination for up to 6 months
Maurer et al <sup>11</sup>	7	N/R, all female	Switzerland	Dominican Republic (5), Ecuador (1), Mexico (1)	Liposuction, abdominoplasty, breast augmentation, breast reduction	N/R	Surgical drainage, implant removal, amikacin/linezolid/moxifloxacin (alone/ combination for up to 6 weeks)
Schnabel et al <sup>12</sup>	19	N/R, all female	United States	Dominican Republic	Liposuction, abdominoplasty, breast implant	N/R	Surgical drainage, long course antibiotic therapy
Engdahl et al <sup>13</sup>	3	44, all female	United States	Dominican Republic	Abdominoplasty, liposuction, breast augmentation	18 weeks	Surgical drainage, 6 months antibiotic therapy with variable combination of ampicillin, cefoxitin, clarithromycin, levaquin
Ruegg et al <sup>14</sup>	1	39, female	Switzerland	Mexico	Breast implant, liposuction	20 weeks	Surgical drainage, clarithromycin (20 weeks), moxifloxacin (6 weeks)
Zosso et al <sup>15</sup>	1	52, female	Switzerland	Dominican Republic	Abdominal liposuction	4 weeks	Surgical drainage, combination of macrolide, rifabutin, moxifloxacin
Schlarb et al <sup>16</sup>	1	30, female	Germany	Turkey	Abdominoplasty	12 weeks	Surgical drainage, moxifloxacin, clarithromycin (3 months)
Yau et al <sup>17</sup>	1	33, female	Australia	Thailand	Facelift	6 weeks	Surgical drainage, cefoxitin and clarithromycin

CDC, Centers for Disease Control and Prevention; N/R, not reported.

8 patients with *M. abscessus*. All of these 8 patients had undergone cosmetic surgery in the Dominican Republic. Over the same time period, there were no reported cases of *M. abscessus* infection complicating >230,000 surgical procedures performed at this medical center or >60,000 performed at Baystate Medical Center (Springfield, MA).<sup>6</sup> This might provide indirect evidence of increased *M. abscessus* complication rates in Dominican Republic as compared to the United States but there has been no definitive study

comparing all data in all patients from both countries, and the logistics of doing so make this near impossible.

Ineffective sterilization of surgical instruments or injectable solutions have been hypothesized as a contributing factor in numerous mycobacterial outbreaks. Inexpensive and low-level chemical methods of sterilization such as usage of quaternary ammonium solutions have been implicated in the outbreak of mycobacterial infection.<sup>29,30</sup> Torres et al reported 7 cases of culture-confirmed RGM wound

infections following liposuction. In these patients, liposuction cannulae were cleaned with tap water and soap followed by low-level disinfection with a commercial quaternary ammonium solution.<sup>29</sup> Following the report of this outbreak, two of the affected surgical facilities switched to high-level disinfection such as ethylene oxide gas sterilization, and no further cases of RGM infections have been reported from these facilities.<sup>29</sup> Because of their minimal effectiveness against mycobacteria, commercial quaternary ammonium solutions are not included in current disinfection recommendations in the United States.<sup>31,32</sup> In another study, isolates from the 12 patients with culture-confirmed RGM infection and an environmental isolate collected from the faucet in a physician's office differed by only 1 to 2 restriction bands, which raises the possibility of RGM outbreak transmission from the potable water supply.<sup>28</sup> Reuse of liposuction cannulas after rinsing with tap water followed by inadequate disinfection, an inappropriate medical environment, and lack of knowledge pertaining to infection control among the medical team members were identified as key factors leading to such infectious complications.<sup>28</sup> In a recent study, nontuberculous mycobacteria (NTM) were detected in 78% of potable water sources collected from 25 states across the United States, of which *M. abscessus* was reported in 12% of the samples.<sup>33</sup> The study also observed statistically significantly higher levels of NTM in chloraminated water than in chlorinated water. Meticulous attention regarding the sterilization techniques is critical to the prevention of the RGM infection outbreaks.

Since RGM infections do not require mandatory reporting to public health departments, the actual incidence of this infection might be considerably higher than reported. Failure of the wounds to heal after conventional treatment should raise concern for atypical infections. It should be noted that the incubation period of RGM infections could vary from weeks to months and the diagnosis should not be discounted based on delayed presentation. For accurate diagnosis, both wound drainage and tissue biopsy should be sent for acid-fast staining, mycobacterial culture, and routine surgical pathology. The RGM will grow on blood agar, MacConkey agar, and Lowenstein-Jensen medium (primarily used for mycobacteria) in about 7 days. The culture sensitivity may be enhanced by also incubating the specimen at 28°C to 30°C (besides the standard 37°C) since some strains of RGM grow at lower temperatures.<sup>34</sup>

Similar to previous reports of RGM infections, our patients predominantly exhibited erythema, tenderness, and serous drainage from surgical wounds. Failure of antibiotics against common pathogens in our patient population (such as *Staphylococcus* and *Streptococcus*) and a lack of bacterial growth on routine cultures raised concern for atypical infection. Treatment of RGM infections depends on the clinical manifestation and antimicrobial sensitivity. A

combination of surgical drainage, removal of prosthetic material, and a prolonged course of culture-directed antibiotic therapy are the appropriate initial treatments.<sup>9-17</sup> Extensive drug resistance is very common in RGM wound infections and optimal therapeutic antibiotic regimens have not been established in controlled studies. Severe infections initially require a multi-week course of intravenous antibiotics, often cefoxitin and amikacin, which covers majority of RGM isolates.<sup>34</sup> While most RGM demonstrate susceptibility of cefoxitin, its poor availability in the United States limits its use in this setting. Amikacin and imipenem are often employed as initial empiric intravenous therapy in such scenarios, in combination with oral clarithromycin or azithromycin while awaiting susceptibility testing. Tobramycin has good activity against *M. chelonae* and tigecycline, and clofazimine may be useful in the treatment of cases that are resistant to amikacin, imipenem, or both.<sup>35,36</sup> Initial parenteral therapy is followed by an oral regimen with a macrolide backbone such as clarithromycin. Oral linezolid is also frequently used as part of combination therapy for RGM, though long term use may be limited by gastro-intestinal tolerability, pancytopenia, and peripheral neuropathy. Total duration of therapy is dependent on severity of infection and clinical response, but may span 2 to 12 months.<sup>6</sup> Clarithromycin can be used alone or as a combination therapy but no prospective trials have compared these options. The single clinical trial using clarithromycin monotherapy reported only 1 case of acquired clarithromycin resistance in a non-compliant patient who prematurely discontinued therapy.<sup>37</sup> When used as a single-drug therapy, Wallace et al have recommended daily usage of clarithromycin for at least 4.5 months.<sup>38</sup> However, both *M. abscessus* and *M. fortuitum* have been found to possess erythromycin ribosomal methyltransferase (*erm*) genes that modify the binding sites for macrolides and confer inducible antibiotic resistance.<sup>38,39</sup> This results in "susceptible" noted at day 3 of incubation and "resistance" by incubation period of 14 days.<sup>40</sup> Clarithromycin resistance has been described in the clinical isolates of *M. abscessus* complex<sup>41</sup> and inducible clarithromycin resistance due to *erm* gene was seen in 2 out of 3 patients in our study. With this knowledge, it would be prudent to use combination therapy when transitioning to oral antibiotic therapy.<sup>40</sup>

A limitation of our study stems from the small sample size and a single institution experience. Our study reports only three medical tourists with RGM wound infections following cosmetic surgery procedures in developing countries. However, the limited number of cases in the literature highlights the rarity of this diagnosis. With the increased frequency of medical tourism and low-cost cosmetic procedures, the suspicion of RGM needs to be entertained for any infection unresponsive to therapy, particularly when the surgery was performed in a developing country.

## CONCLUSIONS

Atypical mycobacterial infections appear to be more common in medical tourists undergoing cosmetic surgery procedures in developing countries. Such an increased incidence might be attributed to endemic infections and inadequate sterilization of surgical instruments. Management is generally delayed by the lack of clinical suspicion resulting in a failure to order mycobacteria-specific cultures. Consulting physicians, including plastic surgeons, should have a low threshold to consider atypical etiologies in such scenarios allowing rapid diagnosis and appropriate treatment.

## Disclosures

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