

Case Report

Management of Infections with Non-Tuberculous Mycobacteria (NTM) After Lipofilling: A Case Report and Literature Review

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Abstract

Infections with atypical mycobacteria are rare but pose considerable diagnostic challenges and potential morbidity. We present a case of *Mycobacterium chelonae* infection following microsurgical breast reconstruction, combined with liposuction and lipofilling, along with a review of the current literature. The diagnosis was delayed due to difficulties in confirmation, leading to prolonged treatment. A typical indicator is the lack of improvement after empirical antibiotic therapy. Diagnosis was confirmed by cultures and specific PCR for nontuberculous mycobacteria after 8 weeks. Staged, limited debridement and prolonged antibiotic combination therapy resulted in eradication, although sequelae remain to be addressed.

Keywords: Breast reconstruction; Infection; Lipofilling; Liposuction; *Mycobacterium chelonae*; Nontuberculous mycobacteria

disfiguring scars, sensitivity disorders, and tissue defects. This article aims to sensitize practitioners to NTM as potential causes of chronic infections and to update current treatment options.

Non-Tuberculous Mycobacteria (NtM)

Non-Tuberculous Mycobacteria (NTM) are acid-fast, non-motile, non-spore-forming rod bacteria classified into Slowly Growing (SGM) and Rapidly Growing (RGM) strains. They are distinct from tuberculosis and leprosy pathogens. Depending on the region, NTM account for up to 50% of mycobacteria detected in laboratories [8] and include over 200 species [11,12]. Despite their ubiquitous presence, they are facultative pathogens, with only a few species regularly causing infections [11,13]. *M. chelonae* and *M. abscessus* are the most significant fast-growing NTMs [1,13,14]. *M. abscessus* 38.7%, *M. fortuitum* 31.5%, *M. chelonae* 15%, *M. abscessus/chelonae* complex 9.6% are the most relevant [4]. Resistance testing often lacks standardization in routine laboratories compared to *M. tuberculosis* complex testing.

Standardized testing can usually only be performed in specialized mycobacterial laboratories, such as the National Reference Center for Mycobacteria.

NTM are found in tap water, soil, air, and occasionally on medical instruments [9,10,13]. Transmission likely occurs via infected materials or airborne droplets, not person-to-person. Their hydrophobic, lipid-rich cell wall facilitates biofilm formation [15], enhancing resistance to antimicrobial substances and survival on various surfaces [11]. *M. abscessus* is more common in patients with lung diseases, especially cystic fibrosis. *M. chelonae* can cause local skin infections and osteomyelitis [1,9,13]. NTM are not contagious but can cause chronic, severe infections in predisposed individuals [16]. Primary infection sites include soft tissues [5,13], with typical triggers being medical instrument penetration, such as injections, liposuction, acupuncture, tattoos [1,17-19] and piercing [13]. Other causative factors include contact lenses, insulin injections, laser eye treatments, mesotherapy [19], Botox and filler injections, catheter placement, marker ink, methylene blue [13,15,20,21] and contaminated implants and transplants [4,15,22,23]. Microbiological detection of fast-growing NTM involves forming colonies on selective nutrient media within 7 days [18], differentiating them from slow-growing strains. Due to their low numbers and optimal growth conditions at lower temperatures, cultural detection can take up to 6-8 weeks.

Case Presentation and Results

A 50-year-old patient underwent liposuction and lipofilling in both breasts after microsurgical double-DIEP flap surgery to address contour deficits (Figure 1). Donor sites were the ventral and lateral abdomen. Seven days post-surgery, the patient presented with local redness and swelling, with unremarkable lab findings. By the fourth week, serous secretion and lump formation began (Figure 2). Routine cultures, microscopy and PCR were negative. Local wound treatment and empirical antibiotic therapy (amoxicillin-clavulanate and ciprofloxacin) were initiated. By the eighth week, serous secretion increased, and CRP levels rose, prompting tissue samples for mycobacterial culture. Antibiotic therapy was adjusted to moxifloxacin and amoxicillin-clavulanate. After 3 months, additional tissue samples and surgical debridement were performed, confirming *M. chelonae*. Treatment with clarithromycin and oral linezolid was initiated (Figure 3). 4 months postoperatively, negative findings of the second tissue sample with culture for non-tuberculous mycobacteria occurred. By the fifth postoperative month, symptoms began to improve, but hypertrophic, painful

scars developed (Figure 4), exacerbating pre-existing depression and PTSD. As side effects of antibiotic therapy fatigue, taste disturbances, daily nausea, paresthesia and fungal infection in toes and soles of feet area as well as genital area appeared, which improved by substitution of vitamin B complex, iron, zinc, and selenium. The patient ceased antibiotic therapy after 5 months. After 2.5 years, no relapse was noted, though hypertrophic, painful scars persisted (Figures 5a/b).

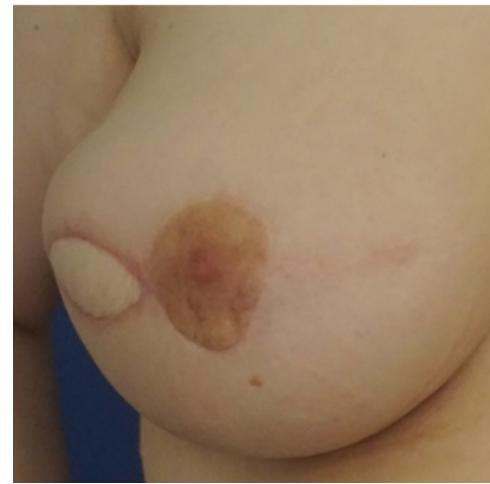


Figure 1: Preoperative situation: post flap surgery.



Figure 2: 4th week: Induration, onset of serous secretion, circumscribed redness.



Figure 3: 3rd month: start Clarithromycin 500mg and Linezolid 600mg for 5 months as well as debridement.



Figure 4: 6th month: signs of inflammation regress, none secretion, fungal infestation foot/genital, resilience reduced, tingling paresthesia in the feet regressing.



Figure 5a: 2.5 years postop: reddened/hypertrophic Scars.



Figure 5b: 2.5 years postop Side view: disfiguring scars.

Discussion

To date, only anecdotal descriptions exist. Padilla et al.'s review of 20 studies from 2003-2017 identified *M. abscessus*, *M. fortuitum*, and *M. chelonae* as the most common causes of NTM soft tissue infections, particularly post-medical tourism [1,6,11]. Infections with *M. chelonae* post-lipofilling are rare [2,5]. Regional differences in infection causes are noted, deficient sterilization procedures frequently were mentioned in medical tourism regions [1].

Frequently, chemical sterilizations with quaternary ammonium compounds, benzalkonium chloride [2,8], or working with unhygienic instruments or contaminated equipment in the operating room are described [1,2,5]. Nontuberculous mycobacteria are relatively resistant to chlorine-containing, mercury-containing and alkaline glutaraldehyde-containing standard disinfectants [15,24]. Mechanical cleaning, thermal steam disinfection, and steam sterilization 134°C, 3200 bar 1.5 h were employed in our case. Usage of small cannula diameter as well as associated technically demanding cleaning and sterilization procedure are additional risk factors. Kim et al. indicated a certain amount of fat necrosis must be expected in lipofilling procedures, especially when executed by surgeons not familiar with the procedure. These areas form an ideal breeding ground, favoring infections. Necrosis rate increases particularly with cryopreserved fat grafts used in multiple procedures, common in Asian countries. Cryopreserved fat grafts pose a higher infection risk during storage [1].

The clinical course can be symptomatic or asymptomatic [13]. A symptomatic course is usually delayed, often 2-4 weeks after the onset of infection and is initially unspecific [1,2,11,15,18], often present initially with localized swelling and redness, progressing to painful lumps, abscesses, ulcerations, and lymph node swelling [1,3,9,13, 21,24]. Rarely, a watery secretion or even sepsis occurs [13,21].

Diagnostic detection of NTM is challenging due to their rarity in postoperative wound infections, as they rather belong to the rare postoperative wound infection pathogens and thus are not initially explicitly in the focus of the treating physician [1,2,9,15,24]. Singh et al. reported a mean time from symptom onset to diagnosis of 11.7 weeks [7]. Diagnosis of presenting case was made within 8 weeks. To date, no standard diagnosis can be identified in the literature [1]. Cultural detection methods are particularly promising [15]. As a rule, however, a smear followed by culture for pathogens and resistances, microscopy after Gram and Ziehl-Neelsen staining give negative results due to insufficient sensitivity [1]. Specific cultural detection methods are particularly promising [15]. As a rule, however, a smear followed by culture for pathogens and resistances, microscopy after Gram and Ziehl-Neelsen staining give negative results due to insufficient sensitivity [1]. As the symptoms usually do not improve in the meantime due to a lack of response to the calculated non-specific antibiotics, more specific detection methods are only then used [3].

To further increase sensitivity, it is recommended to always examine several high-quality samples (e.g. tissue sample instead of swabs) [2,6,19], also to distinguish infection from contamination, as non-tuberculous mycobacteria are ubiquitous in the environment [2]. To examine the cultures for non-tuberculous mycobacteria using a targeted DNA analysis (PCR) is highly recommended. Cultures

can take 6-8, sometimes up to 12 weeks, but are more promising and therefore more sensitive than direct detection methods (direct PCR) [1,2,12]. Direct PCR is a faster method but less sensitive and does not reliably detect non-tuberculous mycobacteria [9]. Non-tuberculous mycobacteria are difficult to treat [25]. NTM are intrinsically resistant to most antibiotics [3,13,4,9, 12,16,24]. As *M. chelonae* is one of the most resistant mycobacteria [4,8,11], identification at the species level and resistance testing in specialized laboratories are crucial [2,12,13].

Histopathological examination complements diagnosis, identifying typical granulomas and signs of chronic inflammation [2,3,12,21]. According to Sardiña et al., the presence of vacuoles is a typical feature and correlates with positive tissue culture and the detection of *M. abscessus* / *M. chelonae* complex [14]. Signs of lymphocytic and neutrophilic, granulomatous inflammation are also indicative [15,24]. Imaging such as ultrasound or MRI aids in visualizing abscesses. Literature shows varying treatment information on *M. chelonae*. Current recommendation is an antibiotic combination of macrolide, aminoglycoside and additional sensitive antibiotic [3,11,13,23]. Macrolides (clarithromycin) appear to have the best effect, but monotherapy is strongly discouraged due to the risk of developing resistance. Treatment should always be given in combination, e.g. with aminoglycoside (tobramycin) [1,13,18,23,24], oxazolidinone (linezolid) [1] or carbapenem (imipenem) or tigecycline [22]. However, it is not uncommon for treatment to be interrupted or discontinued due to severe side effects [6]. Treatment duration of at least 6 months or longer is recommended [1,2,12,13,15,18,26]. Several authors recommend an interdisciplinary approach (infectiologist, microbiologist) [1,12,13], which was also done in the presented case.

Radical surgical removal of contaminated tissue in order to reduce severe scarring, contour deficits or dent formation is recommended [1,3,9,12]. Healing rate with antibiotic therapy alone is reported by Winburn et al. to be 66-73%, together with surgery in 95% of cases [6,9,24,26]. Surgery can go along with surgically induced functional limitations (facial nerve palsy), deformation of soft tissue or bulging, disfiguring scars. This option should therefore only be chosen if conservative methods show no effect [1]. Longlasting side effects such as gastrointestinal disorders (clarithromycin), paresthesia of the extremities (linezolid) or prolongation of the QT interval (azithromycin) can appear [9]. The risk of recurrence of an NTM infection can be between 10-48% after successful treatment [11]. Current treatment recommendations for *M. chelonae* involve a combination of a macrolide, aminoglycoside, and another antibiotic, with clarithromycin showing the best effect. Treatment duration of at least 6 months is recommended, often requiring interdisciplinary collaboration. Radical surgical removal of contaminated tissue may be necessary for severe cases to reduce scarring and contour deficits. Side effects of prolonged antibiotic

therapy can include gastrointestinal disturbances, paresthesia, and QT interval prolongation. Recurrence rates post-treatment range from 10-48%.

Worldwide infection rate caused by *M. chelonae* after lipofilling is rather rare, few cases only have been described. 2015 Kim et al. diagnosed a case of *M. chelonae* infection after lipofilling of 8 ml cryopreserved facial fat using PCR rather than standard cultures. Improvement was achieved with abscess drainage and combination therapy of amikacin, cefoxitin and ciprofloxacin. Too short drug administration led to recurrence. Followed by unknown longer antibiotic treatment finally recovery could be achieved, but accompanied by disfiguring scars and pigmentation on the face [1]. Hammond et al. reported on painful lump formation exclusively on the recipient side 1 week after lipofilling on the buttocks in 2017. Biopsies and cultures for mycobacteria were negative. New cultures using leaking fluid 2 months later and highly specific PCR testing revealed the presence of *Mycobacterium chelonae* [24]. Initial antibiotic treatment with clarithromycin and cotrimoxazole for 6 weeks was followed by clarithromycin and linezolid in accordance with antibiogram. However, the latter had to be replaced by ciprofloxacin after 6 weeks due to paresthesia. Ultimately, healing could only be achieved by generous excision of the affected areas [2]. This resulted in non-concealable, disfiguring gluteal scars on both sides.

Schcolnik et al. reported 2 cases caused by infection with *M. chelonae*, detected 5 months after abdominal liposuction and gluteal lipofilling. Multiple surgical revisions with vacuum sealing and antibiotic triple combination of doxycycline, moxifloxacin and linezolid for 4 months were necessary. The cause was insufficient instrument disinfection by benzalkonium chloride [27,28]. According Escuredo et al. other mycobacterial species such as *M. abscessus* can also lead to infections, shown by 2 cases of breast augmentation by lipotransfer (cosmetic and post-oncological). In the second mentioned case pronounced ulcerations led to ablatio mammae despite the detection of germs 2 weeks later and antibiogram-compliant treatment with amikacin and tigecycline for a further 2 weeks [26]. Jagadeesan et al. reported an *M. chelonae* infection after insulin injection, which was, however, carried out without prior skin disinfection. A 10-week putrid secretion showed no improvement either after antibiotic therapy or after multiple surgical incisions. After a negative smear test, mycobacterial culture and PCR were performed. Healing was achieved with doxycycline and clarithromycin/linezolid for 10 weeks [21]. Similar courses are reported by Terry et al. for non-healing limb ulcerations after penetrating injuries [18] and by Jagadeesan et al. after wart abrasion on the second toe and after laparoscopic removal of an endometriosis [21].

Conclusion

In cases of persistent, refractory skin and soft tissue infections following cosmetic surgery, NTM should be considered as potential infectious agents. Early and specific diagnostic methods should be employed, involving multiple high-quality tissue samples examined in specialized mycobacterial laboratories. Interdisciplinary collaboration with microbiologists and infectiologists is recommended. This article aims to raise awareness of early action to reduce subsequent damage, emphasizing the importance of diagnostic optimization, high-standard disinfection procedures, and the use of single-use instruments.

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Ethical Guidelines: This study has been reviewed by the relevant ethics committee and confirmed that all required guidelines have been met.

Conflict of Interest: There are no conflicts of interest.

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