

Mycobacterium Chelonae Skin Infection Following Intensified Immunosuppression for COVID-19 Pneumonia in a Lung Transplant Recipient : A Case Report

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After bilateral lung transplantation, a 44-year-old man developed coronavirus disease (COVID-19) and received intensified immunosuppressive therapy. After COVID-19, multiple erythematous lesions, accompanied by punctate crusts on the surface, appeared on his right lower leg. Culture of the skin abscess revealed infection with *Mycobacterium chelonae* (*M. chelonae*). Following treatment with clarithromycin, doxycycline, and sitafloxacin, the patient's clinical course was uneventful, and cultures taken from the erythema became negative. This regimen was effective against *M. chelonae* skin infection in immunosuppressed post-lung transplant patients. In diagnostic aspects of *M. chelonae*, Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) followed by multilocus sequence analysis was useful. *Shinshu Med J* 74 : 225—233, 2026

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I Introduction

Mycobacterium chelonae (*M. chelonae*) cutaneous infection is a rare complication experienced by immunosuppressed patients and presents clinical challenges in terms of diagnosis and treatment¹⁾. *M. chelonae* is one of the most common clinically relevant rapid growing mycobacteria (RGM), along with *Mycobacterium fortuitum* and *Mycobacterium abscessus*. Appropriate RGM management requires an understanding of the varying susceptibility patterns of many species and subspecies, as well as diagnostic limitations in accurately differentiating them. Recommended RGM treatment regimens are mainly based on case series and remain unestablished. Clinicians often struggle with the interaction between the antibiotics included in the regimen and the immunosuppressants required

by the patient²⁾³⁾.

In this report, we describe successful treatment of a patient with *M. chelonae* skin infection who was receiving strong immunosuppressive therapy for coronavirus disease 2019 (COVID-19)-induced lung injury after lung transplantation. This report also provides details of polymerase chain reaction (PCR) followed by mass spectrometry used to distinguish *M. chelonae* from related species.

II Case Report

A 44-year-old man was diagnosed with idiopathic pulmonary arterial hypertension in 2017. He had a history of light smoking, consuming approximately three cigarettes per day between 20 and 22 years of age. In October 2021, the patient underwent bilateral lung transplantation from a brain-dead donor. Post-operatively, immunosuppressive therapy with prednisolone, tacrolimus, and mycophenolate mofetil was initiated and no episodes of rejection were observed. Pulmonary hypertension was cured, and maintenance immunosuppressive therapy consisted of predniso-

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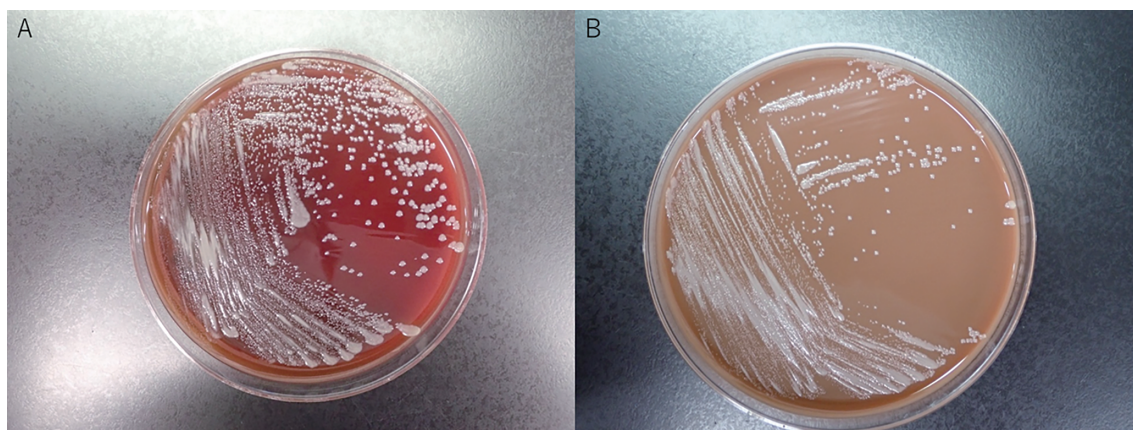


Fig. 1A and B Colony growth on 5 % sheep blood agar (A) and chocolate agar (B) (Becton, Dickinson and Company).

lone 5 mg/day, tacrolimus 1 mg/day (with trough levels of 7–9 ng/ml), and mycophenolate mofetil 500 mg/day.

In July 2024, he developed COVID-19, which was classified as “moderate II” (requiring oxygen therapy) according to the Japanese clinical management guidelines. He received two courses of steroid pulse therapy consisting of methylprednisolone 1000 mg/day for three consecutive days, followed by baricitinib for 14 days. Post-treatment steroid therapy (prednisolone 60 mg/day) was initiated and gradually tapered. However, his respiratory status plateaued, requiring supplemental oxygen via a reservoir nasal cannula (2–3 l/min at rest and 7 l/min during exertion), with a $\text{PaO}_2/\text{FiO}_2$ ratio of approximately 150. Progressive and refractory fibrotic changes persisted, and his clinical condition was discussed at the lung transplant center. The patient was diagnosed with chronic lung allograft dysfunction and discharged at the end of September. The patient was re-registered on the lung transplant waiting list and remained under continued follow-up. The patient developed a left-sided pneumothorax in December 2024 and January 2025, which was managed with observation alone, without chest tube drainage.

In early June 2025, multiple erythematous lesions measuring 3–4 cm in diameter, accompanied by punctate crusts on the surface, appeared on his right lower leg. The patient had no history of hot spring or swimming pool use. Although he kept goldfish, aquarium cleaning was performed by his wife. He was initially treated at a local clinic with oral cefaclor and topical difluprednate ointment, without improvement; sub-

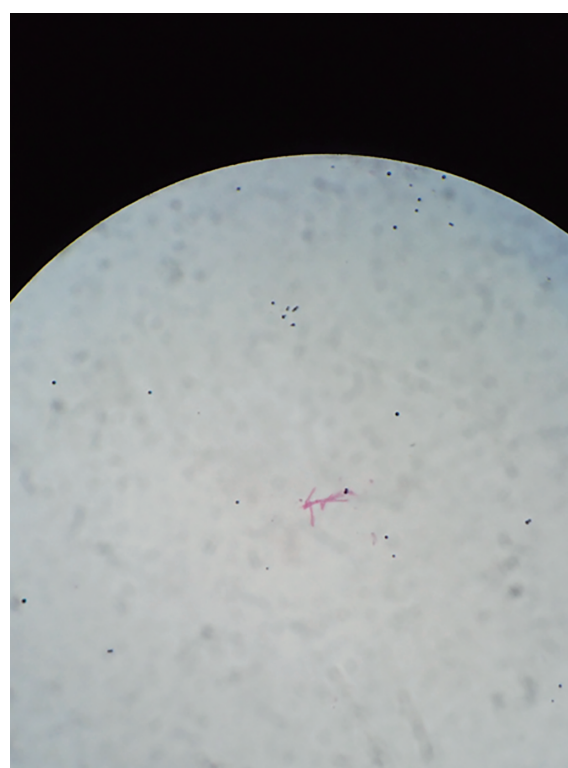


Fig. 2 Culture from a skin abscess with Ziehl-Neelsen staining demonstrating acid-fast bacilli.

sequently, he was referred to the dermatology department of our hospital in July 2025.

A culture obtained from the skin abscess yielded colony growth after four days of incubation on 5 % sheep blood agar and chocolate agar (Becton, Dickinson and Company) at 35 °C in a 5 % CO_2 atmosphere (**Fig. 1A, B**). Ziehl-Neelsen staining of a subsequently obtained specimen from the same lesion detected acid-fast bacilli (**Fig. 2**).

Table 1 Laboratory examination on admission

Measurement parameter	Result	Reference range	Measurement parameter	Result	Reference range
Hematology			Amylase	78 U/l	44-132
White blood cell count	7,480/ μ l	3,300-8,600	BNP	82.8 pg/ml	0-20
Absolute neutrophil count	5,520/ μ l	1,170-6,130	Serology		
Absolute lymphocyte count	1,120/ μ l	350-900	C-reactive protein	0.14 mg/dl	0.00-0.14
Red blood cell count	436×10^4 / μ l	$386-492 \times 10^4$ / μ l	KL-6	1873 U/ml	105-435
Hemoglobin	13.7 g/dl	11.6-14.8	SP-D	118 ng/ml	0.0-109.9
Hematocrit	41.0 %	35.1-44.1	IgG	612 mg/dl	861-1747
Platelet count	13.7×10^4 / μ l	15.8-34.8	Anti-MAC antibody	1.06 U/ml	0-0.69
Blood chemistry			Blood coagulation test		
Total protein	5.4 g/dl	6.6-8.1	PT-INR	1.02	0.85-1.15
Albumin	3.5 g/dl	4.1-5.1	APTT	25.2 sec	20.0-80.0
Blood urea nitrogen	30.7 mg/dl	8.0-20.0	D-dimer	1.1 μ g/ml	0.0-30.0
Creatinine	0.80 mg/dl	0.65-1.07	Therapeutic drug monitoring		
Cystatin C	1.5 mg/l	0.60-0.98	Tacrolimus trough level	9.3 ng/ml	
AST	16 U/l	13-30	Infectious markers		
ALT	18 U/l	10-42	β -D-glucan	<3.81 pg/ml	<20
LDH	256 U/l	124-222	CMV antigenemia assay	Negative	
Total bilirubin	0.94 mg/dl	0.40-1.50			
γ -Glutamyl transferase	136 U/l	13-64			

ALT, alanine aminotransferase ; AST, aspartate aminotransferase ; KL-6, Krebs von den Lungen-6 ; LDH, lactate dehydrogenase ; MAC, *Mycobacterium avium* complex ; PT-INR, prothrombin time-international normalized ratio ; CMV, Cytomegalovirus.

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) (MALDI Biotyper Microflex LT, Bruker Japan ; MBT Compass, MBT Mycobacteria Library v6.0) yielded closely related species within the *M. chelonae* complex, with *M. stephanolepidis* as the top-ranked match (score value 2.06), followed by *M. chelonae* (1.95) and *M. salmoniphilum* (1.88). Because these species are difficult to discriminate reliably using MALDI-TOF MS alone, further species-level identification was performed using multilocus sequence analysis⁴⁾.

Multilocus sequence analysis was conducted using five genetic loci (16S rRNA, hsp65, rpoB, recA, and sodA) comprising a total of 3,534 bp. Multilocus sequence analysis involves performing PCR on multiple specific genes to achieve more accurate identification of RGM strains. The isolate showed the highest sequence similarity to *M. chelonae* (3,511/3,534 bp ; 99.3 %), followed by *M. stephanolepidis* (3,477/3,534

bp ; 98.4 %) and *M. salmoniphilum* (3,411/3,534 bp ; 96.5 %), and was therefore identified as *M. chelonae*.

Multiple erythematous lesions persisted on the right lower leg, and the patient was admitted to our hospital on August 19, 2025. At admission, he was receiving prednisolone 13 mg/day, tacrolimus 0.8 mg/day, mycophenolate mofetil 500 mg/day, itraconazole oral solution (1 % ; 200 mg/day), trimethoprim-sulfamethoxazole 80/400 mg/day, and other medications. He was afebrile, with percutaneous oxygen saturation of 96 % on 3 l/min of supplemental oxygen via a reservoir nasal cannula, which was increased to 5-7 l/min during exertion. Fine crackles were auscultated over the bilateral lower lung fields and the back.

Laboratory findings at admission are summarized in **Table 1**. White blood cell counts and C-reactive protein levels were within normal ranges. Mild renal dysfunction was observed, and tacrolimus trough level (9.3 ng/ml) was within the target range. Serum IgG

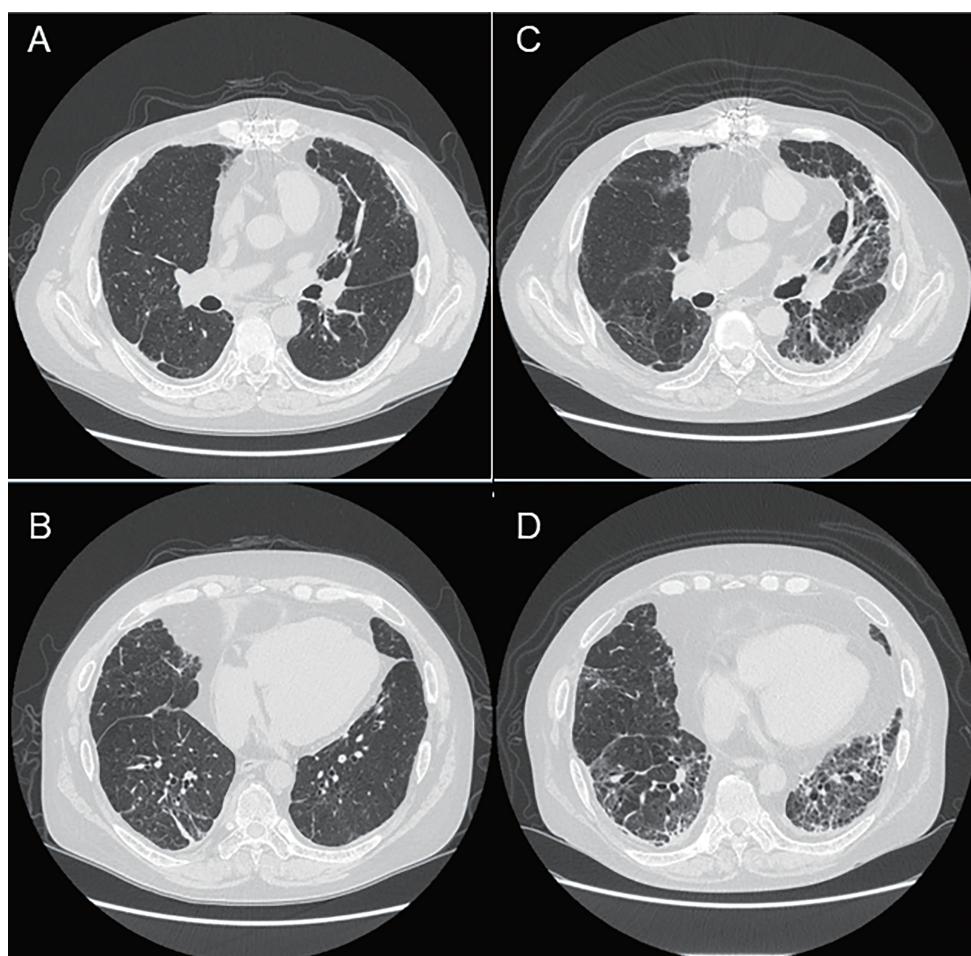


Fig. 3A and B Chest computed tomography images obtained on April 18, 2024, prior to the onset of COVID-19 pneumonia.

Fig. 3C and D Chest computed tomography images obtained at the time of admission.

level was low (612 mg/dl), which was comparable to previous measurements. Tests for anti-GPL-core IgA antibodies were positive. Chest computed tomography (CT) showed gradually progressive emphysematous changes, reticular opacities, and traction bronchiectasis in both lungs; however, there were no new findings suggestive of pulmonary nontuberculous mycobacterial disease (**Fig. 3A–D**). Sputum cultures, including mycobacterial cultures, were negative. Non-contrast CT of the lower extremities revealed epidermal thickening, subcutaneous soft-tissue nodules, and increased attenuation in the right lower leg, without evidence of abscess formation in muscles or bones (**Fig. 4**).

The minimum inhibitory concentrations (MICs) against *M. chelonae* are listed in **Table 2**. Based on

antimicrobial susceptibility testing and interpretation performed according to the CLSI guideline M24 3rd edition⁵⁾ and CLSI supplement M24S 2nd edition⁶⁾, low MICs were observed for tobramycin, doxycycline, ciprofloxacin, and clarithromycin. Although standardized treatment for cutaneous *M. chelonae* infection has not been established, clarithromycin is considered a key drug^{7,8)}. *M. chelonae* lacks the inducible macrolide resistance gene *erm*⁹⁾, and its susceptibility to clarithromycin is generally favorable.

In previous cases at our institution, combination therapy with clarithromycin, doxycycline, levofloxacin or clarithromycin, tobramycin, and imipenem/cilastatin for three weeks, followed by clarithromycin and levofloxacin, resulted in clinical improvement. In the present case, oral therapy was preferred to facilitate

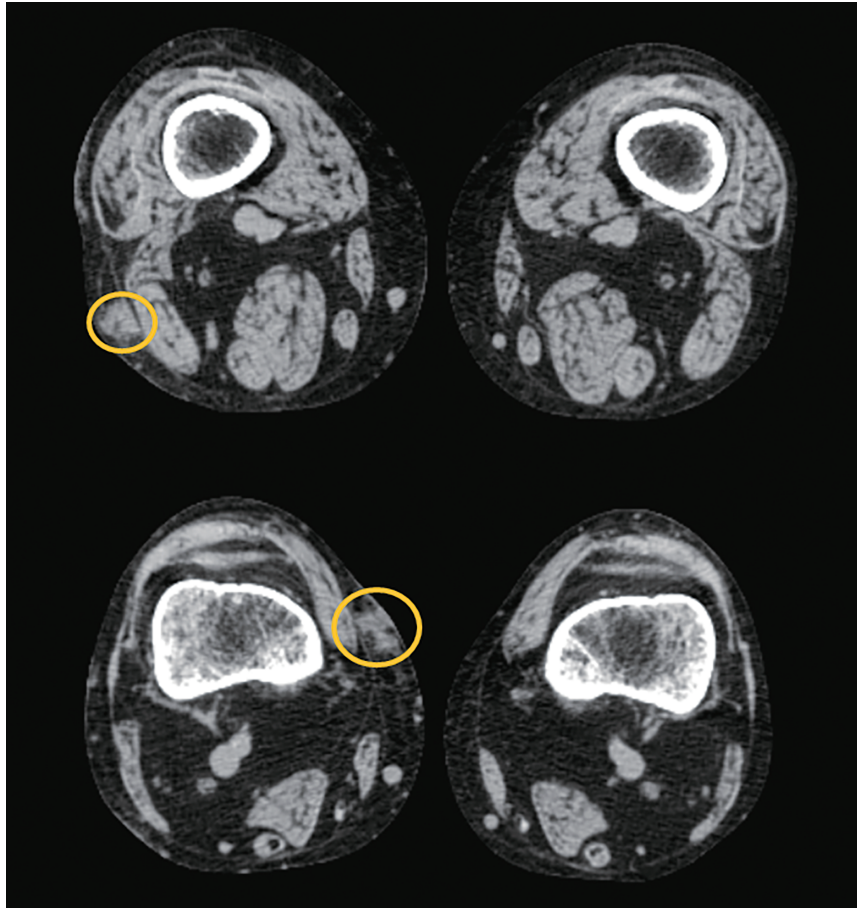


Fig. 4 Non-contrast computed tomography of the lower extremities showing epidermal thickening and subcutaneous soft-tissue nodules in the right lower leg, without evidence of abscess formation involving muscles or bones.

Table 2 Drug sensitivity testing results for our patient

Antibiotics	MIC ($\mu\text{g/ml}$)	Susceptibility*
Tobramycin	2	S
Imipenem/cilastatin	32	R
Faropenem	>64	
Levofloxacin	32	R**
Moxifloxacin	8	R
Trimethoprim-sulfamethoxazole	>152/8	R
Doxycycline	1	S
Meropenem	64	R
Linezolid	16	I
Ciprofloxacin	0.5	S
Sitafloxacin	2	
Amikacin	32	I
Clarithromycin	0.25	S***
Azithromycin	1	

*Based on the CLSI M24 3rd ed 2018, M24S 2nd ed 2023 **Ciprofloxacin and levofloxacin are interchangeable.

***Clarithromycin is representative of newer macrolides (e.g., azithromycin, clarithromycin, roxithromycin).

MIC, minimum inhibitory concentration ; S, susceptible ; I, susceptible, increased exposure ; R, resistant.

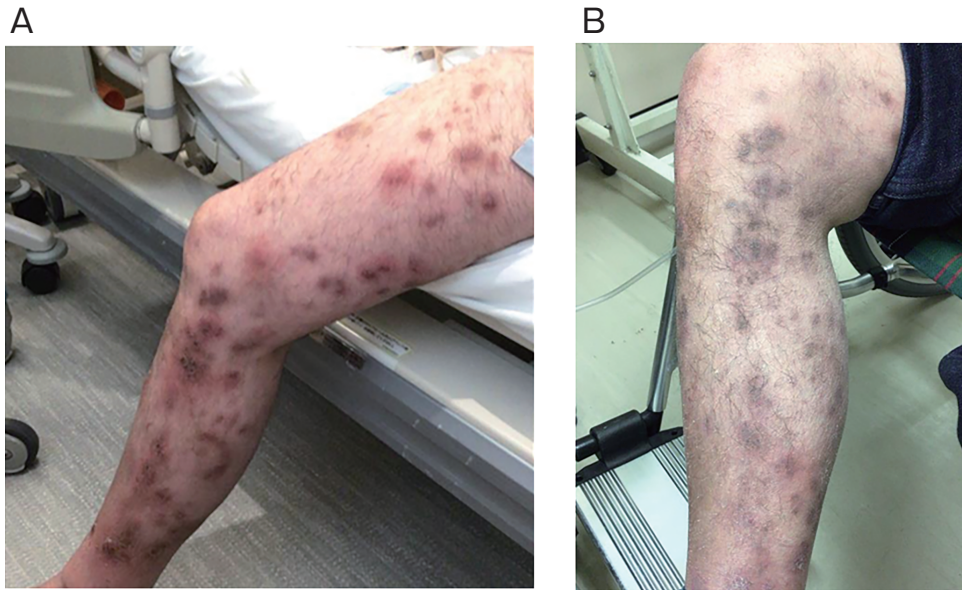


Fig. 5A Clinical photograph of the right lower leg taken on August 19, 2025, before initiation of treatment, showing multiple erythematous lesions measuring 3–4 cm in diameter, with punctate crusts on the surface.

Fig. 5B Clinical photograph of the right lower leg taken on December 4, 2025 (106 days after initiation of treatment), showing that erythema had gradually faded, leaving brownish hyperpigmentation.

transition to outpatient management, and the agents available in our hospital formulary were selected. Following consultation with the lung transplant center, there were concerns that clarithromycin might increase tacrolimus blood levels and worsen renal function. Based on the low MIC, which confirmed susceptibility, clarithromycin was initiated. Tacrolimus trough levels and renal function were closely monitored to manage potential interactions with tacrolimus. The initiation of antimicrobial therapy was scheduled after confirming the MIC results to ensure the selection of an effective macrolide, which was particularly crucial given the potential drug–drug interaction between clarithromycin and tacrolimus. Although multilocus sequence analysis was performed for definitive identification, its results were obtained after the treatment had already been initiated based on the MALDI-TOF MS and MIC findings.

The patient weighed 74.5 kg, and treatment with clarithromycin 800 mg/day, doxycycline 100 mg/day, and sitafloxacin 100 mg/day was initiated on August 20. Mild diarrhea occurred but did not worsen with probiotic therapy. On August 25, tacrolimus trough level increased to 11.3 ng/ml; thus, the dose was re-

duced to 0.4 mg/day, and the trough levels stabilized between 7 and 9 ng/ml. No deterioration in renal function was observed. Prednisolone dose was tapered to 10 mg/day, and the patient was discharged on September 2. The antimicrobial therapy was continued without any major adverse events; erythema gradually faded, leaving a brownish hyperpigmentation (**Fig. 5A, B**).

A repeat mycobacterial culture of the skin lesions performed on August 21 was negative. On November 6, skin biopsy revealed inflammatory cell infiltration composed predominantly of lymphocytes with admixed neutrophils extending from the epidermis to the deep dermis, along with scar-like collagen fiber proliferation. Scattered Langhans-type giant cells were also observed; however, tissue mycobacterial cultures were negative, and these findings were interpreted as post-treatment changes. A treatment duration of approximately six months was planned in consultation with the transplant center.

III Discussion

Herein, we report a case of cutaneous infection caused by *M. chelonae* in a lung transplant recipient follow-

ing COVID-19 treatment. The patient developed multiple painful erythematous nodules on his lower leg after receiving intensive immunosuppressive therapy. Successful management was achieved through a six-month regimen of clarithromycin, doxycycline, and sitafloxacin, while carefully adjusting the dose of tacrolimus to mitigate drug-drug interactions. This case highlights the importance of considering rapidly growing mycobacteria in differential diagnosis of skin lesions in immunocompromised transplant recipients, particularly after additional immunosuppressive therapy, and demonstrates that oral multidrug therapy can be effective with stringent therapeutic drug monitoring.

M. chelonae primarily causes human infection in immunosuppressed patients. The incidence of nontuberculous mycobacterium (NTM) skin infection is reported as 2.0 per 10,000 person per-years in 2000–2009 by USA medical center retrospective study, and in particular, *M. chelonae* skin infection is increasing¹⁾. The increasing trend can be attributed to several factors: (1) increased exposure associated with cosmetic or surgical procedures; (2) host factors, indicated by the rising incidence with age¹⁾. Because no controlled clinical trials of treatment for disease caused by RGM including *M. chelonae* have been performed, selection of regimen depends on case series studies and in vitro susceptibility testing. Accurate identification of RGM determine the outcome of treatment.

Lung transplant recipients require lifelong maintenance immunosuppression, which inherently increases their susceptibility to opportunistic pathogens including RGM⁸⁾¹⁰⁾¹¹⁾. In the present case, we believe that the clinical manifestation of *M. chelonae* was significantly precipitated by the escalation of immunosuppressive therapy for COVID-19. Although the patient's condition was stable under a standard maintenance regimen, the requirement for prolonged and high-dose systemic corticosteroid therapy to manage COVID-19-related respiratory failure likely led to profound suppression of cell-mediated immunity¹²⁾. Such intensive corticosteroid exposure is known to impair macrophage function and T-cell responses, which are essential for controlling mycobacterial pro-

liferation¹³⁾. This temporary but significant intensification of the immunosuppressive state provides an opportunistic window for latent or newly acquired *M. chelonae* to develop into a symptomatic cutaneous infection.

A definitive diagnosis of cutaneous *M. chelonae* infection requires clinical suspicion and microbiological confirmation. In this case, the rapid growth of the pathogen within four days on sheep blood agar and chocolate agar plate was highly suggestive of RGM. Although *M. chelonae* and the *M. abscessus* complex share similar clinical presentations and morphological characteristics, their antimicrobial susceptibility profiles differ significantly, making precise species-level identification crucial for selecting an appropriate treatment regimen. We used MALDI-TOF MS for initial identification, which was subsequently confirmed by multilocus gene sequencing of targets, such as 16S rRNA, hsp65, and sodA^{14)–16)}. After confirming the MALDI-TOF MS results, we attempted to distinguish *M. chelonae* from closely related species using multilocus sequence analysis, which confirmed the species identity with greater accuracy.

In the current clinical landscape in Japan, the diagnostic approach for RGM has shifted significantly. While traditional biochemical tests—such as nitrate reduction and salt tolerance—are included in the comprehensive insurance coverage for bacterial identification, their clinical utility is limited by long turnaround times. In contrast, MALDI-TOF MS is covered by national health insurance and has become the preferred method due to its superior speed and cost-performance. Although multilocus sequence analysis offers the highest accuracy for species identification, it is not currently covered by the public insurance system, making it less accessible for routine bedside diagnostics. Thus, we utilized MALDI-TOF MS for rapid initial identification, supplemented by multilocus sequence analysis to ensure diagnostic reliability in this immunosuppressed patient.

Although treatment selection is typically based on MALDI-TOF MS results in routine clinical practice, more accurate identification of the RGM type using multilocus sequence analysis may contribute to the

selection of appropriate treatment regimens. The integration of these molecular techniques has allowed prompt initiation of a targeted antimicrobial strategy, which is particularly vital in immunocompromised patients owing to the risk of rapid dissemination.

The selection of a treatment regimen for *M. chelonae* should involve a multi-drug approach tailored to the results of antimicrobial susceptibility testing. In the present case, a combination of clarithromycin, doxycycline, and sitafloxacin was administered. Although the isolate was resistant to levofloxacin, it remained susceptible to sitafloxacin, which has been reported to be effective against some fluoroquinolone-resistant NTM strains. A critical challenge in this treatment was the management of drug-drug interaction between clarithromycin and tacrolimus¹⁷⁾. Clarithromycin is a potent inhibitor of cytochrome P450 3A4, which can lead to a significant increase in tacrolimus blood levels¹⁸⁾. Upon initiating clarithromycin, we closely monitored tacrolimus trough levels and preemptively reduced its dose from 0.8 mg to 0.4 mg per day to maintain the therapeutic range and prevent nephrotoxicity. This proactive tacrolimus dose adjustment and stringent monitoring allowed for safe continuation of the necessary antimicrobial therapy without compromising the stability of the transplanted lungs. The novelty of this case lies in the application of multilocus sequence analysis for species-level precision in a lung transplant recipient. Combined with early MIC assessment, this approach ensured high diagnostic accuracy, which is essential for managing complex cases. The

clinical significance of routine multilocus sequence analysis in addition to MALDI-TOF MS remains a subject of debate. In this case, we utilized multilocus sequence analysis to ensure the highest diagnostic certainty, given the patient's profoundly immunosuppressed state. Further studies are needed to define the cost-effectiveness and clinical necessity of routine multilocus sequence analysis for RGM identification in standard clinical practice.

Conclusion

Here, we report a case describing management of a patient with *M. chelonae* skin infection who was receiving strong immunosuppressive therapy for COVID-19-induced lung injury after lung transplantation. A combination therapy regimen containing clarithromycin, which interacts with tacrolimus, is effective against *M. chelonae* skin infections in immunosuppressed patients, such as those after lung transplantation, under close monitoring of blood tacrolimus levels. MALDI-TOF MS followed by multilocus sequence analysis is useful for more accurate identification of the RGM type.

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