

Articles



Successful treatment of *Mycobacterium abscessus* infection with alternate-day half-dose linezolid: A case report and literature review

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Abstract

Mycobacterium abscessus (Mab) is a common rapidly growing non-tuberculous *Mycobacterium* (NTM). On the basis of host immune deficiency (such as positivity for anti-IFN- γ autoantibodies), it can cause a variety of diseases, with pulmonary infection being the most common, followed by skin and soft tissue infections. Currently, the clinical treatment for Mab infections mainly relies on a multi-drug combination regimen centered around macrolides. However, due to the limited number of drugs active against Mab, along with a long treatment course, a high susceptibility to macrolide-induced resistance, and poor treatment compliance caused by adverse drug reactions, clinical treatment is challenging and it is difficult to achieve satisfactory therapeutic outcomes. This article reports a case of skin and soft tissue infection caused by Mab in a patient with a drug allergy constitution and multiple adverse drug reactions. During the maintenance treatment phase, after repeated adjustments to the anti-infective regimen, a treatment strategy was ultimately adopted: taking half the daily dose of linezolid (600 mg, qd) on odd-numbered days and the regular dose of linezolid (600 mg q12h) on even-numbered days, which led to successful treatment. After dose adjustment, the patient's skin lesions completely resolved, and no recurrence was observed during follow-up through December 31, 2025. No further severe myelosuppression occurred under the alternate-day half-dose regimen. Meanwhile, we reviewed relevant literature with the aim of exploring individualized treatment plans for Mab and providing reasonable treatment recommendations for clinicians.

Keywords: *Mycobacterium abscessus*; adverse drug reactions; linezolid; case report

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Introduction

Mycobacterium abscessus (Mab) is widely found in natural environments such as water, soil, and dust and can be contracted by humans and certain animals^[1]. Mab is one of the clinic's most common Rapidly growing mycobacteria (RGM), it was first isolated in 1953 from a subcutaneous abscess-like lesion until 1992, when it was recognized as a separate species^[2]. Mab can cause various diseases, with lung infections being the most common, followed by skin and soft tissue infections^[3]. Clinical manifestations of cutaneous and soft-tissue Mab infections vary widely and may present as subcutaneous nodules, abscesses, cellulitis, ulcers, and sinus tracts^[4], whereas immunocompromised adults may also present with enlarged lymph nodes and systemic symptoms such as metastatic dissemination, septic shock, pulmonary infiltrates, adrenal necrosis, and single or multiple disseminated lesions in the brain parenchyma^[5]. Mab is naturally resistant to most antibiotics, including first-line anti-tuberculosis drugs. The problem of induced resistance to macrolides is becoming increasingly severe, with a long treat-

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ent period and a tendency to relapse after stopping the drug, which has been labeled the "antibiotic nightmare." There needs to be more information on large-sample clinical studies related to Mab infections, and there is still a preponderance of small-sample data or case reports. Here we report on a case of Mab infection of the soft tissues of the skin encountered in our clinical work. The patient tested positive for anti-IFN- γ autoantibodies and had a history of allergies to "sulfonamides and β -lactams". During the treatment, the patient developed an allergy to "quinolones" and adverse reactions to various drugs. After repeatedly adjusting the anti-infective treatment regimen, the patient was finally treated with linezolid at half the daily dose (600 mg, qd, po) on odd-numbered days and linezolid (600 mg, q12h, po) on even-numbered days. Subsequently, no related adverse reactions occurred, and the patient's condition improved and stabilized.

Case introduction

A 72-year-old Chinese female patient weighing 64.5 kg and 158 cm in height (overweight body mass (25.84 Kg/m²)). The patient had a previous history of tuberculosis in 2017 and was on standardized anti-tuberculosis treatment, discontinued after an entire course of treatment as prescribed by the doctor. In 2019, the patient had a recurrence of tuberculosis and was given a full dose and course of antituberculosis treatment, which was discontinued on medical advice after stabilization. The patient

complained of a previous allergy to "sulfonamides and beta-lactams." The patient was hospitalized in the Department of Neurology of our hospital on April 29, 2022, due to weakness of the left side of the limbs, and was admitted to the hospital for a head and neck cranial magnetic resonance examination suggestive of acute-phase cerebral infarction, and was given targeted treatment. However, starting on May 7, 2022, the patient developed a slight rash on the right side of the neck, accompanied by itchy and uncomfortable skin, and on examination, the skin of the right side of the neck was seen to be flushed at the base, with scattered papules of about the size of green beans. Topical topical mucopolysaccharide polysulfate cream was given without improvement. Subsequently, the patient's neck rash gradually became more numerous and extended to the face, forming multiple nodules partially connected into pieces, with a bumpy and irregular surface, accompanied by pain and itching (Figure 1, A). After dermatology consultation, it was considered that local infection and obstruction led to lymphatic vessel dilation. It was recommended to transfer the patient to the dermatology department and complete lymph node and local tissue biopsy for further definitive diagnosis.

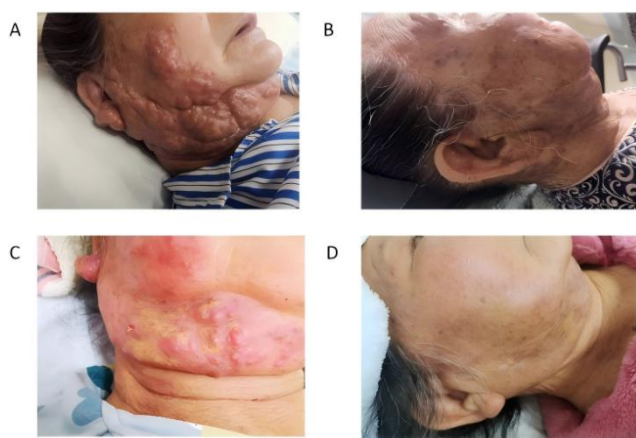


Figure 1. Comparative images of skin before and after treatment. (A) Multiple nodules, some connected to form patches, with irregular and uneven surfaces; (B) Significant improvement in facial rash compared to before; (C) After changing the treatment regimen, the rash on the right side of the neck and face, as well as under the right jaw, gradually increased compared to before; (D) Cheeks one year after treatment: The facial rash has completely resolved.

After the patient was referred to the dermatology department, a skin biopsy at the site of infection was performed on June 9, 2022, and the pathology was suggestive of infectious granulomatous inflammation. After a hospital-wide multidisciplinary consultation, the possibility of fungal infection was considered high, and oral itraconazole 200mg q12h (doubling the first dose) was given for antifungal treatment. After nearly two weeks of antifungal treatment, the patient's skin lesions did not improve; they increased in extent. During this time, tissue specimens were sent out for pathologic diagnosis and macrogene testing. On June 22, 2022, the results from the Department of Dermatopathology, the First Affiliated Hospital of Guangxi Medical University showed: acid-fast bacilli (+), mycobacteria were observed, and infectious granulomatous inflammation was considered. Meanwhile, the metagenomic sequencing results from Guangxi KingMed Diagnostics Institute indicated the presence of 1,490 mycobacterial sequences. On June 25, 2022, skin tissue pathology testing at Guangzhou KingMed Diagnostics Institute detected *Mycobacterium abscessus* (Figures 3 and 4). Mycobacterial culture was attempted using

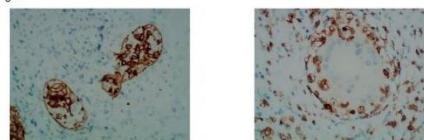
the tissue specimen but yielded no growth, likely due to the small specimen size and prior formalin fixation. Therefore, phenotypic drug susceptibility testing (DST) could not be performed. After combining the above histopathologic and metagenomics results, itraconazole was discontinued on June 27, 2022, and clarithromycin dispersible tablets 500 mg po q12h + amikacin 800mg ivgtt qd + imipenem 1000mg ivgtt q12h + moxifloxacin 400mg po qd were administered. On June 28, 2022, the patient developed skin itching and discomfort, primarily in the limbs. Upon further inquiry into the medical history, it was found that the patient had experienced similar symptoms after previous use of levofloxacin, suggesting a possible allergy to quinolones. Therefore, moxifloxacin was discontinued while the remaining medications remained unchanged, and the patient's skin itching symptoms gradually subsided. On July 28, 2022, after consultation with the Division of Infectious Diseases, it was recommended that the patient be discharged and given clarithromycin 500mg q12h po + minocycline 100mg q12h po for maintenance therapy.

The specimen tested positive via DNA-based metagenomic sequencing for pathogenic microorganisms, with 3 sequences of *Mycobacterium abscessus* detected, along with some colonizing bacteria and/or suspected background microorganisms. Clinical judgment should be made in combination with the patient's clinical manifestations and other auxiliary diagnostic results.

1 List of prokaryotic microorganisms						
Genus				Species		
Type	Latin name	Number of detected sequences	Relative abundance (%)	Latin name	Number of detected sequences	RPM-Ratio
G+	Mycobacteroides	3	75	Mycobacteroides abscessus	3	135.49
2 List of fungi						
Genus				Species		
Latin name	Number of detected sequences	Relative abundance (%)	Latin name	Number of detected sequences	RPM-Ratio	
Not detected						
3 List of DNA viruses						
Genus				Species		
Type	Latin name	Number of detected sequences	Relative abundance (%)	Latin name	Number of detected sequences	RPM-Ratio
Not detected						

Figure 3. Histopathological examination of skin tissue from Guangzhou KingMed Diagnostics Institute.

Microscopic findings:



Diagnostic opinion:
Wax block No. Q2206266 (from the chest area): Skin tissue. No obvious changes were observed in the epidermis. Throughout the entire dermis, multiple focal granulomas were seen, accompanied by necrosis and the formation of multinucleated giant cells. The multinucleated giant cells had a large number of nuclei with irregular distribution. There was extensive infiltration of lymphoid cells, plasma cells, eosinophils, histiocytes, and a small number of neutrophils around the granulomas. Microabscesses were observed in small focal areas. Some lymphoid cells had irregular nuclear shapes and were attracted to the sweat gland epithelium.

Special staining (D-PAS, Gomori methenamine silver (GMS), acid-fast, and Giemsa) performed by Guangzhou KingMed Diagnostics on wax block No. Q2206266 all yielded negative results.

Special staining (PAS, Gomori methenamine silver (GMS), acid-fast, and AB) performed by the submitting institution on wax block No. Q2206266 all showed negative results.

Immunohistochemical results from the submitting institution for wax block No. Q2206266: CD45 scattered positive, CD8 scattered positive, CD4 positive, CD68 positive, CD31 weakly positive (+/-), S100 negative, and CD1a focal positive.

Wax block No. Q2206549 (from the neck area): Skin tissue. No obvious changes were observed in the epidermis. Throughout the entire dermis, multiple focal granulomas were present, accompanied by necrosis and the formation of multinucleated giant cells. The multinucleated giant cells had a large number of nuclei with irregular distribution. There was extensive infiltration of lymphoid cells, plasma cells, eosinophils, histiocytes, and a small number of neutrophils around the granulomas. Some lymphoid cells had irregular nuclear shapes, were attracted to the sweat gland epithelium, and a few were phagocytosed within the multinucleated giant cells.

Special staining results from the submitting institution for wax block No. Q2206549-2: PAS, Gomori methenamine silver (GMS), acid-fast, and AB stains were all negative.

The metagenomic microbial testing result from Uniontime Healthcare (or Kangsheng Huangjiu, depending on the official English name used by the company) is negative.

The metagenomic microbial testing result from Guangxi KingMed Diagnostics headquarters (Guangzhou) is negative.

In summary, considering the molecular findings, the diagnosis is granuloma caused by *Mycobacterium abscessus* infection of the skin. Since immunohistochemical markers CD7 and CD8 showed negative expression in mild atypical lymphoid cells phagocytosed by multinucleated giant cells and in lymphoid cells destroying sweat gland epithelium, and monoclonal rearrangement was detected within a polyclonal background for both TCR β and TCR γ , the possibility of concomitant granulomatous cutaneous T-cell lymphoma is considered. However, given the patient's advanced age and multiple underlying conditions, it is recommended to initiate anti-mycobacterial treatment first and then observe. If the cervical lymph nodes continue to enlarge or the rash does not fully resolve, a complete lymph node and skin tissue biopsy should be performed for further evaluation.

Wax block No. Q2206549-1 was processed at KingMed Diagnostics headquarters (Guangzhou).

—Additional immunohistochemical staining results: CK shows focal destruction of sweat gland epithelium; CD3+, CD5+, CD4+, CD7 and CD8 (both showing slight positivity, with negative expression in lymphoid cells phagocytosed by multinucleated giant cells and in lymphoid cells destroying sweat gland epithelium); PD1-, Ki67 (15% positive).

—Additional in-situ hybridization result: EBER (-) (negative).

—T-cell clonality assessment: In this specimen, monoclonal rearrangement against a polyclonal background was detected at the 197bp region within the D β -JB1/2 interval of TCR β , and at the 176bp region within the V γ -JY1.3/2.3 interval of TCR γ .

—Re-performed microbial metagenomic DNA testing: *Mycobacterium abscessus* was detected (with 3 sequence reads, a relative abundance of 75%, and an RPM-Ratio of 135.49).

Figure 4. Histopathological report of skin tissue from Guangzhou KingMed Diagnostics Institute.

During the out-of-hospital maintenance treatment, the patient began to experience recurrent nausea and vomiting discomfort on August 10, 2022. Considering that minocycline is a newly added drug, gastrointestinal reactions may be related to it, and after symptomatic treatment, symptoms did not improve, minocycline was discontinued. After the patient's gastrointestinal symptoms, such as nausea and vomiting, improved, the treatment was adjusted to clarithromycin 500mg q12h po + linezolid tablets 600mg q12h po anti-infective treatment on August 14, 2022. Dizziness and discomfort, and anemia began on September 2, 2022; symptomatic treatment was given with no improvement in symptoms. On September 18, 2022, the patient was admitted to the infectious diseases unit, and on examination, the facial rash was seen to be significantly better than before (Figure 1, B). Routine blood tests suggested severe anemia, thrombocytopenia, and granulocytopenia (Figure 2), and linezolid was considered to cause bone marrow suppression. Therapeutically, linezolid tablets were suspended, and clarithromycin tablets 500mg q12h po monotherapy continued to be given. After a review of routine blood tests suggesting a rise in hemoglobin and a return to normal granulocytes, the patient was discharged from the hospital and continued to take single-agent clarithromycin tablets 500mg q12h po. The patient's right cervicofacial and right submandibular rashes progressively increased on October 15, 2022 compared with the previous period (Figure. 1, C). The patient presented to the outpatient clinic of the Department of Infectious Diseases on October 29, 2022, and it was considered that the possible therapeutic failure could be due to the induction of drug resistance by clarithromycin. Clarithromycin was discontinued, and treatment was adjusted to rifabutin 300mg qd po combined with linezolid 600 mg qd po. The patient's rash subsided for a time, but then the condition recurred, and the rash increased. After synthesizing the previous treatment history and considering the ineffectiveness of rifabutin and the possible insufficient dosage of linezolid (600 mg, qd, po) (the patient was overweight (25.84 Kg/m²)), rifabutin was discontinued on December 17, 2022, oral anti-infective therapy with linezolid tablets (600 mg, q12h, po) was given. After adjusting the treatment, the patient's rash gradually subsided, but bone marrow suppression reappeared on December 29, 2022, with laboratory findings: platelets 126×10⁹/L, hemoglobin 57 g/L, neutrophils 1.5×10⁹/L, white blood cells 2.1×10⁹/L (Figure 2). Since linezolid (600 mg, q12h, po) resulted in significant bone marrow suppression and the dosage of linezolid (600 mg, qd, po) may be insufficient, the dosage was adjusted to a linezolid tablet dosage of a single day (600 mg, qd, po) with a two-day (600 mg, q12h, po) regimen, as discussed by physicians in the Division of Infectious Diseases and the Department of Pharmacy, beginning on December 29, 2022. After two weeks of adjusting the dosage and administration of linezolid, the rash gradually disappeared, and the repeat blood tests returned to normal. The last in-person follow-up with laboratory testing was on April 15, 2023, showing: platelets 164×10⁹/L, hemoglobin 109 g/L, neutrophils

5.06×10⁹/L, white blood cells 7.36×10⁹/L. As of July 31, 2023, the follow-up patient remained clinically well, and the facial rash had completely subsided on examination (Figure 1, D). A telephone follow-up on December 31, 2025, confirmed that the patient remained clinically well with no rash recurrence, although no laboratory tests were performed at that time. The specific antimicrobial regimen adopted for this patient is shown in Figure 5.

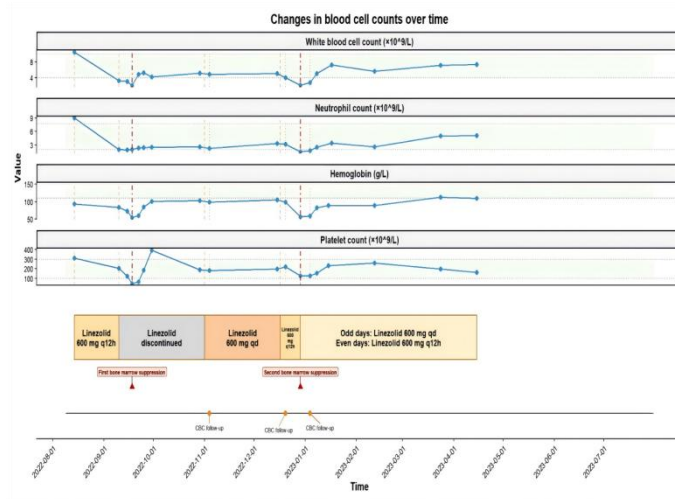


Figure 2. Laboratory results after treatment. (a: White blood cell count (×10⁹/L), reference range: 4–10 ×10⁹/L; b: Neutrophil count (×10⁹/L), reference range: 2–7.7 ×10⁹/L; c: Hemoglobin (Hb) (g/L), reference range: 110–150 g/L; d: Platelet (PLT) count (×10⁹/L), reference range: 100–300 ×10⁹/L)

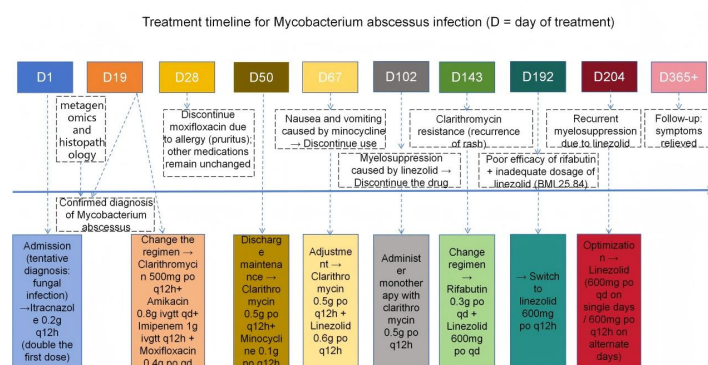


Figure 5. Antimicrobial regimen used by the patient, associated side effects, and interventions during hospitalization.

Considering that the patient had no immunodeficiency caused by diabetes or the use of immunosuppressive agents, but suffered from recurrent tuberculosis and non-tuberculous mycobacterial infections, further investigation was needed to determine the presence of immunodeficiency. Therefore, blood samples were sent out for testing of anti-IFN- γ autoantibodies during the patient's hospitalization. On July 16, 2022, the test result from Wuhan Kindstar Global Diagnostics Laboratory reported: positive for anti-IFN- γ autoantibodies (1:100), confirming the presence of acquired immunodeficiency.

Table 1. Chronological treatment timeline from initial admission to last follow-up

Date	Antimicrobial Regimen	Dose and Frequency	Route	Concurrent Medications	Clinical Events	Adverse Events	Action Taken
April 29, 2022	None	–	–	Targeted therapy for cerebral infarction	Left limb weakness, diagnosed with acute cerebral infarction	None	Admitted to neurology department
May 7, 2022	None	–	–	Mucopolysaccharide polysulfate cream (topical)	Rash on right neck with pruritus	Rash	Topical treatment, no improvement
June 9, 2022	None	–	–	–	Skin biopsy: infectious granulomatous inflammation	None	Biopsy performed
June 9, 2022	Itraconazole	200mg q12h (double first dose)	po	–	Initiated antifungal therapy	None	Treatment started
June 27, 2022	Itraconazole discontinued	–	–	–	Antifungal treatment failed, rash progressed	Treatment failure	Itraconazole stopped
June 27, 2022	Clarithromycin + Amikacin + Imipenem + Moxifloxacin	Clarithromycin 500mg q12h, Amikacin 800mg qd, Imipenem 1000mg q12h, Moxifloxacin 400mg qd	po + ivgtt	–	Initiated empiric anti-mycobacterial therapy	None	Combination therapy started
June 28, 2022	Moxifloxacin stopped, others continued	Same as above (moxifloxacin stopped)	po + ivgtt	–	Skin pruritus (mainly limbs)	Allergic reaction (suspected quinolone allergy)	Moxifloxacin discontinued
July 28, 2022	Clarithromycin + Minocycline	Clarithromycin 500mg q12h, Minocycline 100mg q12h	po	–	Clinical improvement, discharged	None	Discharged on maintenance therapy
August 10, 2022	Clarithromycin + Minocycline	Same as above	po	–	Recurrent nausea and vomiting	Gastrointestinal reaction	Minocycline discontinued
August 14, 2022	Clarithromycin + Linezolid	Clarithromycin 500mg q12h, Linezolid 600mg q12h	po	–	Regimen adjusted after GI symptoms resolved	None	Linezolid initiated
September 2, 2022	Clarithromycin + Linezolid	Same as above	po	Symptomatic treatment	Dizziness, anemia	Anemia	Symptomatic treatment, no improvement
September 18, 2022	Clarithromycin monotherapy	Clarithromycin 500mg q12h	po	–	Facial rash improved; CBC: severe anemia,	Myelosuppression (attributed to	Linezolid paused,

					thrombocytopenia, granulocytopenia	linezolid)	clarithromycin continued
October 15, 2022	Clarithromycin monotherapy	Clarithromycin 500mg q12h	po	–	CBC normalized, but rash gradually increased	Rash recurrence	Outpatient follow-up
October 29, 2022	Rifabutin + Linezolid	Rifabutin 300mg qd, Linezolid 600mg qd	po	–	Suspected clarithromycin-induced resistance	Treatment failure	Clarithromycin stopped, switched to rifabutin + linezolid
December 17, 2022	Linezolid monotherapy	Linezolid 600mg q12h	po	–	Rash initially resolved then recurred; rifabutin ineffective	Treatment failure	Rifabutin stopped, linezolid increased to q12h
December 29, 2022	Linezolid (alternate-day regimen)	Odd days: 600mg qd; Even days: 600mg q12h	po	–	Switched to alternate-day dose regimen	None	Regimen adjusted
January 12, 2023	Linezolid (alternate-day regimen)	Same as above	po	–	Rash completely resolved	None	Clinical improvement
February 1, 2023	Linezolid (alternate-day regimen)	Same as above	po	–	CBC normalized	No severe myelosuppression	Maintenance therapy continued
July 31, 2023	Linezolid (alternate-day regimen)	Odd days: 600 mg qd; Even days: 600 mg q12h	po	None	Follow-up: patient asymptomatic; facial rash completely resolved on examination (Figure 1, D)	None	Continued same regimen; clinical improvement maintained

Footnote: All doses are expressed in milligrams (mg). Route abbreviations: po, orally; ivgtt, intravenous infusion. Frequency abbreviations: qd, once daily; q12h, every 12 hours. CBC, complete blood count; GI, gastrointestinal.

Discussion

NTM are common environmental pathogens, and the incidence of NTM infections has risen globally in recent years; however, their exact incidence rate and prevalence are unknown(6). It is worth noting that NTM prevalence varies significantly across China, with southern and eastern regions having higher NTM prevalence than other regions (7, 8). Unlike Shanghai, the most commonly observed NTM in Guangzhou was Mab, with a higher incidence rate than in Taiwan (30.2%), Korea (26.7%), and Beijing (29.5%) (8, 9). A study in the United States showed that Mab predominated in tap water from surface water(10).

Mab preferentially inhabits ecosystems with higher humidity and temperature, which contributes to their high prevalence in southern China(11). Moreover, the risk factors for NTM infection are host factors such as underlying lung diseases (e.g., bronchiectasis, chronic obstructive pulmonary disease, cystic fibrosis), impaired immunity (e.g., HIV infection, anti-IFN- γ autoantibody positivity.); pharmacological factors such as application of immunosuppressants, chemotherapeutic agents; and environmental factors such as soil, swimming pools, water supply pipes, and healthcare-originated infections(12). The patient in this case showed a positive result in the anti-IFN- γ autoantibody test, indicating possible acquired immunodeficiency. Adult acquired immunodeficiency

syndrome due to anti-IFN- γ autoantibodies was first reported in 2004 (13-15), and patients with positive anti-IFN- γ autoantibodies are mostly Asians, while in China, they are mainly distributed in the southern regions such as Guangxi, Guangdong, and Taiwan(13). IFN- γ plays an essential role in controlling infections with a variety of pathogens. Elevated anti-IFN- γ autoantibodies lead to an increased incidence of infections with pathogens such as NTM, the possible mechanism is that neutralizing anti-IFN- γ autoantibodies at high serum titers inhibit cellular STAT1 phosphorylation by binding to IFN- γ , which in turn inhibits macrophage activation and TNF- α production and affects the function of intrinsic and adaptive immune cells, resulting in a decreased resistance to pathogens such as NTM, fungi, and some specific bacteria (e.g., salmonella, nosodes-like bacteria.)(13,16). Anti-IFN- γ autoantibody-positive immunodeficient populations are prone to recurrent Mycobacterium infections. In this case, the patient had recurrent tuberculosis in 2017 and 2019 and developed a Mab skin soft tissue infection in 2022. To date, patients with adult-onset immunodeficiency caused by anti-IFN- γ autoantibodies lack a standardized management protocol and are primarily treated with prolonged or repeated anti-infective therapy. Current clinical consensus suggests that long-term suppression may be required, but the optimal duration of maintenance therapy remains undefined. For this patient, we plan a structured follow-up schedule including: (1) clinical assessment every 3 months for rash recurrence; (2) complete blood count monitoring every 3 months to detect delayed myelosuppression; (3) annual re-evaluation of anti-IFN- γ autoantibody titers; and (4) immediate re-initiation of anti-mycobacterial therapy if local or systemic symptoms recur. Whether long-term low-dose prophylactic linezolid is necessary will be determined based on serial follow-up outcomes.

It has been demonstrated that the Mycobacterium abscessus complex (MABC) consists of three subspecies, namely Mycobacterium abscessus subsp. abscessus, Mycobacterium abscessus subsp. massiliense, and Mycobacterium abscessus subsp. bolletii(17, 18). Resistance and duration of treatment vary considerably between subspecies, with evidence suggesting that more than 50% of abscessus exhibit persistent Mab culture positivity or relapse after treatment due to induced macrolide resistance during treatment, requiring long-term treatment; in contrast, massiliense does not exhibit induced resistance to macrolides, and therefore has superior treatment efficacy than the other subspecies, with a relatively short duration of treatment (19-21). Importantly, MABC is naturally resistant to a wide range of antibiotics, including almost all first-line anti-mycobacterial drugs(22); therefore, treatment of MABC is complicated, and identification of MABC subspecies and drug susceptibility testing is required prior to administering anti-infective therapy, and effective treatment regimens should be developed accordingly. Unfortunately, MABC subspecies could not be successfully identified in the tissue specimen of our patient, and drug susceptibility testing (DST) results could not be provided due to limited laboratory resources and specimen quality. This constitutes a major limitation of this study, as the lack of subspecies identification and DST reduces the strength of evidence for regimen selection. In future cases, we strongly recommend performing subspecies identification (e.g., via *rpoB* or *hsp65* sequencing) and DST for macrolides, amikacin, imipenem, and linezolid prior to treatment. The absence of subspecies identification and DST limits our ability to tailor therapy based on macrolide susceptibility, which differs between *M. abscessus* subsp. *abscessus* and *M. massiliense*. Our

treatment decisions were therefore guided by clinical response, drug accessibility, and literature-based evidence, so we could only compose a regimen of drugs with anti-MABC activity based on the guidelines of Fever (23) and the Chinese guidelines for diagnosing and treating NTM disease(12). Meanwhile, in the intensive treatment phase, considering that the patient's Mab infection site occurred in the neck and face, which prevented debridement surgery, and according to the drug accessibility in our region, we chose clarithromycin dispersible tablets 500mg po q12h + amikacin 800mg ivgtt qd + imipenem 1000mg ivgtt q12h + moxifloxacin 400mg po qd. However, the patient developed an allergic rash during the process. After inquiring about the history of a similar rash with the application of levofloxacin, it was hypothesized that he might be allergic to fluoroquinolones, so moxifloxacin was discontinued. After three weeks of intensive treatment, the patient's condition improved significantly, and we then switched to oral drug maintenance therapy. However, the patient developed successive severe gastrointestinal reactions to the drugs used (minocycline) as well as recurrence of facial rash (presumably with possible clarithromycin-induced resistance), which led us to think of another drug, linezolid, which belongs to the oxazolidinone class. Accumulating evidence suggests that in vitro antimicrobial activity was shown to be better against Mab linezolid isolated from China(24-30). Moreover, the average detection rate of linezolid-resistant Mab in China was relatively low at 7.3%, which was similar to that in India (7%) (31) but significantly lower than that in the UK (63%) (32) and South Korea (20%). The mechanism of this regional difference in resistance needs to be better understood, it may be related to the fact that linezolid is a recently introduced new antimicrobial drug in developing countries such as China and India, where it has been used for antimicrobial therapy for a relatively short time and therefore exhibits a lower rate of resistance to linezolid by Mab isolates in these regions. This was the key to the ultimate success of this patient's monotherapy with linezolid in the maintenance phase.

Linezolid achieves its bacteriostatic effect by inhibiting the initiation of protein synthesis on the bacterial 50S ribosome. Systemic absorption of orally administered linezolid is close to 100%, has low binding to serum proteins (31%), and provides adequate access to most of the body's tissue compartments, including bone, alveolar, and cerebrospinal fluids (33). The adult dose is 600 mg once, twice a day, administered intravenously or orally, and no dose adjustments are required in patients with renal or hepatic insufficiency (34). This patient was well treated with the routine administration of 1200 mg/d of linezolid, and examination showed that the facial rash had subsided significantly from the previous dose, however, severe anemia and thrombocytopenia developed, forcing us to discontinue it temporarily. Clinical adverse effects of linezolid-induced myelosuppression are common, and the incidence is exceptionally high after more than two weeks of drug use(35-40). The results of a Meta-analysis by Agyeman et al. (41) showed that the percentage of myelosuppression occurred in 507 patients with the application of linezolid to treat drug-resistant tuberculosis was 32.90%. THIROT et al. (42) reported 248 adverse drug reactions (ADRs), 43 cases of thrombocytopenia, and 17 cases of anemia in patients treated with linezolid in four Belgian hospitals in 2016. GUAN et al. (43) retrospectively analyzed the occurrence of ARD in 118 cases treated with linezolid and found thrombocytopenia in 58 cases (50.00%). BOUNTHAVONG et al. (44) reported 54 cases of thrombocytopenia in 1361 patients taking linezolid, which

resolved after discontinuation of the drug. The mechanism of linezolid-induced myelosuppression is complicated because linezolid inhibits protein synthesis in bacterial ribosomes and inhibits mitochondrial protein synthesis, mitochondrial dysfunction results in adverse reactions in the hematologic system (45). It has also been shown that linezolid also causes downstream cellular deficits, with a significant increase in the level of apoptosis in the blood cells of treated patients (46). In conclusion, linezolid causing granulocyte deficiency and anemia is a widespread adverse reaction and should be taken seriously. Careful observation during the application, primarily when linezolid is used for more than one week, and routine laboratory monitoring should include once-weekly complete blood counts, basal metabolic function, and liver and renal function tests (40, 47).

In this case, the rash increased further during the discontinuation of linezolid, so we reactivated linezolid therapy after the myelosuppression resolved. Based on previous adverse reactions to the usual linezolid dosage of 1200 mg/d, we decided to reduce the dosage given, considering that the dose was too high. A study by B.A. Brown-Elliott et al. (48) confirmed that reducing the dose of linezolid to 600 mg/d reduced side effects such as peripheral neuropathy, anemia, gastrointestinal symptoms, and thrombocytopenia while maintaining anti-MABC activity. The guideline from Fever (23) recommends that good in vivo anti-MABC activity can be maintained by applying linezolid 300 mg/d during the maintenance period. Deng J et al. (49), on the other hand, concluded that the use of linezolid together with vitamin B6 reduced linezolid-associated hematopenia. However, an earlier study that included 24 patients on more than a 2-week course of linezolid found that preemptive use of vitamin B6 did not prevent myelosuppression (50). Therefore there is no clear and adequate prophylaxis for linezolid-induced myelosuppression. Combining the above information with the patient's overweight body mass and the fact that we applied a therapeutic dose of linezolid 600 mg/d, the efficacy was not good. It has been shown that dosage or dosing regimen changes can improve linezolid effectiveness (51). The rationale for the alternate-day half-dose regimen is supported by linezolid's pharmacokinetic/pharmacodynamic (PK/PD) properties against *Mycobacterium abscessus*. Linezolid exhibits time-dependent killing against *M. abscessus* (52), and as a time-dependent antibiotic, its efficacy is primarily determined by the duration of time that drug concentration exceeds the MIC ($\%T > MIC$). The pharmacokinetic properties of linezolid further support the feasibility of extended-interval dosing. The pharmacokinetic properties of linezolid have been well characterized. Linezolid exhibits approximately 31% plasma protein binding to serum albumin. The elimination half-life of linezolid is 5–7 hours (33), and achieves excellent tissue penetration, with lung epithelial lining fluid concentrations approximating serum concentrations, showing a penetration rate of approximately 100% (53). In patients with diabetic foot infections, linezolid tissue penetration ratios (tissue free AUC to plasma free AUC) were 1.27 for infected wound tissue and 1.42 for healthy thigh tissue, indicating sustained target-site exposure (54). These favorable PK/PD properties enable prolonged maintenance of therapeutic concentrations even with extended dosing intervals. This provides a theoretical basis for extending the dosing interval (55). Hematologic toxicity of linezolid, particularly thrombocytopenia and anemia, exhibits concentration-dependent and time-dependent characteristics. Thrombocytopenia correlates strongly with trough concentration

($C_{\min}$), while leukopenia correlates with cumulative exposure time (56). By administering half the daily dose (600 mg qd) on odd days and the full regimen (600 mg q12h) on even days, the patient's weekly total dose was reduced by approximately 25% compared to the standard 1200 mg/day, while maintaining effective drug exposure on alternating days. This strategy likely lowered the steady-state trough concentration, thereby mitigating myelosuppression without sacrificing efficacy, as the intermittent but sustained exposure remained above the MIC for most of the treatment period.

The rationale for selecting an alternate-day half-dose regimen over simple dose reduction (e.g., 600 mg qd or 300 mg q12h) was based on the patient's clinical response: 600 mg qd was insufficient to control the infection (rash recurred), while 600 mg q12h was effective but caused myelosuppression. Compared with other alternative strategies, vitamin B6 supplementation has not been shown to prevent linezolid-induced myelosuppression (50). Tedizolid, a newer oxazolidinone, may have a better safety profile but is not widely available in China and has less evidence for *M. abscessus* (57, 58). Hematopoietic growth factors (e.g., G-CSF, erythropoietin) were considered but not used due to cost and the patient's preference to avoid additional injections. From a cost-benefit perspective, the alternate-day regimen reduced weekly linezolid consumption by 25% (from 8400 mg to 6300 mg per week), resulting in proportional drug cost savings. In China, the average cost of linezolid treatment for a comparable infection was approximately ¥17,228 per course (59). A 25% dose reduction would therefore save approximately ¥4,300 in drug costs alone. In contrast, standard full-dose therapy (600 mg q12h) with adjunctive hematopoietic growth factor support would incur additional expenses: G-CSF (approximately ¥200 – 400 per injection) and erythropoietin (approximately ¥100 – 200 per injection), both requiring frequent subcutaneous administration over weeks to months. Moreover, growth factors do not address the underlying cumulative drug toxicity, provide no benefit for thrombocytopenia, and carry risks including bone pain and splenic rupture. Therefore, our dose-reduction strategy offers superior cost-effectiveness by directly reducing drug acquisition costs and avoiding growth factor-related expenses, while simultaneously mitigating the root cause of myelosuppression.

Evidence supporting intermittent dosing in other mycobacterial infections further justifies our approach. In tuberculosis, intermittent linezolid-containing regimens (e.g., three times weekly) have been widely used, demonstrating acceptable efficacy and lower toxicity (60). In *Mycobacterium avium* complex (MAC) infections, intermittent macrolide dosing has also been reported (61). Although evidence for intermittent linezolid dosing specifically against *M. abscessus* remains limited, the above experience provides indirect support for our strategy. We closely monitored the patient's condition and laboratory indexes, and the patient's rash gradually subsided, and the repeated blood tests showed that all three systems were typical. We follow up with the patient regularly, and as of December 31, 2025, the patient still maintains a satisfactory therapeutic effect. A systematic literature search (PubMed, Embase, Cochrane Library) using the terms ('*Mycobacterium abscessus*' OR 'NTM') AND ('linezolid' OR 'oxazolidinone') AND ('intermittent' OR 'alternate-day' OR 'dose reduction') did not identify any previously published cases with a similar dosing strategy. It is important to note that other cases of linezolid treatment for *M. abscessus* infections have been reported using standard dosing regimens (600 mg q12h). However, the alternate-day half-dose strategy described here

has not been previously reported. This study has several limitations, including the lack of subspecies identification and DST. We will attempt to address these issues through ongoing follow-up and future studies. Nevertheless, this case provides preliminary evidence that an alternate-day dosing regimen with varying daily doses may be a viable option for selected patients who cannot tolerate standard dosing due to myelosuppression.

The treatment process of this patient is undoubtedly tricky; the patient himself belongs to the allergic body (previous sulfonamides, β -lactams allergy); standardized treatment process has appeared for moxifloxacin allergic reaction, minocycline, and clarithromycin gastrointestinal reaction, as well as linezolid myelosuppression and other multiple adverse drug reactions. However, after our team continuously reviewed the relevant literature and timely adjusted the dosing regimen, satisfactory results were finally achieved. This case from the selection of antimicrobial drugs, drug dosage and usage adjustment in accordance with the evidence of evidence-based medicine, but also fully embodies the importance of individualized anti-infective program in clinical practice, for the clinical diagnosis and treatment of MABC provides a brand new idea. The limitations of this study are, firstly, that the sensitivity of a particular drug is judged by its clinical effects. This is due to the impact of insufficient allocation of healthcare resources and poor patient compliance; we are unable to achieve the ability to adjust the daily dose of linezolid by detecting the blood concentration of linezolid to ensure the efficacy of the treatment and the safety of the medication. Secondly, the patient has acquired immunodeficiency with positive anti-IFN- γ autoantibodies. An additional limitation is that follow-up after July 31, 2023, was conducted via telephone only (most recently on December 31, 2025), without confirmatory laboratory testing. Therefore, asymptomatic cytopenia or subclinical recurrence cannot be completely excluded. The duration of linezolid maintenance therapy and the necessity for long-term low-dose prophylactic medication remain unclear, and we will attempt to address these issues through ongoing follow-up management of this patient in the later stage. The alternate-day half-dose linezolid regimen described here is not recommended for routine use but may be considered in select patients who: (1) have confirmed or suspected linezolid-induced myelosuppression on standard dosing; (2) require prolonged maintenance therapy for non-tuberculous mycobacterial infections; (3) cannot tolerate full-dose linezolid due to cytopenias, and in whom alternative agents are limited. Importantly, this strategy represents an individualized therapeutic attempt rather than a validated standard. Its generalizability is limited by the lack of therapeutic drug monitoring (TDM), absence of subspecies identification, and single-case design. Prospective studies or larger case series with PK/PD guidance are needed to establish safety and efficacy before broader application.

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Abbreviations

AUC: area under the curve
 CAMs: cell adhesion molecules
 DAMPs: Damage-associated molecular patterns
 DEGs: Differentially Expressed Genes
 DL: drug-likeness
 Enet: elastic network
 FA :folic acid
 GBM: generalized lifting regression model
 GO: Gene Ontology
 GSEA: Gene Set Enrichment Analysis
 GSVA: Genome Variation Analysis
 ICD: Immunogenic Cell Death

KEGG: Kyoto Encyclopedia of Genes and Genomes

LOOCV: leave-one-out cross-validation

LPS: lipopolysaccharide

OB:oral bioavailability

PAMPs: Pathogen-associated molecular patterns

PCA: Principal component analysis

PCD:Programmed cell death

PRRs: Pattern recognition receptors

plsRcox: partial least squares regression

qRT-PCR: quantitative real - time polymerase chain reaction

ROC: receiver operating characteristic

RSF: random survival forest

SDH: succinate dehydrogenase

SuperPC: supervised principal component analysis

TCM: traditional Chinese Medicine

TCMSP: Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform

DECLARATIONS

Ethics approval and consent to participate

Not applicable

Date availability statement

The datasets presented in this study can be found in online repositories. The names of therepository/repositories and accession number(s) can be found in the article.The detailed description of data availability can be found at the following links: (<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi>).

Competing interests

We declare that the authors have no competing interests in this paper.

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Authors' contributions

Qiuli Chen, Yongbing Yu and Fanyan Ou conceived the idea for the study and designed the overall research framework. Qiuli Chen, Yongbing Yu and Fanyan Ou developed the experimental methods used in the study.Junzhi Yang was responsible for developing and implementing the software used for data analysis.Binbin Li and Lixiong Zeng collected and organized the data used in the study. Fanyan Ou, Houyu Gan and Guo Qian were responsible for cleaning and preprocessing the raw data. Qiuli Chen, Yongbing Yu and Fanyan Ou wrote the first draft of the manuscript.Binbin Li and Guo Qian created the visualizations and figures for the paper. Kanglai Wei, Jie Yang, Jihua Feng and Jianfeng Zhang supervised the entire research process.All authors contributed to the review and editing of the manuscript.All authors discussed, revised, and proofread the manuscript.

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