Successful Treatment of Soft Tissue *Mycobacterium chelonae* Infection With a Tedizolid-Containing Regimen

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Introduction

Mycobacterium chelonae is a rapid-growing, non-tuberculous mycobacteria (NTM). It is ubiquitous in the environment including water, soil, milk, and fruit. Although a relatively rare pathogen, it has been associated with infections of soft tissue, lung, joints, and the central nervous system.[1] Infections primarily occur in immunocompromised individuals such as organ transplant recipients or chronic steroid users.

Given its relatively rare incidence, there are little data to support treatment regimens for *M. chelonae*. Historically, treatment has included clarithromycin, though there have been growing reports of acquired resistance and treatment failure when patients are treated with clarithromycin monotherapy. Due to this growing resistance, additional antibiotics such as aminoglycosides or fluoroquinolones have been increasingly utilized in conjunction with a macrolide.[1] Treatment often includes multiple antibiotics for an duration of at least 4-6 months.[3]

Due to this paucity of data, selecting a treatment regimen for multidrug-resistant (MDR) *M. chelonae* can be difficult. Studies have shown successful treatment of *M. chelonae* in an immunocompromised patient using the combination of both clarithromycin and linezolid, however linezolid is poorly tolerated over long treatment courses and this study noted frequent adverse events including thrombocytopenia, myalgia and mitochondrial toxicity due to the use of linezolid.[4]

Tedizolid is a newer oxazolidinone that has been shown to have lower mean inhibitory concentrations (MICs) when treating many NTM, including *M. chelonae,* as compared to linezolid. Tedizolid has also been shown to have reduced instance of bone marrow suppression and other serious adverse events when compared to linezolid.[5] As there are no prior documented cases of *M. chelonae* treated with tedizolid, we discuss a case of such in the setting of a non-healing wound after a dog bite.

Case Description

A 37-year-old man with a history of HIV (last viral load undetectable, CD4 count 696 cells/mm^3 [37%]) taking rilpivirine-emtricitabine-tenofovir alafenamide and dolutegravir (history of M184V mutation) initially presented to clinic 5 days after a dog bite to his right thigh. Out of concern for acute soft tissue infection, the patient was empirically treated with a 10-day course of amoxicillin-clavulanate. When the wound failed to heal, he was then treated with a 7-day course of TMP-SMX, followed by courses of cefuroxime and clindamycin.

He continued to notice intermittent purulent drainage despite 3 courses of oral antibiotics over a 2 month period. Due to poor wound healing despite visits to the wound care clinic and the additional of topical mupirocin he was sent to the infectious disease clinic which was not aware of his wound prior to this time.

Deep swab samples were obtained in clinic and sent for bacterial, fungal, and acid-fast bacilli cultures. Ultimately, cultures were positive only for *M. chelonae*. No other organisms were identified. Sensitivities showed susceptibility to azithromycin, gentamicin, tobramycin, linezolid, and tigecycline. Resistance included amoxicillin-clavulanate, TMP-SMX, cefepime, ciprofloxacin, doxycycline, and minocycline (Table 1). Due to the patient's HIV status, in conjunction with MDR *M. chelonae* infection, the decision was made to initiate a multidrug treatment plan. The patient was started on combination treatment with linezolid 300 mg PO daily, azithromycin 500 mg PO daily, and tobramycin 7 mg/kg IV three times weekly. In conjunction with antibiotics, total excision of the abscess was performed early during the treatment course.

As an extended treatment duration of 6 months was anticipated, the decision was made to replace linezolid with tedizolid due to its reduced risk for bone marrow toxicity and other serious adverse reactions in comparison to linezolid. The patient was started on tedizolid 200 mg PO daily after completing 6 days of linezolid. After 6 weeks of treatment with IV tobramycin, this was discontinued as planned. The patient remained on tedizolid and azithromycin for the remainder of his 6 month treatment duration.

The patient tolerated 6 months of combination treatment with tedizolid and azithromycin without any significant side effects. His blood counts, renal function, and hepatic function remained stable. The wound completely healed without further complication.

Images

Antibiotic	MIC (mcg/mL)	Interpretation
Amikacin	<=8	*Susceptible*
Augmentin	>32/16	Resistant
Azithromycin	<=16	*Susceptible*
Cefepime	>32	Resistant
Cefotaxime	>64	Resistant
Cefoxitin	>128	Resistant
Ceftriaxone	>64	Resistant
Ciprofloxacin	4	Resistant
Clarithromycin	<=0.25	*Susceptible*
Clofazimine	<=0.5	*Susceptible*
Clofazimine/Amikacin	<=0.5/2	*Susceptible*
Doxycycline	>16	Resistant
Gentamicin	4	*Susceptible*
Imipenem	8	Intermediate
Kanamycin	<=8	*Susceptible*
Linezolid	8	*Susceptible*
Minocycline	>8	Resistant
Moxifloxacin	2	Intermediate
Tigecycline	<=0.25	*Susceptible*
Tobramycin	<=2	*Susceptible*
TMP/SMX	>4/76	Resistant

Table 1. Antimicrobial sensitivities from tissue sample.

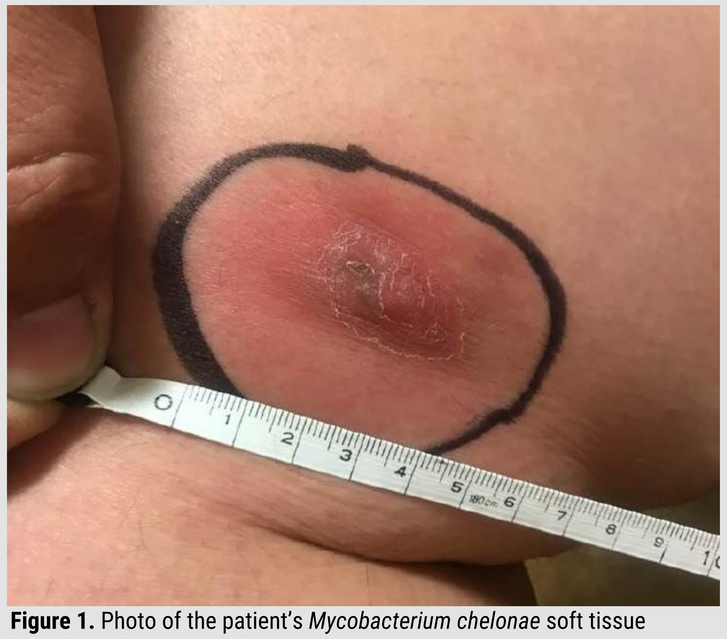

Figure 1. Photo of the patient's *Mycobacterium chelonae* soft tissue infection prior to surgical excision.

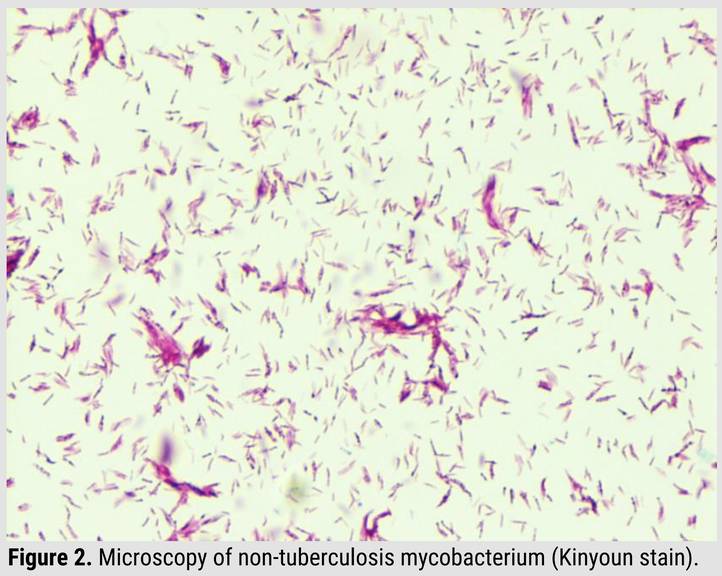

Figure 2. Microscopy of non-tuberculosis mycobacterium (Kinyoun stain). *labmedicineblog.com/tag/mycobacterium/*

Discussion

Although a relatively rare pathogen, *M. chelonae* can present a problematic infection, particularly with rising prevalence of MDR NTM. Current treatment recommendations have largely been based upon prior case reports. The American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) recommend "multidrug macrolide-based therapy based on susceptibility testing results and surgical resection."[6] However, these guidelines also state that there are no drug combinations with proven efficacy.

As linezolid has been shown to have significant toxicity when used for longer than 2 weeks duration, we propose the utilization of tedizolid for treatment of *M. chelonae* infection. This medication has lower risk of bone marrow toxicity compared to linezolid, and is therefore a preferred medication for treatment of MDR infection requiring a prolonged course. Although cost is a major barrier to tedizolid at this time, as cost is eventually reduced, we propose tedizolid as a well tolerated and convenient oral medication for treatment of MDR NTM infections requiring prolonged treatment courses.

Other medications traditionally used for *M. chelonae* infection, including aminoglycosides, are often limited by their potentially serious nephrotoxicity and ototoxicity. Furthermore, the need for IV infusions is often burdensome for patients. Tedizolid alleviates many of these potential treatment pitfalls.

Based upon our case report, we propose tedizolid can be considered as part of a multidrug regimen to treat MDR *M. chelonae*. Tedezolid has reduced toxicity as compared to other antibiotics recommended for treatment of *M. chelonae* infection.

Learning Points

- When encountered with a chronic non-healing infection despite multiple treatments with antibiotics, consider a Mycobacterium infection
- Consider NTM infections particularly in immunocompromised patients (e.g. HIV, chronic steroid use, biologics, etc.)
- Tedizolid should be considered as part of a multi-drug regimen for patient's with *M. chelonae* infection, particularly with multi-drug resistant *M. chelonae*.

References

1. Stelzmueller I, Dunst KM, Wiesmayr S, Zangerie R, Hengster P, Bonatti H. Mycobacterium chelonae skin infection in kidney-pancreas recipient. *Emerg Infect Dis*. 2005;11(2):352–354. doi:10.3201/eid1102.040902

2. Spencer S. Jang and Dwight C. Hirsh (*2002*). Rapidly Growing Members of the Genus *Mycobacterium* Affecting Dogs and Cats. Journal of the American Animal Hospital Association: May/June 2002, Vol. 38, No. 3, pp. 217-220.

3. Verghese E, Jabri A, Watkins RR. Successful Treatment of a Renal Abscess Caused by *Mycobacterium chelonae*: A Case Report [published correction appears in Open Forum Infect Dis. 2018 Nov 08;6(3):ofy264. Jabr, Ahmad [corrected to Jabri, Ahmad]]. *Open Forum Infect Dis*. 2018;5(9):ofy196. Published 2018 Aug 16. doi:10.1093/ofid/ofy196

4. Parize P, Hamelin A, Veziris N, Morand PC, Guillemain R, Lortholary O, Dupin N. Induction therapy with linezolid/clarithromycin combination for Mycobacterium chelonae skin infections in immunocompromised hosts. J Eur Acad Dermatol Venereol. 2016 Jan;30(1):101-5. doi: 10.1111/jdv.12965. Epub 2015 Feb 11.

5. Barbara A. Brown-Elliott, Richard J. Wallace Jr. *In Vitro* Susceptibility Testing of Tedizolid against Nontuberculous Mycobacteria. Journal of Clinical Microbiology May 2017, 55 (6) 1747-1754; DOI: 10.1128/JCM.00274-17

6. Novosad SA, Beekmann SE, Polgreen PM, et al. Treatment of Mycobacterium abscessus Infection. *Emerging Infectious Diseases*. 2016;22(3):511-514. doi:10.3201/eid2203.150828.

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