Infection and Drug Resistance

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Efficacy, Safety, and in vitro Sensitivity of Omadacycline in the Treatment of Brucellosis: A Case Series Study

Zhu Zeng[1,*], Hongdong Tan[2,*], Beibei Wu[3], Qiuting Jiang[1], Ying Ye[4], Yanping Zhang[5], Yiyi Wu[6], Yunsong Yu[7], Hua Zhou[8]

[1]Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China; [2]Department of Spinal Infection Surgery, Shandong Public Health Clinical Center, Jinan, People's Republic of China; [3]Institute of Microbiology Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, People's Republic of China; [4]Department of Infectious Disease, The First Affiliated Hospital of Anhui Medical University, Hefei, People's Republic of China; [5]Department of Infectious Disease, The Third People's Hospital of Changzhou, Changzhou, People's Republic of China; [6]Department of Infectious Disease, The First Affiliated Hospital of Ningbo University, Ningbo, People's Republic of China; [7]Department of Infectious Disease, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China; [8]Department of Respiratory and Critical Care Medicine, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Hua Zhou, Department of Respiratory and Critical Care Medicine, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, People's Republic of China, Email zhouhua1@zju.edu.cn

Purpose: Treatment options for brucellosis are limited. Omadacycline demonstrates strong antibacterial activity against a broad spectrum of bacteria. However, the efficacy of omadacycline against *Brucella* spp. remains unclear.

Patients and Methods: We screened brucellosis patients who received omadacycline from April to July 2023 across five hospitals in China and conducted in vitro experiments to evaluate the activity of omadacycline against different *Brucella* species.

Results: A total of 13 patients were included, all of whom received omadacycline as part of a combination regimen. Within this cohort, 11 were diagnosed with Brucella spondylitis, and 8 of these underwent surgical intervention. Omadacycline was administered as second-line therapy in 10 (76.9%) patients due to uncontrolled symptoms and as empirically in the remaining 3. Following the initiation of an omadacycline-containing regimen, symptoms of fever and/or back pain improved rapidly, regardless of whether it was used as empirical or second-line therapy. The median time from omadacycline initiation to defervescence was 3 days, and to relief of back pain was 7 days. The median duration of omadacycline treatment was 32 days, and it was administered in combination with other agents, including rifampicin and cephalosporins. The regimen was well tolerated, with only one patient experiencing mild nausea. In vitro, omadacycline demonstrated consistent activity against all tested *Brucella* species.

Conclusion: In this case series, omadacycline-containing regimens were well tolerated and associated with rapid symptomatic improvement. These findings support further evaluation in prospective comparative studies.

Keywords: *Brucella*, brucellosis, omadacycline, case series, susceptibility

Introduction

Brucellosis is a widespread zoonotic disease caused by *Brucella* species that primarily affects domestic and wild animals but can be transmitted to humans through direct contact with infected animals or their secretions, or via ingestion of contaminated meat, unpasteurized milk, or dairy products. Tetracycline derivatives remain the most effective antibiotics for treating brucellosis,[1] with the World Health Organization (WHO) recommending a 6-week combination regimen of doxycycline and rifampin in 1986.[2] Although current treatments yield a high cure rate, ongoing efforts remain focused on improving therapeutic options. The limitations associated with current standard regimens include an increased risk of adverse effects due to the prolonged treatment duration, as well as clinically relevant drug–drug interactions.[1]

https://doi.org/10.2147/IDR.S574932
Received: 17 October 2025
Accepted: 13 April 2026
Published: 21 April 2026

Moreover, *Brucella* spp. are facultative intracellular pathogens and the limited intracellular penetration of conventional agents may impede bacterial eradication and contribute to disease relapse, particularly in complicated forms such as osteoarticular involvement.[1,3] Brucella spondylitis represents one of the most severe manifestations of brucellosis and can lead to serious complications, including permanent neurological deficits or even death. The reported incidence of Brucella spondylitis varies from 2% to 60% in the literature.[3] Prolonged antibiotic therapy remains the cornerstone of treatment for brucellar spondylitis, with combination regimens of two or three antibiotics used to prevent relapse. The optimal duration of therapy for osteoarticular involvement is approximately 3 to 6 months, and surgery may be required for a specific subset of patients, particularly those with bone destruction or progressive neurological deficits.[4] However, current therapeutic outcomes are suboptimal. A retrospective study conducted in China, which included 821 patients with brucellar spondylitis, reported a relapse rate of approximately 3.45% among those treated with antibiotics alone.[5] This persistent risk of relapse underscores the urgent need for novel and more effective therapeutic regimens for the management of Brucella spondylitis.

Future directions in the treatment of human brucellosis are increasingly focused on shortening treatment duration, minimizing toxicity, enabling oral administration, and identifying agents with enhanced intracellular activity.[1] Several studies suggest that tetracycline derivatives may provide an alternative therapeutic strategy. Cascio et al demonstrated that a 3-week regimen of oral minocycline combined with intravenous rifampin resulted in a lower relapse rate compared to doxycycline plus rifampin/streptomycin for brucellosis[2] Tigecycline, which shares a similar chemical structure with minocycline, has been shown to possess a minimum inhibitory concentration $(MIC)_{90}$ for *Brucella* isolates ranging from 0.064 to 0.125 mg/L[6] and has been proposed as a potential therapeutic alternative for brucellosis.[7]

Omadacycline is a novel aminomethylcycline antimicrobial available in both intravenous and oral formulations. It exhibits broad-spectrum activity against Gram-positive and Gram-negative aerobic, anaerobic, and atypical bacteria [6] and was approved by the US Food and Drug Administration (FDA) in 2018 for the treatment of community-acquired bacterial pneumonia and acute skin and skin structure infections.[8] Compared to doxycycline, omadacycline exhibits higher liposolubility, superior tissue penetration, a lower potential for drug–drug interactions, and better oral tolerability,[9] making it a potential alternative for brucellosis. Notably, its reported favorable safety profile offers a potential alternative for patients intolerant to doxycycline or those at risk of drug-related hepatotoxicity. However, clinical data on its efficacy and tolerability in brucellosis remain limited.

This study aimed to expand current knowledge by investigating the in vitro activity of omadacycline against *Brucella* and reporting clinical experiences with omadacycline in the treatment of brucellosis in a cohort of patients from five medical centers in China.

Materials and Methods

Patients

This observational retrospective study was conducted at five medical centers in China between April and August 2023. Consecutive patients (≥18 years old) with a definitive diagnosis of brucellosis who received omadacycline as part of their antimicrobial treatment regimen were reviewed and followed up. The enrolled patients included those who were treated with omadacycline as empirical treatment before the pathogen was identified and continued the treatment for at least 2 weeks after diagnosis. In another group, patients received standard antimicrobial therapy (such as a combination of doxycycline and rifampicin or streptomycin) but exhibited persistent symptoms, leading to the addition of omadacycline as part of second-line therapy. Patients who received omadacycline for less than 14 days were excluded from the study.

Brucellosis was diagnosed based on clinical signs compatible with the disease and at least one of the following criteria:[2] 1) isolation of *Brucella* spp. from blood, other fluids, or tissue; 2) a ≥1:160 standard tube agglutination (STA) titer of antibodies to *Brucella spp*., 3) the metagenomic next-generation sequencing (mNGS) of plasma or tissue indicates positive nucleic acid for *Brucella spp*. Spondylitis was diagnosed based on physical examination and radiological or magnetic resonance imaging (MRI) studies.[3]

Uncontrolled symptoms were mainly defined as the persistence of both of the following after at least 5 days of standard combination therapy: (1) Persistent fever (temperature >38°C for more than 72 hours) after exclusion of other

causes of pyrexia; and (2) Clinically unimproved back pain, indicated by a Numerical Rating Scale (NRS) pain score that was unchanged or worse from baseline, accompanied by persistently elevated or plateauing inflammatory markers (C-reactive protein, CRP).

Defervescence was defined as a temperature <37.3°C sustained for more than 48 hours, in the absence of any antipyretic medications (eg, NSAIDs or acetaminophen). Relief of back pain was defined as patient-reported improvement in pain, including a decrease in the Numerical Rating Scale [NRS] score from baseline, or a reduction in the frequency of analgesic use.

Treatment

Antimicrobial therapy before the diagnosis of brucellosis is defined as empirical treatment, while antimicrobial therapy after the diagnosis of brucellosis is defined as first-line therapy. The antimicrobial treatment replaced after the first-line therapy is defined as second-line therapy.

In accordance with the China Brucellosis Diagnosis and Treatment Guidelines, surgical intervention was indicated for patients presenting with spinal instability or progressive neurological deficits.[5] Preoperative management consisted of a minimum three-week course of anti-Brucella therapy. Surgery was deferred until the patient had remained afebrile for at least five days and inflammatory markers CRP showed a consistent downward trend.

Data Collection and Follow-Up

Demographic and clinical information were collected from medical records. For each patient, demographic characteristics such as sex, age, city of residence, history of ingesting unpasteurized dairy products, history of brucellosis infections, and exposure to infected animals, as well as clinical information including signs and symptoms, laboratory findings, history of disease relapse, and treatment regimens were recorded.

Relapse was defined as the reappearance of symptoms or signs of the disease or a new positive blood culture after therapy.[10] Following therapy, all patients were re-examined on an outpatient basis at regular 1-month intervals for 12 months, or whenever clinical symptoms reappeared. Follow-up data were collected until August 2024.

Statistical Analysis

This retrospective case series used only descriptive statistics. No comparative or inferential analyses were performed; the findings are descriptive and hypothesis-generating.

In vitro Activity of Omadacycline

The antimicrobial susceptibility of the *Brucella* spp. isolates for rifampicin, moxifloxacin, streptomycin, and omadacycline was performed using the Etest strips (Liofilchem srl, Roseto degli Abruzzi, Italy) according to the manufacturer's recommendations and in accordance with the 2016 guidelines of the Clinical and Laboratory Standards Institute[7] at the Zhejiang Provincial Center for Disease Control and Prevention. *Escherichia coli* ATCC 25922 was used as a quality control strain. Solutions of the *Brucella* spp. isolates (adjusted turbidity, 0.5 McFarland standard) were coated on Mueller–Hinton Agar medium (Beijing Solarbio Science & Technology Co., Ltd., Beijing, China), +5% defibrinated horse blood and 20 mg/L β-NAD, then an E-test strip was attached, and incubated for 72 h at 37°C. After a 72-h incubation period, as determined by the appearance of an even lawn of bacteria, the MIC values were determined as the intersection of the applicable inhibition ellipse displayed by the E-test strips.[11] Among the seven strains of *Brucella* spp., 544A, 1330S, and sheep 1 were reference strains, while the remaining three clinical strains were obtained from blood cultures. The strain 2319 was isolated from the blood of case 1 in this study. Two strains, 2153 and 2162, were isolated from patients in Hangzhou in April 2023; however, these two patients were not enrolled in the study. There is no specific breakpoint for antimicrobial susceptibility testing of *Brucella* spp. in the guidelines provided by the Clinical and Laboratory Standards Institute or the European Committee on Antimicrobial Susceptibility Testing.

Study Approval

This study was approved by the Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (Registration No. IIT20230657A). Informed consent was obtained from all participants. This study strictly complies with the principles outlined in the Declaration of Helsinki. Rigorous measures were adopted to protect patient privacy and data security during the collection, analysis, and storage of clinical data.

Results

Patient Characteristics

A total of 13 consecutive patients with brucellosis were enrolled, all of whom were Han Chinese. The characteristics of the patients are summarized in Table 1. All patients were diagnosed with brucellosis for the first time, including 84.6% (11/13) with spondylitis. Blood cultures were performed for 10 patients, with five yielding positive results. The STA test was conducted for all patients, with nine (69.2%) testing positive. Metagenomic next-generation sequencing (mNGS) was performed in four patients (1 blood sample and 3 tissue samples), all were positive. Five patients were diagnosed through blood culture; two were diagnosed through mNGS after negative blood cultures, and the remaining six were diagnosed based on STA. Among the six patients whose diagnosis was based solely on STA results, all were from regions with a high incidence of brucellosis and had a documented history of definitive exposure, in addition to testing positive by the Rose Bengal Test (RBT). In all cases, the diagnosis was further supported by a repeat positive STA result.

Due to the clinical manifestations of brucellosis mimicking many other diseases, it often presents diagnostic challenges. The median interval from the onset of the first symptom to diagnosis was 20 days (range, 8 to 89 days) in our study. At the onset of illness, the main presenting symptoms were fever (12/13, 92.3%), back pain (10/13, 76.9%) and malaise/weakness (9/13, 69.2%). The median duration from illness onset to defervescence was 28 days (range, 13 to 117), and the median duration to relief of back pain was 43 days (range, 32 to 142). Additionally, grade 1 transaminase elevations were observed in 3 patients (23.1%) before the initiation of omadacycline therapy, including 1 patient with a history of cirrhosis who experienced concomitant elevation of transaminases and bilirubin (both were grade 1).

Table 1 Demographic Data of 13 Patients with Brucellosis

Characteristic	n
Total of subjects	13
Age (range, years)	60 (35–72)
Male	11
Residential area	
Rural areas	11
Suburban areas	1
Urban area	1
History of contact with suspicious animals	
Yes	12
Indeterminate	1
Etiological evidence*	
Blood culture	5/10
Serological tests	9/13
Metagenomic next generation sequencing of plasma or tissue	4/4
Symptoms	
Fever	12
Back pain	10
Malaise/Weakness	9

Note: *positive/underwent test.

Treatment

The concurrent antimicrobials prescribed with omadacycline are shown in Table 2, and the most common concomitant antibiotic regimen was rifampicin and cephalosporins. Three patients received omadacycline as empiric and first-line antibiotic therapy. Ten patients received various antibiotic combinations as first-line treatment, with the combination of

Table 2 Case Summaries of 13 Patients with Brucellosis

Case NO.	Age/ Gender	Infection Location	First Line Antimicrobials and Duration (Days)	Reasons for Switching to Omadacycline	Second Line Antimicrobials and Duration (Days)	Subsequent Antibiotics Post-Omadacycline (days)#	Treatment Related Adverse Events
1	60/M	Blood	Omadacycline, Levofloxacin (48)	/	/	Doxycycline, Rifampicin (14)	NO
2	60/M	Bloodstream, Vertebrae	Omadacycline, Rifampicin, Ceftizoxime (32)	/	/	Doxycycline, rifampicin, levofloxacin, cefdinir (225)	NO
3	50/M	Bloodstream, Vertebrae	Omadacycline, Levofloxacin, Ceftriaxone (26)	/	/	Levofloxacin, Rifampicin, Minocycline (174)	NO
4	72/M	Inguinal lymph nodes	Doxycycline, Rifampicin (7)	Fever	Omadacycline, Rifampicin, Ceftizoxime (46)	Doxycycline, Rifampicin (35)	NO
5	65/F	Bloodstream, Vertebrae	Doxycycline, Rifampicin (4)	Fever	Omadacycline, Rifampicin, Ceftriaxone (22)	Rifampicin, Levofloxacin, Doxycycline (32)	NO
6	48/M	Vertebrae	Doxycycline, Rifampicin (22)	Fever	Omadacycline. Rifampicin, Ceftizoxime (37)	Doxycycline, Rifampicin, Levofloxacin, Cefaclor (197)	NO
7	34/M	Vertebrae	Doxycycline, Rifampicin, Ceftriaxone (27)	Fever	Omadacycline, Rifampicin, Ceftizoxime (41)	Doxycycline, Rifampicin, Levofloxacin, Cefdinir (90)	NO
8	63/M	Vertebrae	Doxycycline, levofloxacin (20)	Back pain	Omadacycline, Rifampicin, Ceftizoxime (34)	Doxycycline, rifampicin, levofloxacin, cefdinir (210)	NO
9	58/M	Vertebrae	Amikacin, Cefuroxime, SMZ-TMP (36)	Back pain	Omadacycline, Rifampicin, Ceftizoxime (27)	Doxycycline, rifampicin, Levofloxacin, Cefdinir (245)	NO
10	61/M	Vertebrae	Doxycycline, Rifampicin, Ceftriaxone, Levofloxacin (14)	Fever	Omadacycline, Rifampicin, Ceftizoxime (30)	Doxycycline, Rifampicin, Levofloxacin, Cefdinir (238)	NO

(*Continued*)

https://doi.org/10.2147/IDR.S574932

Table 2 (Continued).

Case NO.	Age/ Gender	Infection Location	First Line Antimicrobials and Duration (Days)	Reasons for Switching to Omadacycline	Second Line Antimicrobials and Duration (Days)	Subsequent Antibiotics Post-Omadacycline (days)#	Treatment Related Adverse Events
11	61/M	Vertebrae	Doxycycline, Rifampicin, Ceftriaxone, Levofloxacin (28)	Fever	Omadacycline, Rifampicin, Ceftizoxime (25)	Doxycycline, Rifampicin, Levofloxacin, Cefdinir (35)	NO
12	49/M	Vertebrae	Doxycycline, Rifampicin (23)	Fever	Omadacycline, Rifampicin, Ceftizoxime (29)	Doxycycline, Rifampicin, Levofloxacin, Cefdinir (266)	NO
13	45/F	Bloodstream, Vertebrae	Doxycycline, Rifampicin, Ceftriaxone (28)	Back pain	Omadacycline, Rifampicin, Ceftizoxime (39)	Doxycycline, Rifampicin, Levofloxacin, Cefdinir (42)	Nausea

Notes: Case 1–3 received omadacycline as first line antibiotic treatment, case 4–13 received omadacycline as second line antibiotic treatment; #Subsequent antibiotics post-discharge.

doxycycline and rifampicin being the most common choice (8/10, 80%) (Table 2). Among these patients who received omadacycline as second-line treatment, the median duration of the first line antibiotic regimen for brucellosis was 22.5 days (range, 4 to 36), seven were switched to omadacycline due to uncontrolled fever, while the remaining three were switched for uncontrolled back pain (Figure 1).

All patients showed significant improvement in clinical symptoms after receiving omadacycline. The median time from the initiation of omadacycline to defervescence was 3 days, regardless of whether it was used as first or second-line therapy (Figure 1). Notably, among the second-line patients, 20.0% (2/10) had uncontrolled fever for more than 20 days during prior first-line treatment (Figure 2). Three patients received omadacycline for uncontrollable back pain, and the median duration from the start of omadacycline to relief of back pain was 7 days (Figure 1). Omadacycline was initiated intravenously (200 mg once as a loading dose, followed by 100 mg daily as a maintenance dose) and maintained throughout hospitalization. At discharge, patients were transitioned to oral formulations. Since oral omadacycline is not covered under China's health insurance system, only three patients received the oral formulation after discharge (300 mg

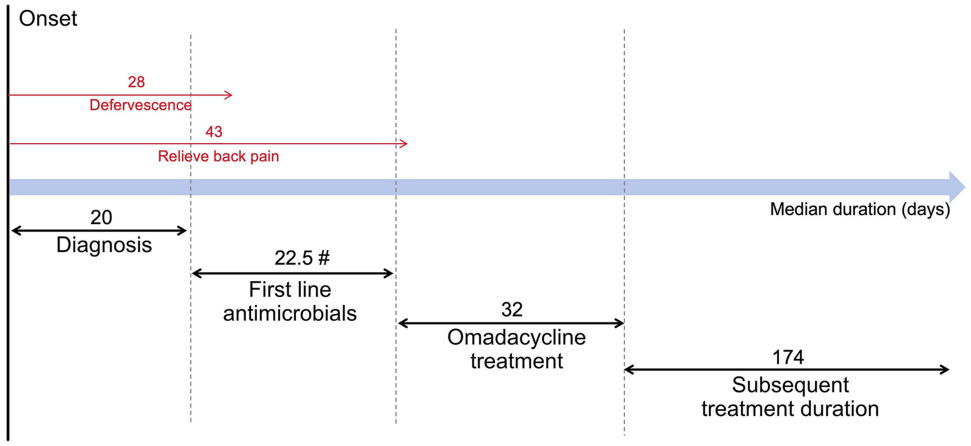

Figure 1 Timeline of patients with Brucellosis after onset of illness.
Note: # Median duration of first-line antibiotic therapy for 10 patients who received omadacycline as second-line therapy.

https://doi.org/10.2147/IDR.S574932

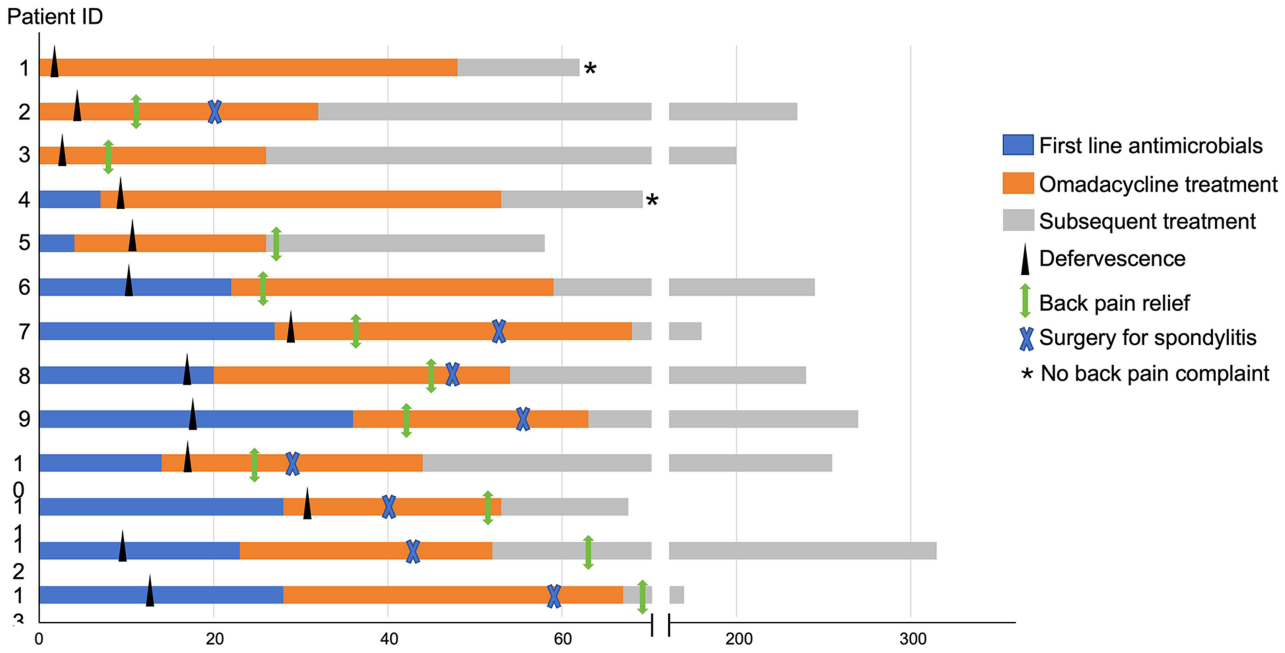

Figure 2 Timeline of patients with brucellosis treated with antibiotic.

daily, with treatment duration ranging from 7 to 42 days). The remaining ten patients were switched to alternative regimens. The most commonly used sequential therapy following omadacycline was doxycycline in combination with rifampicin, with a median treatment duration of 174 days (range: 14 to 266 days). In the current series, only one patient experienced mild nausea during omadacycline treatment, which was relieved after symptomatic treatment.

In this study, 84.6% (11/13) of patients were diagnosed with *Brucella* spondylitis, with back pain and fever being the predominant symptoms. Among these, 72.7% (8/11) received surgical intervention. Each patient received combination

Table 3 MICs (mg/L) of 4 Antimicrobial Agents to *Brucella Spp*

Source	Strain	Rifampicin	Moxifloxacin	Omadacycline	Streptomycin
Reference strains	544A *Brucella abortus*	0.25	0.063	0.5	1
	1330S *Brucella suis*	0.25	0.063	0.25	1
	Sheep 1 *Brucella melitensis*	0.25	0.125	0.25	2
Clinical isolations	RM66 *Brucella canis*	0.25	0.125	0.5	1
	2153 *Brucella melitensis*	0.5	0.063	0.25	2
	2162 *Brucella abortus*	1	0.0125	0.25	2
This study case 1	2319 (S) *Brucella melitensis*	0.5	0.063	0.25	2

Notes: MICs were determined for the seven *Brucella* strains described in the Methods section, including one isolate from Case 1.

https://doi.org/10.2147/IDR.S574932

antibiotic therapy including omadacycline prior to surgery and achieved basic control of clinical symptoms and serum inflammatory markers before the procedure (see Methods, Treatment section).

Chronic inflammation, along with in-acute-phase chronic inflammation, were the most commonly observed pathological changes in spinal brucellosis. Since *Brucella* spondylitis requires a longer course of antibiotics than uncomplicated brucellosis, 72.7% (8/11) of patients received a combination of three antibiotics for more than 3 months. Three patients showed suboptimal adherence to the post-discharge oral medication regimen and discontinued treatment after approximately one month (Table 2).

Follow Up

To assess treatment efficacy and adverse events, all patients were followed up weekly for the first month after discharge, then monthly via telephone during treatment and bimonthly after treatment discontinuation. During the one-year follow-up period, no patients were lost to follow-up. Follow-up assessments revealed that patients experienced relief from pain and fever, regained mobility, and showed radiographic improvement with stable disease, with no evidence of relapse up to the final follow-up.

In vitro Activity of Omadacycline

The MICs of four antimicrobial agents (rifampicin, moxifloxacin, omadacycline, and streptomycin) are summarized in Table 3. A total of 7 strains were detected. For reference strains (B. abortus 544A, B. suis 1330S, B. melitensis Sheep 1), MIC of omadacycline ranged from 0.25 to 0.5 mg/L, comparable to rifampicin (0.25 mg/L), moxifloxacin (0.063–0.125 mg/L), and streptomycin (1–2 mg/L). For isolate 2319 from case 1, the omadacycline MIC was 0.25 mg/L. Overall, omadacycline exhibited consistent in vitro activity against all tested *Brucella* strains.

Discussion

Since *Brucella* can persist in host macrophages, evading the human immune system for prolonged periods,[12,13] 5–20% of patients experience relapse or therapeutic failure despite adequate antibiotic treatment.[14,15] Current treatment principles for brucellosis advocate for prolonged treatment durations combined with antimicrobial regimens effective in the intracellular acidic environment.[1,16] Tetracyclines are considered highly effective against *Brucella*, with doxycycline being the most widely used antibiotic for human brucellosis.[17] Several studies have suggested that tetracycline derivatives may offer superior efficacy compared to tetracycline itself and are promising treatments for brucellosis.[1,17] Rubinstein et al identified minocycline as the most effective antibacterial drug against *Brucella* melitensis,[18] a finding confirmed by Cascio A retrospective study by Cascio et al showed that a combination of intravenous rifampin and oral minocycline administered for 3 weeks resulted in the lowest relapse rate (17%).[2] Dizbay et al demonstrated that tigecycline exhibits good in vitro activity against *Brucella* and may be a potential candidate for future therapeutic regimens[6] As a tetracycline derivative, omadacycline has been shown to possess high liposolubility, superior tissue and macrophage cell penetration,[9] and better oral bioavailability and tolerability, suggesting its potential as a treatment for brucellosis.[19]

In this study, omadacycline demonstrated in vitro activity against the tested *Brucella* spp. isolates, with low MIC values (Table 3). This finding is consistent with the established antimicrobial spectrum of this agent. Previous studies have confirmed that omadacycline possesses antibacterial activity against a broad range of pathogens, including various Gram-positive and Gram-negative bacteria, as well as atypical pathogens, including intracellular organisms.[20] However, clinical efficacy does not always correlate with in vitro susceptibility.[21] Pathogen elimination in vivo is governed by an intricate interplay with the host's defense network,[22] particularly for intracellular pathogens such as *Brucella*. Furthermore, the clinical effectiveness of omadacycline is inherently dependent on its pharmacokinetic/pharmacodynamic (PK/PD) properties, specifically its capacity for tissue penetration and intracellular distribution.[23] Therefore, evaluating the efficacy of omadacycline in patients with brucellosis is particularly important. Unfortunately, to our knowledge, no relevant prospective, randomized controlled clinical research data are currently available. The goal of brucellosis treatment is to control the acute illness and prevent complications and relapses.[24] In this study, we found that most patients experienced rapid remission of clinical symptoms, such as fever and back pain, following omadacycline

treatment. Furthermore, no patient experienced a relapse during the 12-month follow-up. We speculate that this may be related to the high intracellular concentration of omadacycline in tissue, macrophages, and neutrophils, as reported in previous literature.[19] Given the non-specific symptoms of brucellosis, many patients require a prolonged period to achieve a definitive diagnosis. Omadacycline, as a new broad-spectrum antibiotic, is widely used in empirical anti-infective therapy. This study confirms that *Brucella* is sensitive to omadacycline, indicating that its empirical use does not delay patient recovery before a definitive diagnosis is made. In our study, three patients received omadacycline as empirical first-line treatment, and their symptoms were significantly alleviated, with all patients ultimately recovering.

For osteoarticular brucellosis, the ability of omadacycline to penetrate bone tissue and achieve adequate intracellular concentrations is of critical importance. While direct pharmacokinetic data on omadacycline in human bone are currently lacking, preclinical studies have provided relevant insights. In a rat model of osteomyelitis, administration of omadacycline resulted in high bone tissue-to-plasma concentration ratios, suggesting a potential for distribution into bone tissue.[25] Furthermore, preliminary evidence supports the activity of omadacycline against intracellular pathogens, including nontuberculous mycobacteria, as demonstrated in both in vitro macrophage infection models[9] and documented clinical cases.[26] The symptomatic improvement observed in patients with osteoarticular brucellosis in this study also suggests the potential efficacy of omadacycline-containing regimens for this patient population. Future research should focus on characterizing omadacycline concentrations in bone and macrophages to establish a stronger pharmacological rationale for its use in osteoarticular brucellosis.

Adverse events associated with omadacycline, including nausea, vomiting, increased creatinine, and elevated transaminase levels, have been reported in clinical trials.[27] Despite the longer duration of treatment in our case series (range, 22 to 48 days), omadacycline appears to be safe, well-tolerated, and feasible for treating brucellosis. Furthermore, omadacycline was used off-label as part of a first-line treatment regimen in case 3, based on its expected low hepatotoxicity and high susceptibility against *Brucella*. This patient had been diagnosed as a hepatitis B virus carrier with liver cirrhosis prior to brucellosis, with baseline transaminase and bilirubin levels elevated to grade 1. During treatment, the patient did not experience severe complications, with transaminase and bilirubin levels remained stable Two additional patients without a history of liver disease had a grade 1 increase in transaminase levels prior to second-line omadacycline, and returned to normal after symptomatic treatment during subsequent omadacycline treatment. It is important to note that *Brucella* can inherently trigger abnormal liver function, and long-term drug therapy may exacerbate liver damage, further increasing the liver's burden. Tuohutaerbieke reported that the prevalence of drug-induced liver injury (DILI) in brucellosis inpatients receiving drug therapy was 9.08%, with rifampin being the primary drug associated with DILI.[28] Additionally, symptomatic treatment with antipyretic analgesics and herbal medicine use often leads to liver injury in the clinical treatment of brucellosis in mainland China. The authors also emphasized that the effects and interactions of different drugs require comprehensive consideration, as the combined use of multiple drugs may increase the incidence of DILI.[28] Given the prevalence of DILI in brucellosis, a personalized treatment plan should be tailored to the patient's baseline liver function. According to available data, the risk of serious liver and kidney injury associated with omadacycline is relatively low.[29,30] Moreover, omadacycline is neither a substrate, inducer, nor inhibitor of the major CYP enzymes, which reduces the potential for drug interactions involving these enzymes.[31] This makes omadacycline a promising alternative therapeutic option for patients prone to DILI. Based on available evidence, omadacycline warrants future investigation as: (1) a second-line alternative for patients with intolerance or contra-indications to standard therapies (eg, doxycycline, rifampin); and (2) a potentially safer choice for individuals with baseline liver impairment or a high risk of hepatotoxicity. However, as a novel antibiotic, the application of omadacycline for brucellosis still requires confirmation through large-scale clinical studies, as well as a balanced evaluation that considers drug accessibility, health insurance policies, and individual patient characteristics.

Additionally, this study highlights the role of mNGS in diagnosing *Brucella* infection, which is consistent with previous studies.[32] Due to the variable and non-specific clinical manifestations of brucellosis, diagnosis is often delayed in non-endemic, high-incidence areas.[32] Serologic tests are the fundamental diagnostic tools for brucellosis. Currently, the clinical diagnosis primarily relies on STA and culture. Although culture is considered the gold standard, it has a high false-negative rate and is time-consuming, which can delay treatment. For example, in case 4 of this study, the patient was diagnosed with brucellosis through mNGS of an inguinal lymph node biopsy sample only after 28 days of fever and

negative blood cultures. As an unbiased assay, mNGS has been widely used to detect infectious pathogens and has ushered in a new era in the diagnosis of infectious diseases, especially for rare or unexpected pathogens. It has been shown to offer higher diagnostic efficacy compared to traditional methods.[33] Yao et al compared the diagnostic value of mNGS with conventional methods in *Brucella* spondylitis and found that the sensitivities of STA and bacterial culture were 625% and 20.8%, respectively, with negative predictive values of 20.8% and 28.0%, respectively. In contrast, mNGS had a sensitivity of 83.3% and a negative predictive value of 55.6%, both significantly higher than those of conventional methods.[32] Consistent with previous studies, we found that mNGS showed the highest diagnostic sensitivity (100%), while the sensitivities of SAT and culture were 69.2% and 50%, respectively, in our current study.

However, several limitations should be considered when interpreting the results of this study. First, as an observational study with a small sample size, the findings are subject to potential bias. Additionally, the retrospective design precluded the acquisition of certain data; for instance, daily NRS scores for back pain were not available for all patients. Symptomatic improvement was therefore inferred from surrogate markers, including changes in analgesic requirements and qualitative descriptions in clinical progress notes. While informative, these measures are inherently subjective and may introduce variability in outcome interpretation.

Moreover, although all patients showed clinical improvement after initiating omadacycline-containing regimens, the observed outcomes were influenced by multiple confounding factors, including the use of concomitant antibiotics (eg, rifampicin, doxycycline, cephalosporins), surgical intervention in selected spondylitis cases, and potential selection bias related to treatment switching for persistent symptoms. As such, the clinical improvements cannot be attributed solely to omadacycline. Furthermore, the use of oral omadacycline for the full treatment course in China is currently limited by its exclusion from national health insurance coverage. In this study, all patients subsequently transitioned to other antibiotic regimens, which further complicates the interpretation of omadacycline-specific efficacy. Finally, due to strict biosafety regulations in China—where *Brucella* is classified as a Category B notifiable infectious disease—the transportation and handling of clinical isolates are restricted to authorized institutions such as the Centers for Disease Control and Prevention. Consequently, only one *Brucella* spp. isolate in this study was available for in vitro susceptibility testing, which may limit the generalizability of our findings. Nonetheless, this case series provides valuable real-world evidence regarding the feasibility and tolerability of omadacycline-containing regimens for brucellosis.

Conclusion

Based on clinical data and in vitro susceptibility testing, we conclude that omadacycline-containing regimens may represent a feasible therapeutic option for brucellosis, particularly in cases with intolerance or hepatotoxicity risk. Given the inherent limitations of this retrospective study, these findings warrant confirmation in larger, prospective controlled trials.

Acknowledgments

We also thank all colleagues who contributed data to this study.

Funding

This work was supported by research grants, including the Research and Development Program of Zhejiang Province (2023C03068, 2023C02036), the Key R&D Plan of the Ministry of Science and Technology of China (2022YFC2504502), the National Natural Science Foundation of China (82272338). The funders had no involvement in the study design, data collection and analysis, the decision to publish, or the preparation of the manuscript.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Bosilkovski M, Keramat F, Arapovic J. The current therapeutical strategies in human brucellosis. *Infection*. 2021;49(5):823–832. doi:10.1007/s15010-021-01586-w

2. Cascio A, Scarlata F, Giordano S, Antinori S, Colomba C, Titone L. Treatment of human brucellosis with rifampin plus minocycline. *J Chemother*. 2003;15(3):248–252. doi:10.1179/joc.2003.15.3.248
3. Spernovasilis N, Karantanas A, Markaki I, et al. Brucella spondylitis: current knowledge and recent advances. *J Clin Med*. 2024;13(2):595. doi:10.3390/jcm13020595
4. Unuvar GK, Kilic AU, Doganay M. Current therapeutic strategy in osteoarticular brucellosis. *North Clin Istanb*. 2019;6(4):415–420. doi:10.14744/nci.2019.05658
5. Wang K, Gu Z, Liu Q, et al. Clinical epidemiological characteristics and treatment outcomes of Brucella spondylitis in Ningxia, China: a 12-year single-center retrospective study. *BMC Infect Dis*. 2025;25(1):1567. doi:10.1186/s12879-025-12101-z
6. Dizbay M, Kilic S, Hizel K, Arman D. Tigecycline: its potential for treatment of brucellosis. *Scand J Infect Dis*. 2007;39(5):432–434. doi:10.1080/00365540601105756
7. Pappas G, Papadimitriou P, Christou L, Akritidis N. Future trends in human brucellosis treatment. *Expert Opin Investig Drugs*. 2006;15(10):1141–1149. doi:10.1517/13543784.15.10.1141
8. Vacalis S, Brunton S, Gindi J. Omadacycline in skin infections and pneumonia: a review of the evidence. *J Fam Pract*. 2022;71(5 Suppl):S10–S21. doi:10.12788/jfp.0424
9. Jahanbakhsh S, Howland J, Ndayishimiye Uwineza MO, et al. Evaluation of omadacycline against intracellular Mycobacterium abscessus in an infection model in human macrophages. *JAC Antimicrob Resist*. 2023;5(5):dlad104. doi:10.1093/jacamr/dlad104
10. Nimri LF. Diagnosis of recent and relapsed cases of human brucellosis by PCR assay. *BMC Infect Dis*. 2003;3(1):5. doi:10.1186/1471-2334-3-5
11. Ma HR, Xu HJ, Wang X, et al. Molecular characterization and antimicrobial susceptibility of human Brucella in Northeast China. *Front Microbiol*. 2023;14:1137932. doi:10.3389/fmicb.2023.1137932
12. Lecaroz C, Blanco-Prieto MJ, Burrell MA, Gamazo C. Intracellular killing of Brucella melitensis in human macrophages with microsphere-encapsulated gentamicin. *J Antimicrob Chemother*. 2006;58(3):549–556. doi:10.1093/jac/dkl257
13. Guo X, Zeng H, Li M, et al. The mechanism of chronic intracellular infection with Brucella spp. *Front Cell Infect Microbiol*. 2023;13:1129172. doi:10.3389/fcimb.2023.1129172
14. Mile B, Valerija K, Krsto G, Ivan V, Ilir D, Nikola L. Doxycycline-rifampin versus doxycycline-rifampin-gentamicin in treatment of human brucellosis. *Trop Doct*. 2012;42(1):13–17. doi:10.1258/td.2011.110284
15. Pappas G. The peculiar ways of Brucella survival: looking through the keyhole. *Virulence*. 2010;1(6):473–474. doi:10.4161/viru.1.6.13200
16. Solera J, Martinez-Alfaro E, Espinosa A. Recognition and optimum treatment of brucellosis. *Drugs*. 1997;53(2):245–256. doi:10.2165/00003495-199753020-00005
17. Ariza J, Bosilkovski M, Cascio A, et al. Perspectives for the treatment of brucellosis in the 21st century: the Ioannina recommendations. *PLoS Med*. 2007;4(12):e317. doi:10.1371/journal.pmed.0040317
18. Rubinstein E, Lang R, Shasha B, et al. In vitro susceptibility of Brucella melitensis to antibiotics. *Antimicrob Agents Chemother*. 1991;35(9):1925–1927. doi:10.1128/AAC.35.9.1925
19. Gotfried MH, Horn K, Garrity-Ryan L, et al. Comparison of omadacycline and tigecycline pharmacokinetics in the plasma, epithelial lining fluid, and alveolar cells of healthy adult subjects. *Antimicrob Agents Chemother*. 2017;61(9). doi:10.1128/AAC.01135-17
20. Karlowsky JA, Steenbergen J, Zhanel GG. Microbiology and preclinical review of omadacycline. *Clin Infect Dis*. 2019;69(Suppl 1):S6–S15. doi:10.1093/cid/ciz395
21. Mantur BG, Amarnath SK, Shinde RS. Review of clinical and laboratory features of human brucellosis. *Indian J Med Microbiol*. 2007;25(3):188–202. doi:10.4103/0255-0857.34758
22. Pan T, Lee JW. A crucial role of neutrophil extracellular traps in pulmonary infectious diseases. *Chin Med J Pulm Crit Care Med*. 2024;2(1):34–41. doi:10.1016/j.pccm.2023.10.004
23. Rodvold KA, Burgos RM, Tan X, Pai MP. Omadacycline: a review of the clinical pharmacokinetics and pharmacodynamics. *Clin Pharmacokinet*. 2020;59(4):409–425. doi:10.1007/s40262-019-00843-4
24. Skalsky K, Yahav D, Bishara J, Pitlik S, Leibovici L, Paul M. Treatment of human brucellosis: systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2008;336(7646):701–704. doi:10.1136/bmj.39497.500903.25
25. Karau MJ, Schmidt-Malan SM, Cunningham SA, et al. Activity of omadacycline in rat methicillin-resistant staphylococcus aureus osteomyelitis. *Antimicrob Agents Chemother*. 2022;66(1):e0170321. doi:10.1128/AAC.01703-21
26. Rizzo AR, Moniri NH. Omadacycline for management of Mycobacterium abscessus infections: a review of its effectiveness, place in therapy, and considerations for use. *BMC Infect Dis*. 2022;22(1):874. doi:10.1186/s12879-022-07857-7
27. O'Riordan W, Cardenas C, Shin E, et al. Once-daily oral omadacycline versus twice-daily oral linezolid for acute bacterial skin and skin structure infections (OASIS-2): a Phase 3, double-blind, multicentre, randomised, controlled, non-inferiority trial. *Lancet Infect Dis*. 2019;19(10):1080–1090. doi:10.1016/S1473-3099(19)30275-0
28. Tuohutaerbieke M, Li X, Yin Y, et al. The characteristics, prevalence, and risk factors of drug-induced liver injury among brucellosis inpatients in Xinjiang, China. *Front Pharmacol*. 2021;12:657805. doi:10.3389/fphar.2021.657805
29. Opal S, File TM, van der Poll T, Tzanis E, Chitra S, McGovern PC. An integrated safety summary of omadacycline, a novel aminomethylcycline antibiotic. *Clin Infect Dis*. 2019;69(Suppl 1):S40–S47. doi:10.1093/cid/ciz398
30. Kovacs SJ, Ting L, Praestgaard J, et al. An open-label study of the impact of hepatic impairment on the pharmacokinetics and safety of single oral and intravenous doses of omadacycline. *Antimicrob Agents Chemother*. 2020;64(11). doi:10.1128/AAC.01650-20
31. Flarakos J, Du Y, Gu H, et al. Clinical disposition, metabolism and in vitro drug-drug interaction properties of omadacycline. *Xenobiotica*. 2017;47(8):682–696. doi:10.1080/00498254.2016.1213465
32. Yao X, Zhao G, Wang L, Jia C. Study on the value of second-generation sequencing technology in the clinical diagnosis of osteoarticular brucellosis. *J Orthop Res*. 2024;42(10):2327–2335. doi:10.1002/jor.25867
33. Zhou H, Larkin PMK, Zhao D, et al. Clinical impact of metagenomic next-generation sequencing of bronchoalveolar lavage in the diagnosis and management of pneumonia: a multicenter prospective observational study. *J Mol Diagn*. 2021;23(10):1259–1268. doi:10.1016/j.jmoldx.2021.06.007