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CASE REPORT

A 68-Year-Old Man with Multiple Comorbidities Presents with a Weeping Wound of the Left Lower Extremity: A Case Report

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Abstract

In cases of cellulitis, identification of a specific pathogen is often not possible on clinical grounds, and in our institution the recommended practice for empiric treatment of skin infections is to cover for the usual pathogens, such as *Staphylococcus aureus* and *Streptococcus pyogenes*. This article describes the management of a 68-year-old man in whom the choice of appropriate antibiotic treatment for suspected cellulitis was complicated by many factors, including several known risk factors for recurrent cellulitis, multiple comorbid conditions, and the patient's wish to leave hospital as soon as possible. Given this patient's clinical syndrome, coverage for methicillin-resistant *S. aureus* was part of the treatment decision, and to enable a prompt discharge, an effective oral treatment was needed for him to take at home. These and other considerations that guided the selection of omadacycline as appropriate antibiotic therapy for this patient are discussed.

Keywords: Cellulitis, *Clostridium difficile* infection, Comorbidities, Methicillin-resistant *Staphylococcus aureus*, Omadacycline, Oral treatment, Recurrent cellulitis, Risk factors, Weeping wound

1. Introduction

This article describes the management of a patient in whom the choice of appropriate antibiotic treatment for suspected cellulitis was complicated by multiple factors. The patient had several known risk factors for recurrent cellulitis and multiple comorbid conditions, and he also wished to leave hospital as soon as possible.

A 68-year-old man presented to his primary care physician for a weeping wound in the lower left extremity (LLE) 2 days after hitting his leg while fixing a car engine, with progressive cellulitis following the injury. The patient was referred to the emergency department (ED) for evaluation for potential deep vein thrombosis (DVT) and treatment of LLE cellulitis. His notable medical history included chronic obstructive pulmonary disease, treated with prednisone 5 mg daily, a T2N1 small-cell carcinoma of the hilar region, for which he had received chemotherapy and radiotherapy, a history of alcohol use, and depression treated with paroxetine. Although not confined to bed, the patient was wheelchair bound (secondary to cervical and lumbar stenosis) and overweight. He also had a history of *Clostridium difficile* infection (CDI). He had experienced multiple previous episodes of LLE cellulitis and had failed treatment with cephalexin and sulfamethoxazole/trimethoprim.

The initial workup revealed that the patient had a temperature of 97.8 °F, pulse rate of 99 beats/minute, blood pressure 115/81 mmHg, oxygen saturation 96%, and respiratory rate 16 breaths/minute. An ultrasound scan of the LLE was negative for DVT, and physical examination indicated LLE cellulitis.

Preliminary laboratory findings showed a slightly elevated white blood cell count (WBC) of 12.4×10^9/L (normal range for men[1] = $5–10 \times 10^9$/L) and elevated serum creatinine level 1.6 mg/dL (normal range for adult male[2] = 0.74–1.35 mg/dL). Blood cultures obtained before hospital admission were found to be negative.

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2. Case

The patients' clinical course is summarized in Fig. 1. The patient was admitted to a general medical floor and started treatment with vancomycin and ceftriaxone (in our center, this regimen is typically prescribed in the ED and continued in the hospital setting). The patient lived a significant distance away (1.5-h journey time) and expressed interest in leaving hospital quickly. As such, the process of obtaining omadacycline was started on the day of admission and approval for coverage was returned on Day 2. Oral omadacycline was prescribed as it is an effective treatment with activity against both methicillin-resistant *Staphylococcus aureus* (MRSA) and streptococci. The patient was discharged from the hospital on Day 3 with omadacycline sample pack and instructions to take the first loading dose of 450 mg the night of discharge and a second loading dose of 450 mg the following day. The patient then completed a further 10 days of oral omadacycline 300 mg once daily, for a total of 14 days of antibiotic treatment.

The patient was referred to his primary care physician for follow-up after completion of the course of oral omadacycline. Improvement in LLE cellulitis was noted on Day 8 and resolution was documented on Day 17 (14 days after discharge from hospital and 5 days after treatment ended), with no requirement for further treatment for this condition. No adverse events were noted during the period of treatment with oral omadacycline.

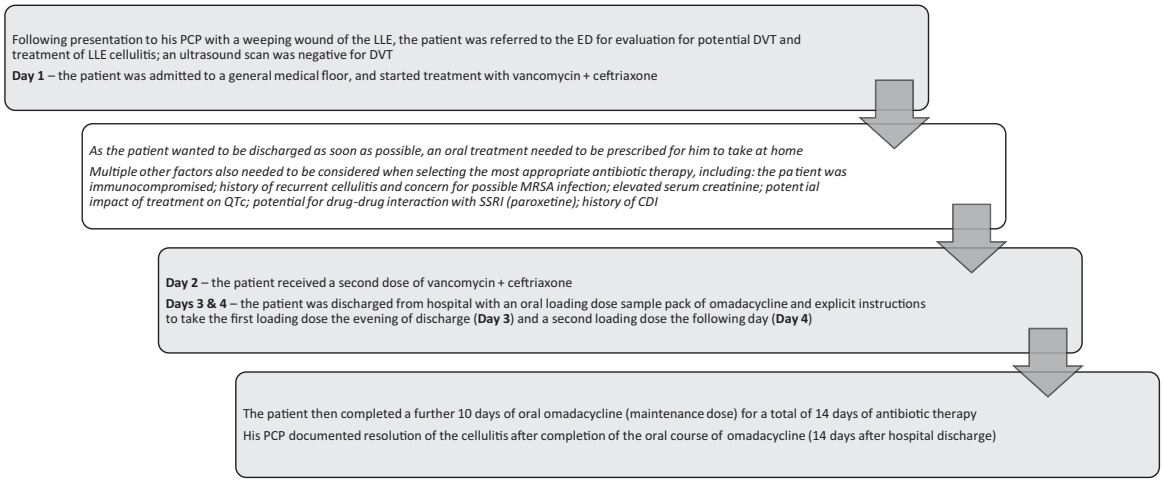
3. Discussion

Definitive antimicrobial therapy was required for this patient, and the case was complicated by multiple factors that needed to be considered when selecting the most appropriate antibiotic therapy.

3.1. Medical and social history

The patient was overweight, and had a history of lung cancer and alcohol use; these are all known risk factors for recurrent cellulitis. The primary general risk factors for recurrent cellulitis are (lower-extremity) lymphoedema, obesity, and a history of cancer.[3-7] A weak association has also been noted between diabetes, as well as alcohol use disorder and recurrent cellulitis,[5,6] and a case–control study including 398 patients receiving prophylactic treatment with benzathine penicillin and more than 8000 controls underscores the significance of diabetes in recurrent cellulitis.[8]

This patient was also immunocompromised due to receiving treatment with prednisone (although at a physiologic dose). The interactions of antibiotic therapies with host immunity are being increasingly recognized, and the properties of the tetracycline and oxazolidinones classes of antibiotics might explain the higher efficacy of omadacycline compared with linezolid in treating acute bacterial skin and soft tissue infections in patients with diabetes (Table 1).[9] Neutrophil dysfunction in patients with diabetes makes them more susceptible to infection with Gram-negative pathogens, and



CDI, *Clostridioides difficile* infection; DVT, deep vein thrombosis; ED, emergency department; LLE, left lower extremity; PCP, primary care physician; SSRI, selective serotonin reuptake inhibitor

Fig. 1. Clinical course of the patient's wound management.

Table 1. Comparison of omadacycline with linezolid

	Omadacycline	Linezolid
Antibiotic class	Tetracycline	Oxazolidinone
Administration	Intravenous and oral	Intravenous and oral
Spectrum of coverage	Broad coverage against Gram-positive and fastidious Gram-negative bacteria[25,21]	All clinically important Gram-positive bacteria[26,27]
Risk of SSRI paroxetine drug−drug interaction[15]	No risk	Potential risk of serotonin syndrome/toxicity
Efficacy in patients with diabetes mellitus susceptible to gram-negative bacterial infection[9]	High efficacy with collateral anti-inflammatory properties	Low efficacy due to neutrophil dysfunction

SSRI, selective serotonin reuptake inhibitor

thereby likely to benefit from the broader−spectrum activity of tetracyclines like omadacycline rather than oxazolidinones: oxazolidinones like linezolid have been shown to be dependent on neutrophil function, potentially compromising the potency of this drug class; and tetracyclines show collateral anti-inflammatory properties not seen in other antibiotic classes.[9]

3.2. Antibiotic coverage for likely pathogens

In cases of cellulitis, identification of a specific pathogen is often not possible on clinical grounds, and in our institution the recommended practice for empiric treatment of skin infections is to cover for the usual pathogens, such as *S. aureus* and *Streptococcus pyogenes.* Given the patient's clinical syndrome, coverage for MRSA was also part of the treatment decision. Recurrence is high in patients with skin infections caused by MRSA,[10] and there was concern for underlying MRSA in this patient because he had experienced multiple previous episodes of cellulitis and had failed treatment with cephalexin and sulfamethoxazole/trimethoprim. Blood cultures are a common means of identifying a bacterial pathogen, but the yield is low, and the results only marginally affect treatment.[11] Elderly patients with acute onset of illness, high fever, and a significant elevation in WBC, as well as patients who are immunocompromised, may most benefit from blood cultures.[11] However, in this patient, blood cultures were found to be negative.

3.3. Impact on kidney function

The patient presented with serum creatinine 1.6 mg/dL, which is above normal. This was considered a relative contraindication to using sulfamethoxazole/trimethoprim, because this can decrease creatinine secretion to the distal tubule and, though it does not affect glomerular filtration rate, it can cause a rise in creatinine.[12-14]

3.4. Possible impact on QTc

After considering the patient's kidney function, weight, and sedentary lifestyle, even though a QT interval measurement had not been obtained, it was decided not to risk prescribing an antibiotic with known impact on QTc. Although a fluoroquinolone would provide MRSA coverage, there was caution about the use of this antibiotic class in this case.

3.5. Risk of drug−drug interactions

As the patient was also taking the selective serotonin reuptake inhibitor (SSRI) paroxetine, treatment with linezolid would not be ideal due to the potential risk of serotonin syndrome/toxicity.[15]

3.6. History of CDI

The patient's history of CDI was also considered a significant concern and drove the decision to avoid using antibiotics that are known to have a high association with CDI and favor the use of a tetracycline. As the patient had a history of lung cancer, the National Comprehensive Cancer Network guidelines for the prevention and treatment of cancer-related infections were also consulted.[16] These guidelines recommend reducing unnecessary antibiotic use and, noting the link between use of fluoroquinolones and severe CDI as well as MRSA infections, they recommend caution regarding excess use of fluoroquinolones.

Tetracyclines are associated with a low risk of CDI, compared with high-risk antibiotics such as fluoroquinolones and clindamycin.[17-19]

3.7. Social, economic, and other factors

The patient expressed interest in leaving the hospital as soon as possible, and if there is no longer a clinical need for hospitalization (as indicated by a negative blood culture), we wanted to avoid the cost

of the patient remaining in hospital only for administration of antibiotic therapy. The substantial cost of the one-time dose of IV antibiotics was also considered, as access to higher-cost antibiotics may be difficult due to their use being restricted in our institution. There may be barriers to use for newly available antibiotics, such as omadacycline, to become part of the standard of care in a hospital setting. Some physicians may not be familiar with the full range of antibiotics available to them, instead opting for what they believe will work. They may be uncertain of the best option in cases such as these, where the patient wishes to be discharged and is not required to remain as an inpatient. Obtaining approval for the use of omadacycline was straightforward, and it was delivered to the patient by the specialty pharmacy, enabling him to be discharged without concern that he would be without medication. The Infectious Diseases Society of America recommends using the same antibiotic, if possible, when switching from IV to oral treatment.[20] As omadacycline is approved as both IV and oral formulations,[21] if an IV loading dose had been given instead of the two oral loading doses, this patient could still have completed the course of treatment with once-daily oral maintenance doses of omadacycline at home. As once-daily oral dosing is associated with better dose-taking compliance compared with oral antibiotics with more frequent dosing regimens (e.g., three or four times daily), this was considered another potential advantage of this treatment choice.[22]

The favorable clinical outcome seen in this patient with LLE cellulitis is consistent with findings in patients with acute bacterial skin and skin structure infections in two phase 3 clinical trials of omadacycline, OASIS-1[23] and OASIS-2.[24] In OASIS-1, 38.9% (n = 123) of the patients who received omadacycline had cellulitis; in OASIS-2, 24% (n = 86) of the patients who received omadacycline had cellulitis or erysipelas. In OASIS-1, the patients received IV omadacycline initially and could then switch to oral omadacycline after 3 days, and in OASIS-2 patients received oral omadacycline throughout; in both studies, omadacycline was found to be non-inferior to linezolid with a similar safety profile.

4. Conclusion

In this patient with LLE cellulitis and multiple comorbidities, including a history of CDI, and in whom underlying MRSA infection was considered likely, 14 days of antibiotic therapy (ceftriaxone and vancomycin for 2 days, oral loading doses of omadacycline for 2 days, and oral omadacycline maintenance dose for 10 days) resulted in resolution of the LLE cellulitis with no further treatment being required. Switching from IV antibiotic therapy to oral omadacycline enabled the patient to return home as soon as possible, according to his wishes, thereby avoiding the need for prolonged and costly inpatient treatment solely to receive treatment. Moreover, in the environment of the COVID-19 pandemic, we feel that enabling effective treatment to occur in the patient's home is especially pertinent, because discharging the patient from hospital as quickly as possible is likely to reduce risk of transmission of infection within the hospital setting and also minimize the burden on hospital capacity.

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Notes on patient consent

Informed consent was obtained from the patient.

Conflict of interest

Speakers Bureau and Consultant, Paratek Pharmaceuticals, Inc.

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