

Dalbavancin Use for the Treatment of Methicillin-resistant *Staphylococcus aureus* Pneumonia

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Abstract

Dalbavancin is a lipoglycopeptide with a long half-life that allows infrequent dosing. It is indicated for the treatment of acute bacterial skin and skin structure infections caused by susceptible organisms, including *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA). Although this agent has been used off-label clinically, there are minimal data in infections outside the current indications. We report a case of a 28-year-old nonadherent male with HIV presenting with pneumonia due to MRSA that was treated with dalbavancin. The patient was admitted to the hospital with classic pneumonia symptoms, and sputum cultures and bronchoalveolar lavage grew MRSA. Other infections were ruled out. The patient was initially treated with vancomycin, but subtherapeutic concentrations prompted a change to dalbavancin upon discharge. The patient was readmitted 11 days later with the complaints of hemoptysis and shortness of breath, with unchanged imaging. However, no evidence of MRSA was found at this time. Utility of dalbavancin for other disease states has profound implications, particularly in patients with poor medication adherence.

Keywords: Dalbavancin, lipoglycopeptide, methicillin-resistant *Staphylococcus aureus*, pneumonia

INTRODUCTION

Pneumonia represents one of the most frequent infectious diseases, and complications occur in up to 50% of patients.^[1] Although methicillin-resistant *Staphylococcus aureus* (MRSA) is an uncommon cause of pneumonia, MRSA coverage is recommended for both health care-associated and ventilator-associated pneumonia.^[2]

Dalbavancin, a lipoglycopeptide, is indicated for acute bacterial skin and skin structure infections (ABSSSI). Dalbavancin demonstrates potent MRSA activity (minimum inhibitory concentration [MIC]₉₀ of 0.06 mg/L), potentially making it an option for the treatment of other infections.^[3] This case is unique because it is the first reported use of dalbavancin for MRSA pneumonia.

CASE REPORT

A 28-year-old nonadherent male with HIV (last absolute CD4 = 4 cells/cmm) presented with a 3-day history of productive cough, shortness of breath, severe fatigue, and fever. Based on a hospital admission 22 days prior, the patient was empirically

started on vancomycin and cefepime for health care-associated pneumonia (HCAP) and trimethoprim/sulfamethoxazole for possible pneumocystis pneumonia (PCP). Baseline blood, urine, and other results were negative, including tests for tuberculosis, PCP, cytomegalovirus, influenza, parainfluenza, respiratory syncytial virus, and adenovirus. Induced sputum cultures grew MRSA [Table 1], and cefepime was discontinued on day 3.

On day 5, a bronchoalveolar lavage (BAL) revealed numerous macrophages in the right upper lobe. Chest X-ray revealed interval worsening of bilateral infiltrates and pleural effusions compared to previous scans. Computed tomography (CT) chest displayed large areas of airspace consolidation predominantly involving the lower lobes associated with pulmonary nodules surrounded by ground glass, likely reflective of multifocal

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Table 1: Susceptibility testing

Antimicrobial	Initial isolates, MIC (mg/L)	Interpretation	Subsequent isolates, MIC (mg/L)	Interpretation
Clindamycin	0.25	Susceptible	≤0.12	Susceptible
Erythromycin	≥8	Resistant	≥8	Resistant
Gentamicin	≤0.5	Susceptible	≤0.5	Susceptible
Linezolid	2	Susceptible	2	Susceptible
Oxacillin	≥4	Resistant	≥4	Resistant
Tetracycline	≤1	Susceptible	≤1	Susceptible
Trimethoprim + sulfamethoxazole	≥320	Resistant	≥320	Resistant
Vancomycin	≤0.5	Susceptible	1	Susceptible

MIC=Minimal inhibitory concentration

pneumonia. On day 7, BAL remained positive for MRSA. Vancomycin was recommended for 14 days of anti-MRSA therapy. Vancomycin trough concentrations remained subtherapeutic (approximately 10 mg/L) throughout the hospitalization despite dosing adjustments, only approaching therapeutic concentrations (14.8 mg/L) on day 9. Therefore, on day 12, the patient was discharged with a one-time 1500 mg dose of dalbavancin.

Eleven days post-discharge, the patient was readmitted with complaints of weakness, aching, hemoptysis, shortness of breath, abdominal pain, and nausea. The patient was placed on a nonrebreather mask and admitted to the medical intensive care unit due to increased oxygen requirements. Chest X-ray revealed extensive bilateral infiltrates unchanged from previous images. CT of the chest revealed an interval increase in multifocal areas of consolidation in the lower lobes, with pulmonary nodules surrounded by ground-glass consolidations and central bronchograms consistent with multifocal pneumonia. Based on this presentation, he was treated for HCAP with vancomycin, cefepime, and azithromycin. Blood cultures, galactomannan, Fungitell[®], histoplasma antigen, blastomyces antigen, urine pneumococcal antigen, and urine legionella antigen were negative. Sputum cultures revealed no evidence of MRSA.

A bronchoscopy and biopsy were not completed due to his critical state. Since other tests were negative, clindamycin and primaquine were started for PCP coverage. Despite initial improvement, his oxygen requirements increased, he was re-intubated, and ultimately succumbed after cardiac arrest and multiorgan failure on hospital day 7.

DISCUSSION

Currently, no data exist regarding dalbavancin for the treatment of pneumonia. In the treatment of ABSSSI, dalbavancin displayed similar efficacy to vancomycin without added adverse effects, despite high potency.^[4]

Telavancin, another lipoglycopeptide, has been utilized for treating MRSA pneumonia with a high success (81.8%).^[5] However, telavancin is infrequently prescribed due to increased risk of renal toxicity and drug/laboratory interactions compared to vancomycin. Dalbavancin has yet to display either of

these limitations and also boasts a half-life >1 week. The once-weekly dosing may render this agent advantageous in certain populations.^[3]

In this case, nonadherence (confirmed by clinical records), progression of illness, and an inability to obtain therapeutic vancomycin concentrations prompted the discussion of dalbavancin as a treatment option. While this patient ultimately succumbed, it is encouraging that MRSA in the lungs was not identified in repeated sputum cultures, suggesting eradication by dalbavancin.

While this is the first report of dalbavancin utilization for the treatment of pneumonia, it is not without limitations. First, we do not have patient-specific pharmacokinetic data. Based on age and renal function, it can be assumed that it is comparable to population pharmacokinetics. In addition, with a vancomycin MIC of ≤1 mg/L, the initial vancomycin should have eradicated the infection. However, our patient never achieved therapeutic vancomycin concentrations during treatment. The suggested area under concentration/MIC ratio for successful treatment of MRSA pneumonia would likely not have been met.

CONCLUSION

After recurrent MRSA-positive respiratory, sputum, or BAL cultures, and an inability to obtain therapeutic concentrations with vancomycin as an inpatient, our nonadherent patient with HIV received a one-time dose of dalbavancin for the treatment of MRSA pneumonia. He returned to the hospital 11 days postdischarge with respiratory complaints, but sputum cultures at that time were negative, suggesting that dalbavancin helped eradicate MRSA. Although the use of and optimal dosing for MRSA pneumonia will require further investigation, this report suggests that dalbavancin may be an option in difficult cases with few alternative options.

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Conflicts of interest

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