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Daptomycin for methicillin-resistant *Staphylococcus aureus* infections of the spine

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Abstract

BACKGROUND: Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is increasingly common. Treatment with vancomycin-based therapy is often unsuccessful. Daptomycin is a relatively new lipopeptide antibiotic with potent activity against MRSA.
PURPOSE: To describe the successful management of MRSA infection involving the spine.
STUDY DESIGN: Two case reports of MRSA infection, one involving epidural and lumbar subdural abscesses, the other with osteomyelitis and discitis.
METHODS: Two cases are described, one with lumbar epidural and subdural abscesses and the other with osteomyelitis and discitis of the spine. Switching from vancomycin to daptomycin plus rifampin-based therapy resulted in patient improvement that allowed discharge from the hospital.
RESULTS: Both patients recovered fully from their infection.
CONCLUSIONS: Daptomycin is a safe and effective option for the treatment of MRSA infection involving the spine.

Keywords: Methicillin-resistant *S. aureus*; Bacteremia; Epidural abscess; Lumbar subdural abscess; Osteomyelitis; Discitis; Daptomycin; Vancomycin

Introduction

Infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is increasingly common in the hospital setting, accounting for 60% to 70% of all nosocomial infections [1]. Compared with methicillin-susceptible *S. aureus* (MSSA) infections, MRSA infections are 1.8–2.1 times more likely to result in death [2–4]. Vancomycin has been the standard therapy for MRSA infection, but increasing evidence indicates decreasing effectiveness of vancomycin for *S. aureus* infection. Of a total of 6,003 *S. aureus* isolates from the University of California at Los Angeles, the percentage with a vancomycin minimum inhibitory concentration (MIC) of 1 μg/mL was significantly higher in 2004 than in 2000 (70.4% vs. 19.9%, $p<0.01$) [5].

The rise in MRSA MIC for vancomycin is troubling. Data indicate that vancomycin MICs of 1–2 μg/mL are associated with a clinical success rate of 10%, compared with 56% for MICs ≤0.5 μg/mL [6]. Similarly, the mortality rate for MRSA bacteremia rises with the MRSA MIC, from 24% when the MIC is ≤0.5 μg/mL to 35% when the MIC is 2 μg/mL [7]. Local data have revealed that 61% of MRSA blood isolates at our hospital had a vancomycin MIC of 2.0 μg/mL and an additional 37% had an MIC of 1.5 μg/mL by E-test. Such evidence points to the need for alternative therapies with potent activity against MRSA.

Daptomycin is a lipopeptide with excellent activity against most aerobic Gram-positive pathogens, including those resistant to methicillin, vancomycin, and linezolid [8,9]. Daptomycin is rapidly bactericidal but does not cause cell lysis [10–13]. The US Food and Drug Administration has approved daptomycin for the treatment of complicated skin and skin structure infections caused by susceptible pathogens as well as for bacteremia, including right-sided endocarditis, caused by MSSA or MRSA [9]. A systematic review has recently shown daptomycin's effectiveness for treatment of patients with bone and joint infections [14].

Data on daptomycin penetration into the CNS are limited. In a rabbit model, daptomycin penetration into the inflamed and noninflamed meninges was approximately 5%

FDA device/drug status: approved for this bacteremia, not epidural abscess, discitis, or osteomyelitis (daptomycin).

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and 2%, respectively [15]. In this report, we describe two cases of spinal infections in which daptomycin was used with favorable outcomes.

Case reports

Case 1

Clinical presentation

A 30-year-old white male with altered mental status, lethargy, and increasing fever was admitted to the intensive care unit. He had a history of a motor vehicle accident 10 years ago that required a left-sided hemipelvectomy. He has an extensive history of intravenous (IV) drug abuse. On hospital admission, a lumbar puncture revealed white cells of 190,000/mm^3, red cells 3/mm^3, neutrophils 64%, and lymphocytes 36%. One of two blood cultures was positive for *Staphylococcus*. Vital signs were temperature 38.8 °C, pulse 112/min, respirations 36/min, and blood pressure 140/72 mm Hg. His erythrocyte sedimentation rate (ESR) was 75 mm/h. Physical examination revealed mild nuchal rigidity, distant heart sounds without murmur, decreased breath sounds with bilateral rales and occasional wheeze, decreased muscle mass, and the left hemipelvectomy. There were no stigmata of endocarditis.

Initial course

The clinical impression was meningitis. Because of the patient's history of increasing back pain and the clinical findings, lumbar epidural abscess and pyogenic meningitis were suspected. Given the history of IV drug abuse, infection with MRSA was considered likely. He received one dose each of gentamicin and ceftriaxone in the emergency department, but this was changed to vancomycin, ceftriaxone, and levofloxacin pending further workup. A computed tomography (CT) scan revealed an epidural abscess of the lumbar spine. Unenhanced and enhanced magnetic resonance imaging (MRI) of the lumbar spine demonstrated a large epidural abscess extending from L1 through the superior aspect of L5 (Fig. 1). Paraspinal abscess formation was noted extending through the left L1–L2 and L2–L3 neural foramina.

Surgery

Surgery on the third hospital day confirmed lumbar epidural abscess and also showed lumbar subdural abscess. The patient underwent a decompression lumbar laminectomy of L4–L5 with microscopic drainage of the epidural and subdural abscesses.

Further course

Sensitivities of the blood cultures drawn on admission and of the CSF culture drawn before surgery showed MRSA sensitive to vancomycin, rifampin, tetracycline, and cotrimoxazole and resistant to oxacillin, erythromycin, and levofloxacin. Because the vancomycin trough level was subtherapeutic (<3 μg/mL) despite administering 3.5 g in

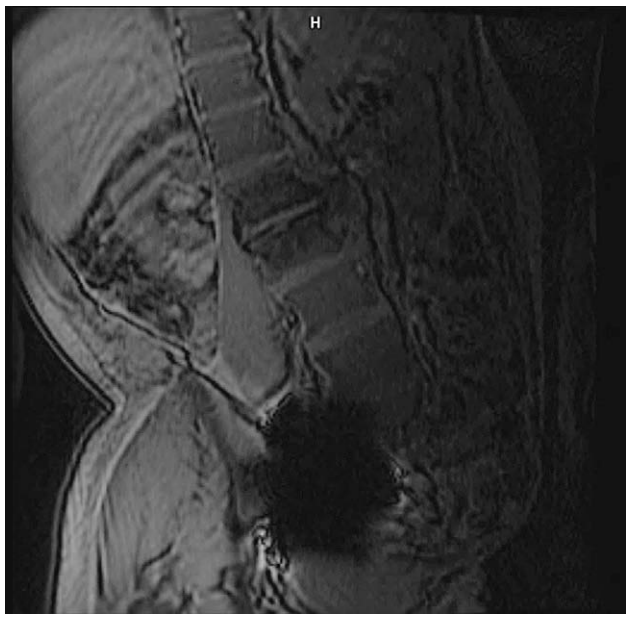

Fig. 1. MRI of the lumbar spine demonstrating a large epidural abscess extending from L1 through the superior aspect of L5.

divided daily doses, the antibiotic regimen was changed to oral rifampin 600 mg (initially IV but changed to oral when the patient was taking oral medications) and daptomycin 450 mg IV daily (8 mg/kg/d). The patient's condition subsequently improved. A blood culture drawn on the fifth hospital day, and blood and CSF cultures drawn on the eighth hospital day, yielded no growth. The patient continued to recover and received rifampin and daptomycin for 6 weeks. Daptomycin was well tolerated and no adverse events were reported during therapy. There were no clinically relevant changes in laboratory values and no adverse changes were noted on physical examination that might have been attributable to the treatment regimen. Creatine kinase levels ranged from 13 to 22 U/L for the duration of therapy. The patient subsequently received 3 months of oral double-strength trimethoprim-sulfamethoxazole twice daily after completing IV antibiotic therapy. At his 6-month follow up, there was no evidence of infection and his sedimentation rate, which had been 21 mm/h at the end of treatment, was clinically stable, remaining in the range of 20–29.

Case 2

Clinical presentation

A 72-year-old man presented with chest pain (6–9/10) radiating to his back. He had a past history of prostate cancer, left knee total arthroplasty, and nephrostomy tubes that recently had been replaced with ureteral stents. He had no notable examination findings except for a fever of 38.2 °C and a 1/6 systolic murmur heard best at the left sternal border. He had a normal white blood cell count, but had a creatinine of 1.6 mg/dL and an ESR of 84 mm/h. He was taking cotrimoxazole chronically for MRSA bacteriuria and bicalutamide for prostate cancer.