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Successful Treatment of Methicillin-Resistant *Staphylococcus aureus* Meningitis with Daptomycin

To the Editor—Methicillin-resistant *Staphylococcus aureus* (MRSA) meningitis is an uncommon cause of acute bacterial meningitis that is associated with a high mortality rate [1]. Because of limited therapeutic options and difficulty achieving therapeutic drug concentrations in the CSF, the treatment of these drug-resistant organisms remains challenging. Although the mainstay of treatment traditionally has been vancomycin, there are case reports of successful treatment with teicoplanin and linezolid [2, 3]. Daptomycin is a bactericidal agent that has the potential to treat CNS infections caused by multidrugresistant gram-positive organisms. Here, we describe a case of MRSA meningitis with septic brain emboli successfully treated with intravenous daptomycin in a patient with a vancomycin allergy.

A 41-year-old woman was admitted to the hospital because of recent onset of slurred speech, fever, and right arm tremor. Her medical history was significant for systemic lupus erythematosus with chronic kidney disease necessitating hemodialysis after failed renal transplantation. The patient had a history of multiple hospitalizations, most recently for catheter-related bacteremia due to MRSA. Treatment was complicated by the development of leukocytoclastic vasculitis caused by vancomycin therapy; therefore, therapy was changed to linezolid.

At admission to the hospital, the patient's temperature was 37.9°C, and her blood pressure was 118/51 mmHg. On physical examination, she had a right thigh dialysis graft with an open wound draining purulent discharge. Initial laboratory data included a WBC count of 23,000 cells/mL with 14% band forms.

While in the emergency department, the patient experienced a seizure and was intubated to protect the airway. A lumber puncture was performed, which revealed a WBC count of 410 cells/mL, an RBC count of 230 cells/mL, a glucose level of 44 mg/dL, and a protein level of 102 mg/dL. Empirical treatment with cefepime, ampicillin, and linezolid was initiated. On the second hospital day, cultures of CSF and blood samples grew MRSA. The MIC of vancomycin was determined to be 0.5 mg/dL with use of the VITEK system (bioMe´rieux). Because of both the patient's history of a vancomycin allergy and the possibility of graft infection, daptomycin was administered (6 mg/kg every 48 h) with rifampin, and treatment with the other antibiotics was discontinued.

The MRSA isolate was susceptible to daptomycin, with an MIC of 1 mg/dL (determined according to E-test [ABiodisk]). CT revealed septic emboli in the brain, and transesophageal echocardiography revealed no valvular vegetations or myocardial abscess. On hospital day 3, the thigh graft was removed. On hospital day 10, the patient was extubated. Her hospital course was also complicated by spontaneous pneumothorax and gastrointestinal bleeding. Additional blood cultures showed no growth after antibiotic therapy was initiated. The patient completed 42 days of daptomycin therapy; upon discharge to a skilled nursing facility, she was awake, alert, and without any residual neurologic deficits.

S. aureus is a rare cause of acute bacterial meningitis, accounting for 1%–9% of all cases [1]. There have been case

reports of treatment using intravenous or intrathecal teicoplanin and linezolid [2, 3], but the usual therapeutic choice in cases of MRSA meningitis is vancomycin with or without rifampin. However, vancomycin is bacteriostatic and slow-acting, and MRSA isolates are demonstrating increasing MICs [4]. In addition, clinical studies of vancomycin in the treatment MRSA meningitis are limited. Vancomycin has poor CSF penetration in the absence of inflamed meninges or when administrated with dexamethasone [5, 6].

For patients who develop a reaction to vancomycin, treatment of MRSA meningitis remains clinically challenging.

Daptomycin is a cyclic lipopeptide derived from *Streptomyces roseosporus* [7]. The mode of action is unique; it binds to bacterial membranes in the presence of physiological levels of calcium ions [8]. Daptomycin has potent bactericidal activity against gram-positive bacteria that is concentration-dependent. Unlike agents that are active against the cell wall, daptomycin causes rapid bactericidal activity without cell lysis, which could reduce the release of bacterial molecules and lessen the inflammatory response [9–11]. For CNS infections in animal models, Cottagnound et al. [12] demonstrated eradication of pneumococcal meningitis with daptomycin. In a rabbit meningitis model, daptomycin displayed significantly superior bactericidal activity, compared with vancomycin therapy, in treating *S. aureus* infection. When given at a dose of 6 mg/kg, the penetration of daptomycin into inflamed meninges was 5%; daptomycin was, therefore, significantly more effective than vancomycin in sterilizing CSF. The level of penetration in noninflamed meninges was 2% [13].

Our patient experienced clinical improvement and her blood cultures showed no growth soon after administration of daptomycin was initiated. Although daptomycin dosage is not well established for dialysis-dependant patients, we used a dosage of 6 mg/kg every 48 h (which is the approved dosage for bloodstream infections).

Given our patient's clinical response, additional CSF studies for drug levels and confirmation of sterilization were not performed. Indeed, further study is needed in humans to evaluate the CNS penetration of daptomycin in inflamed meninges and its efficacy for treating MRSA CNS infection. In conclusion, this case suggests that daptomycin is a potentialalternative for patients who are not able to tolerate vancomycin for the treatment of MRSA meningitis.

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