Available online at www.sciencedirect.com
ScienceDirect
Diagnostic Microbiology and Infectious Disease 60 (2008) 437–440
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Diminished vancomycin and daptomycin susceptibility during prolonged bacteremia with methicillin-resistant *Staphylococcus aureus*

Jason W. Bennett[a,*], Clinton K. Murray[a], Robert L. Holmes[b], Jan E. Patterson[c], James H. Jorgensen[d]

[a]*Department of Medicine, Brooke Army Medical Center, Fort Sam Houston, TX 78234, USA*
[b]*Department of Infectious Diseases, Wilford Hall Medical Center, San Antonio, TX 78201, USA*
[c]*Department of Medicine (Infectious Diseases) and Pathology, University of Texas Health Science Center and South Texas Veterans Health Care System, San Antonio, TX 78229, USA*
[d]*Department of Pathology, University of Texas Health Science Center, San Antonio, TX 78229, USA*

Received 5 June 2007; accepted 10 November 2007

Abstract

An elderly patient with methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia was treated sequentially with vancomycin plus rifampin then daptomycin plus gentamicin. The MRSA strain developed diminished susceptibility to vancomycin (MIC increase and tolerance), daptomycin, and gentamicin, and resistance to rifampin during therapy.
© 2008 Elsevier Inc. All rights reserved.

Keywords: Vancomycin tolerance; Daptomycin resistance; MRSA bacteremia; Minimum inhibitory concentration; Bactericidal effect

A 94-year-old woman with advanced dementia was admitted to our medical center with a 1-week history of fever and worsening mental status despite receiving 5 days of levofloxacin (500 mg by mouth daily) for a presumed urinary tract infection. Blood cultures drawn at the time of admission and throughout her hospital course demonstrated methicillin-resistant *Staphylococcus aureus* (MRSA) (Fig. 1). Diagnostic workup including imaging studies and transthoracic echocardiography did not reveal an infectious source. The course of antimicrobial therapy is described in Fig. 1. Vancomycin was dosed 1 g once or twice daily to obtain serum trough levels >15 μg/mL.

In an effort to understand the patient's unremitting bacteremia in the face of aggressive antimicrobial therapy, 16 of the patient's MRSA isolates recovered during a 27-day hospital course were assessed for antimicrobial susceptibility, antimicrobial killing effects of different antibiotics, and the genetic relatedness of her isolates.

Broth microdilution antimicrobial susceptibility testing was performed using in-lab prepared frozen panels in accordance with the methods of the Clinical and Laboratory Standards Institute (CLSI, 2006a, M7-A7). In order to assess possible subtle increases in MIC, one-half $\log_2$ concentrations of vancomycin were prepared. All MICs were interpreted using the latest CLSI criteria (CLSI, 2006b, M100-S16). *S. aureus* ATCC® 29213 was used as the quality control organism.

The bactericidal effects of vancomycin, daptomycin, and selected drug combinations were determined by time-kill curve assays according to the procedures described by the CLSI (CLSI, 1999, M26-A). Vancomycin assays were performed using isolates from hospital day (HD) 1, HD9, and HD26. Daptomycin was used for isolates HD9 and HD26. Test concentrations were prepared at 2 and 4 times the vancomycin MIC and 4 times the daptomycin MIC for each isolate. Isolate HD9 was also tested against the combinations of vancomycin at 2 times the MIC with rifampin or with gentamicin. Tolerance was defined as <3 $\log_{10}$ reduction in colony-forming unit

* Corresponding author. Infectious Disease (MCHE-MDI), Brooke Army Medical Center, 3851 Roger Brooke Drive, Fort Sam Houston, TX 78234, USA. Tel.: +1-210-916-4355; fax: +1-210-916-0388.
E-mail address: jason.bennett@amedd.army.mil (J.W. Bennett).

0732-8893/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.diagmicrobio.2007.11.002

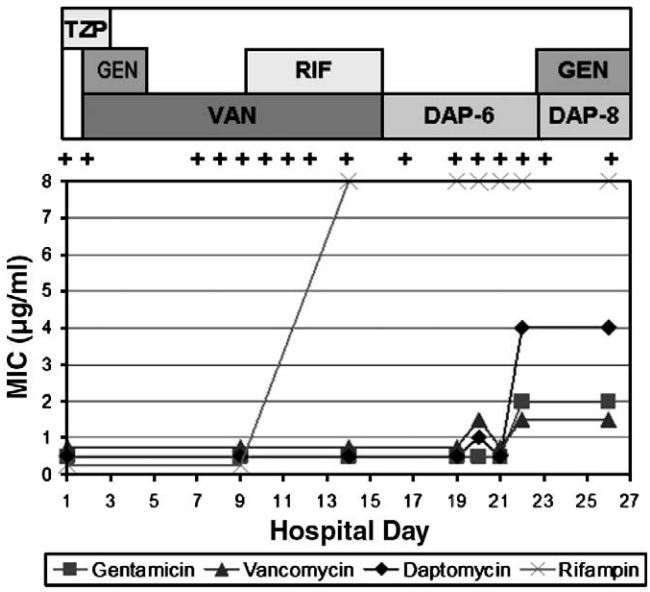

Fig. 1. Antibiotic susceptibility testing of selected MRSA isolates by microbroth dilution and antibiotic regimen by hospital date. MRSA isolates in blood cultures are indicated by +. Antibiotic dosing was as follows: piperacillin–tazobactam (TZP), 3.375 g iv qid; gentamicin (GEN), 60 mg iv tid; vancomycin (VAN), 1 g iv once or twice daily based on serum trough levels. Trough levels >15 µg/mL on all but 4 days (HD3, 8.7 µg/mL; HD12, 8.1 µg/mL; HD13, 13 µg/mL; HD15, 11.9 µg/mL), rifampin (RIF), 300 mg po tid. RIF MICs were either <0.25 or >8 µg/mL; daptomycin (DAP), 6 mg/kg iv daily then increased to 8 mg/kg daily.

(CFU)/mL following 24-h incubation (Bradley et al., 1978; Norden and Keleti, 1981).

All of the patient's MRSA isolates were resistant to ciprofloxacin, clindamycin, erythromycin, and trimethoprim–sulfamethoxazole but susceptible to doxycycline, minocycline, linezolid, and vancomycin. The initial isolate was susceptible to rifampin (MIC <0.25 µg/mL), but resistance (MIC >8 µg/mL) was observed in all isolates following 6 days of rifampin and vancomycin combination therapy (Fig. 1). The vancomycin MIC of the initial isolate was 0.75 µg/mL, but by HD9, the MIC increased to 1.5 µg/mL. The daptomycin MIC of the initial isolate was 0.5 µg/mL but increased to 4 µg/mL on HD22 after 6 days of 6 mg/kg dosing (Fig. 1). The MIC of gentamicin increased from 0.5 to 2 µg/mL by HD22 (Fig. 1). Five MRSA isolates from different times during the hospital course were identical by pulsed-field gel electrophoresis (PFGE) (pulse type USA100.0137) with *Sma*I-restricted DNA according to the CDC PulseNet protocol (McDougal et al., 2003).

Time–kill assays performed with vancomycin did not demonstrate antibiotic tolerance at either 2 or 4 times the MIC for isolate HD1, whereas HD9 and HD26 both demonstrated tolerance to vancomycin at both antibiotic concentrations (Fig. 2). At 4 times the MIC with HD9 and HD26 isolates, daptomycin was rapidly bactericidal with a >3 $\log_{10}$ decrease in CFU/mL in 4 h despite the increase in MIC to 4 µg/mL (Fig. 2). The addition of gentamicin to

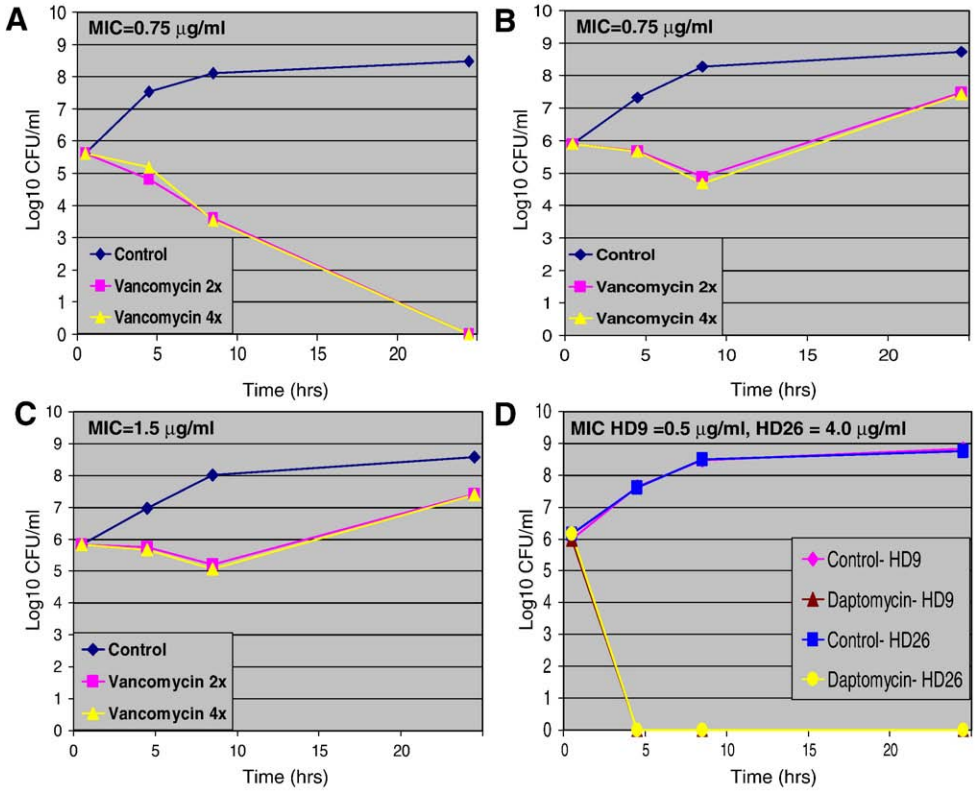

Fig. 2. Time–kill assays for MRSA isolates HD1, HD9, and HD26. Vancomycin concentrations were 2 or 4 times the isolate MIC for HD1 (A), HD9 (B), and HD26 (C). Daptomycin concentration was 4 times the isolate MIC for HD9 (D) and HD26 (D).

Download English Version:

https://daneshyari.com/en/article/3348136

Download Persian Version:

https://daneshyari.com/article/3348136

Daneshyari.com