Case Report

Use of Daptomycin for the Treatment of Methicillin-Resistant Coagulase-Negative Staphylococcal Ventriculitis

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Received 19 January 2012; Accepted 13 March 2012

Academic Editor: Dianne L. Atkins

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Coagulase-negative staphylococci (CoNS) are the main pathogens causing hospital-acquired external-ventricular-drain (EVD-) and lumbar-drain- (LD-) associated meningitis and ventriculitis. The treatment of these infections can be challenging and may require combination of intraventricular and intravenous administration of antibiotics. Limited animal data demonstrate rapid daptomycin bactericidal activity, adequate penetration in the setting of inflamed meninges, and extended half-life in the ventricles Steenbergen et al. (2009). There are limited clinical data using daptomycin intravenously and/or intraventricularly for the treatment of central nervous system infections (CNS) Elvy et al. (2008), Stucki et al. (2007), Lee et al. (2008) and Wallace et al. (2009). We report here our experience in the treatment of an EVD-related infection.

1. Case Report

A 52-year-old female with history of hypertension, smoking, alcohol dependence, and coronary vascular disease with recent myocardial infarction was admitted due to acute change in mental status. The patient had a spontaneous intraventricular hemorrhage, and an emergency bedside ventriculostomy was performed. Her hospital course was marked by persistent fevers in spite of multiple negative blood, cerebrospinal fluid (CSF), and urinary cultures. She received empiric levofloxacin intravenously 750 mg daily and vancomycin 1 gram intravenously every 12 hours until day 9 of hospitalization. Her neurologic function steadily improved, and the ventriculostomy was discontinued on day 11. However, her CSF cultures on that day yielded coagulase-negative staphylococcal (CoNS) species. Vancomycin 1 gram and rifampin 600 mg intravenously were administered every 12 hours. On day 15, computerized tomography (CT) of the head demonstrated increased intraventricular hemorrhage requiring reinsertion of an external ventriculostomy. Repeated CSF analysis demonstrated elevated WBC (57 cells/mm3 and protein 149 mg/dL) with decreased glucose (67 mg/dL). CSF cultures yielded CoNS again. Cultures of CSF continued to yield CoNS for the next three days despite the addition of daptomycin intravenously at 10 mg/kg (dosed at actual body weight) daily. As a result, intraventricular daptomycin was added on day 18, 10 mg daily for the first two days and then every other day. Culture of CSF became sterile on day 25 following 7 days of daptomycin intravenously and intraventricular therapy in addition to continued administration of intravenous vancomycin and rifampin. The second ventriculostomy was discontinued on day 38 (as was rifampin administration). Intravenous daptomycin and vancomycin were discontinued on day 55 after 37 days of dual treatment. Mental status progressively improved during this time.

Daptomycin peak and trough levels in the CSF were measured on day 29, and day 30, respectively (correlating to day 10 following the start of intravenous and day 11
following the start of intraventricular daptomycin). The peak 
CSF level (following intravenous and intraventricular ad-
ministration) was 6.30 mcg/mL on day 29 and the trough 
CSF level was 1.39 mcg/mL on day 30. The serum trough 
level on day 30 was 20.15 mcg/mL, and the minimum in-
hibitory concentration (MIC) of CoNS to daptomycin was
<1 mcg/mL.

The remaining hospital course was complicated with respir-
atory failure requiring tracheostomy and ventilation sup-
port, ventilator-associated pneumonia, sacral pressure ulcer,
and Clostridium difficile colitis. The patient was successfully
discharged on day 65 to a rehabilitation center.

2. Discussion

Data in animal models support rapid bactericidal activity
of daptomycin. Early studies of MRSA ventriculitis in ani-
mals demonstrate daptomycin achieving greater bactericidal 
activity, more rapid killing kinetics, longer intraventricular 
half-life than vancomycin, minimal cell wall lysis, and signif-
icant reduction in host inflammatory reaction and cortical 
injury [1]. Several clinical reports describe successful use 
of daptomycin for the treatment of various CNS infections (e.g.,
meningitis, septic brain emboli, EVD-associated ventriculi-
tis, etc.) caused by gram-positive bacteria (e.g., meticillin-
resistant Staphylococcus aureus, Enterococcus faecalis, etc.) [2–
5]. Doses of daptomycin used ranged from 6 to 12 mk/kg 
for intravenous administration and 5 to 10 mg every other 
day for intraventricular administration. Daptomycin was 
chosen either due to failure or adverse events of standard 
antibiotics early on in the course of the infection. Recent 
pharmacokinetic study of a single intravenous 10 mg/kg dose 
in patients with indwelling external CSF shunts menin-
gitis/ventriculitis demonstrated CSF penetration of 11.5% 
corrected for protein binding) [6].

In our patient, the addition of intravenous daptomycin 
was precipitated by persistent growth of CoNS in spite of 
treatment with vancomycin and rifampin. The decision to 
add intraventricular administration of daptomycin was made 
due to continued neurosurgical need for the ventriculostomy 
and potential limited CSF penetration of intravenous dap-
tomycin. We found trough CSF levels of daptomycin to be 
2-fold greater than the MIC for CoNS with peak levels well 
over 6-fold greater. These levels were obtained in the setting 
of both intravenous and intraventricular administration of 
daptomycin, and we cannot comment on the penetration 
and/or efficacy of intravenous daptomycin alone in this 
setting (or the need to add intraventricular daptomycin rou-
tinely). The impact of synergy between rifampin and dap-
tomycin was not quantitated in our patient, and we do not 
believe continued use of vancomycin provided additional 
benefit in this case. Our patient’s outcome was similarly 
successful as previous CNS infections treated with dapto-
mycin.

We feel more clinical data are needed to delineate con-
sistent daptomycin CSF penetration and role for intraven-
tricular administration of daptomycin in CNS infections in 
conjunction with removal of involved prosthetic devices.

Financial Support

This study was supported in part by the BMA Medical 
Foundation and the Beatrice Snyder Foundation.

Acknowledgment

The authors wish to thank Maria Amodio-Groton, PharmD,
Clinical Science Director, Cubist Pharmaceuticals Inc, Lex-
ington, Massachusetts for technical assistance.

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