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ORIGINAL ARTICLE

# The use of ceftaroline fosamil in methicillin-resistant *Staphylococcus aureus* endocarditis and deep-seated MRSA infections: a retrospective case series of 10 patients

**Jennifer C. Lin · Gregory Aung · Amy Thomas · Maximillian Jahng · Scott Johns · Joshua Fierer**

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**Abstract** There are many limitations to the current antibiotics used for the treatment of severe methicillin-resistant *Staphylococcus aureus* (MRSA) infections. Ceftaroline is a new fifth-generation cephalosporin approved for the treatment of skin and soft tissue infections caused by MRSA and community-acquired pneumonia. We propose that ceftaroline can also be used successfully in more severe MRSA infections, including endocarditis. We conducted a retrospective chart review in a university-affiliated Department of Veterans Affairs hospital in San Diego, California (USA) of ten inpatients treated with ceftaroline for severe MRSA infection, including five cases of probable endocarditis (including two endocardial pacemaker infections), one case of pyomyositis with possible endocarditis, two cases of pneumonia (including one case of empyema), two cases of septic arthritis (including one case of prosthetic joint infection), and two cases of osteomyelitis. Seven of the 10 patients achieved microbiological cure. Six of the 10 patients achieved clinical cure. Seven patients were discharged from the hospital. Three patients were placed on comfort care and expired in the hospital; one achieved microbiological cure before death, and two remained bacteremic at time of death. In most patients, ceftaroline was effective for treatment of MRSA bacteremia and other severe MRSA infections. Adverse effects seen included rash, eosinophilia, pruritus, and *Clostridium difficile* infection. Ceftaroline can be a safe and effective drug for treatment of severe MRSA infections, and further comparative studies are warranted.

**Keywords** Methicillin-resistant *Staphylococcus aureus* (MRSA) · Ceftaroline · Endocarditis · Osteomyelitis · Bacteremia

J. C. Lin (✉) · J. Fierer
Division of Infectious Diseases, Department of Medicine, University of California San Diego, 9500 Gilman Drive #0711, San Diego, CA 92093, USA
e-mail: jenclin@gmail.com; j9lin@ucsd.edu

G. Aung · S. Johns
Department of Pharmacy, Veterans Affairs (VA) Healthcare System, San Diego, CA, USA

A. Thomas
Thomas J. Long School of Pharmacy and Health Sciences, University of the Pacific, Stockton, CA, USA

M. Jahng
Department of Pharmacy, New Mexico Veterans Affairs (VA) Healthcare System, Albuquerque, NM, USA

J. Fierer
Medical Service, Veterans Affairs (VA) Healthcare System, San Diego, CA, USA

J. Fierer
Department of Pathology, University of California San Diego, San Diego, CA, USA

## Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is widespread both in hospitals and in the community. Meta-analyses showed increased mortality from MRSA infections compared to methicillin-susceptible *S. aureus* (MSSA) infections [1, 2], in part because of the inferiority of vancomycin compared to beta-lactam antibiotics [3, 4]. Although vancomycin has been the standard therapy for severe MRSA infections, the need for new treatment options has been increased by the rising minimum inhibitory concentration (MIC) for treatment of MRSA [5]. Ceftaroline fosamil is a novel cephalosporin with a high affinity for staphylococcal

penicillin-binding proteins, including PBP2a [6]. Ceftaroline was approved by the FDA for the treatment of community-acquired pneumonia (CAP) and acute bacterial skin and skin structure infections (ABSSSI) based on multicenter randomized Phase III trials [7–10] and was recently reported to be effective therapy for a small number of cases of MRSA endocarditis and bacteremia [11]. This article describes the successful use of ceftaroline in the treatment of MRSA bacteremia and various deep-seated MRSA infections.

## Patients and methods

With approval from our Institutional Review Board, we retrospectively reviewed the charts of all patients at the Veterans Affair Hospital in San Diego, CA (USA) diagnosed with severe MRSA infections who were treated with ceftaroline between March 2011 and October 2011. Patients were identified by querying a list of infectious disease consultations during this period, because all positive blood cultures result in an infectious disease consultation, or through a query of the pharmacy department database indicating which patients had received ceftaroline. Infective endocarditis was diagnosed clinically. Patients were presumed to have endocarditis if they had prolonged bacteremia (>48 h) with no other source and were suspected to have an intravascular source of infection. A transesophageal echocardiogram (TEE) was not always obtained for reasons of co-morbidities in some cases and patient refusal in others.

Microbiological results were evaluated for all patients to determine pathogen identity and susceptibility. The isolates were identified and tested for susceptibility by the Vitek system and by E test (bioMérieux, Durham, NC, USA). Information gathered from individual case records included patient age, gender, diagnoses, antibiotic treatment, adverse effects, and final outcome.

Patients were treated with ceftaroline if they failed to clinically respond to treatment with vancomycin, relapsed after vancomycin therapy, or if they had adverse effects limiting vancomycin therapy. Linezolid was not used because we had several cases of bacteremia. Although daptomycin is also an option for treatment of MRSA, controlled trials have failed to show its superiority to vancomycin [5]. Additionally, several of our patients had pneumonia, for which daptomycin would have been inappropriate.

Ceftaroline dosage and duration were based on a number of factors including age, weight, renal function, presumed tissue penetration, and distribution of ceftaroline. Ceftaroline dosed at 600 mg IV every 12 h achieves adequate $\%T >$ MIC in ABSSSI, but higher dosing may be required to achieve this goal at more difficult-to-penetrate infection sites. As ceftaroline exhibits a fairly short half-life (1.6 h after 1 dose and 2.7 h after 28 doses [12]),we dosed our patients with normal renal function (glomerular filtration rate, GFR >60 ml) as we would other IV cephalosporins with comparable half-lives, every 8 h. If the GFR was <60 ml, we either lowered the dose to 400 mg every 8 h or prolonged the dosing interval (patients 2, 4, 5, 6, and 7). Although dosing every 8 h was the goal for the Department of Infectious Diseases and the Department of Pharmacy overseeing the care of the patients, individual practitioners may have opted for a different treatment regimen. In some cases (patients 1 and 10), patients were started on every 12 h dosing as per the drug label but then switched to every 8 h dosing at the recommendation of the infectious diseases consultant. As this was a retrospective chart review, we could not enforce standardized treatment regimens.

The primary endpoints were clinical cure and microbiological cure. Clinical cure was defined as resolution of all signs and symptoms of infection or improvement such that no further antimicrobial therapy was necessary. Microbiological cure was defined as negative cultures after antimicrobial therapy; eradication was presumed if an adequate source specimen was not available to culture but the patient was assessed as a clinical cure. Failure was defined as persistent signs and symptoms of infection, persistently positive blood cultures while on ceftaroline, relapse after stopping ceftaroline, or death if that could be attributed to ongoing infection.

## Results

Ten patients fit our criteria, including five with probable endocarditis, two cases of pneumonia, two cases of septic arthritis, two cases of osteomyelitis, and one case of pyomyositis (Table 1; multiple diagnoses in patients 3 and 4). All ten patients had failed other anti-MRSA medications before the initiation of ceftaroline. We achieved microbiological cure in seven of ten patients; six of the ten patients achieved clinical cure. Three patients were assigned to comfort care and expired in the hospital; one evidenced microbiological cure before death. The two treatment failures had received 4 days (patient 5) and 8 days (patient 6) of treatment, respectively.

### Endocarditis

Patients 1 through 5 were probable cases of endocarditis. Four patients had clear blood cultures after 3–7 days of ceftaroline.

Patient 1 was a patient on the palliative care service who was found to have MRSA bacteremia. No clear source was identified, but he was presumed to have endocarditis or another intravascular source of infection because of

**Table 1** Case summaries

| Patient Age (years)/ gender | Diagnoses | Positive cultures[a] | Antimicrobial MIC (mg/l)[b] | Ceftaroline dose and duration[a] | Prior and concurrent anti-MRSA Agents | Renal function (CrCl in ml/min) | Microbiological cure[c,d] | Clinical cure[e] | Adverse drug reactions | Patient outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| 1<br>66/M | Endocarditis (probable) | Blood: days *1, 3* | Vancomycin[#] (2)<br>Daptomycin[#] (0.75)<br>Ceftaroline[#] (0.5) | 600 mg IV every 12 h on days 5–20<br>600 mg every 8 h on days 20–47 | Vancomycin IV days 1–5 | CrCl = 71 mL/min | Yes (day 11) | No | *C. difficile* infection | Day 47: Patient died after care withdrawn (metastatic prostate cancer on palliative care). Last negative blood culture on day 11 |
| 2<br>53/M | Endocarditis (probable)<br>Pulmonary septic emboli | Blood: days *1,* **2, 3, 4** | Vancomycin (1)<br>Ceftaroline[#] (0.5) | 600 mg IV every 12 h on days 2–55 | Daptomycin IV 7 mg/kg/day days 1–2<br>Linezolid IV days 1–5<br>Gentamicin IV days 2–4 | CrCl = 21–56 mL/min | Yes (day 5) | Yes | None | Day 55: Discharged off all anti-MRSA antibiotics<br>Day 259: Patient died from leukemia while on palliative care. Last negative blood culture on day 252 |
| 3<br>80/M | Endocarditis (probable)<br>Infected pacemaker<br>Septic hip | Blood: days *1, 4–7, 9, 15–18, 20* | Daptomycin[#] ($\leq$2)<br>Ceftaroline[#] (0.5)<br>Vancomycin (2) | 600 mg IV every 8 h on days 20–42 | Vancomycin IV days 2–9, 52–66<br>Daptomycin 7 mg/kg daily on days 10–51<br>Gentamicin days 3–4, 9<br>Rifampin days 51–52 | CrCl = 23–43 mL/min | Yes | Yes (day 22) | Fever, rash, and eosinophilia (day 41) | Day 7: Proximal femur resected<br>Day 42: Antibiotics changed to Vancomycin due to rash and allergy<br>No recurrence 120 days after end of treatment. |
| 4<br>55/M | Endocarditis (possible)<br>Pyomyositis of pectoral muscle at site of previous tunneled dialysis catheter | Blood: days *1–2,* **3–6**) | Vancomycin (0.5, 1, 2)<br>Ceftaroline[#] (0.75) | 200 mg IV every 12 h on days 3–9 | Vancomycin IV days 1–3<br>Clindamycin IV days 2–3 | End-stage renal disease on hemodialysis thrice weekly<br>CrCl < 10 mL/min | Yes | Yes (day 7) | None | Day 9: Discharged home on vancomycin IV for 6 weeks<br>Patient refused muscle debridement and TEE<br>No recurrence of bacteremia 7 months after end of treatment |
| 5<br>85/M | Endocarditis (probable)<br>AICD pocket infection | Blood: days *1–2,* **3, 4, 5, 6, 7** | Vancomycin (2)<br>Ceftaroline[#] (0.25) | 400 mg IV every 12 h on days 3–6 | Vancomycin IV days 1–3<br>Gentamicin IV days 1–6<br>Rifampin day 6 | CrCl = 15–20 mL/min | No | No | None | Day 6: Made comfort care and died. AICD pocket infection without removal of AICD resulting in cardiac arrest |

**Table 1** continued

| PatientAge (years)/ gender | Diagnoses | Positive cultures[a] | Antimicrobial MIC (mg/l)[b] | Ceftaroline dose and duration[a] | Prior and concurrent anti-MRSA Agents | Renal function (CrCl in ml/min) | Microbiological cure[c,d] | Clinical cure[e] | Adverse drug reactions | Patient outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| 6<br>88/M | Pneumonia | Sputum: days *1, 7*<br>No subsequent cultures | Vancomycin (1) | 400 mg IV every 8 h on days 8–15 | Vancomycin IV days 1–8 | CrCl = 49 mL/ min | No | No | None | Day 15: Made comfort care<br>Day 18: Care withdrawn; patient died |
| 7<br>64/M | Recurrent pneumonia with empyema due to bronchopleural fistula | Pleural fluid: days *0* (prior to admission), **2, 3**<br>No subsequent cultures<br>No positive blood cultures | Vancomycin (0.5)<br>Daptomycin[#] (0.125)<br>Ceftaroline[#] (0.38) | 400 mg IV every 8 h on days 1–31 and days 58–87 | During previous admissions:<br>Vancomycin IV, minocycline PO, co-trimoxazole PO, linezolid PO | CrCl = 52 mL/ min | Yes (clinical and radiographic, no surveillance pleural fluid cultures) | Yes | *C. difficile* associated diarrhea | Day 92: Discharged home on minocycline. No recurrence of empyema in following 12 months |
| 8<br>60/F | Prosthetic knee septic arthritis<br>Bacteremia | Blood: day *1* (cleared day 3)<br>Joint fluid/ tissue: days *1*, **63, 65** (surgery day 65) | Vancomycin (1)<br>Linezolid (4)<br>Ceftaroline[#] (0.5) | 600 mg IV every 8 h on days 2–23 | Vancomycin IV days 1–2<br>Rifampin 600 mg po q24 h days 1–24 | CrCl = 70 mL/ min | No | No | Day 9: Eosinophilia<br>Day 22: Pruritus | Day 2: Right knee incision and drainage<br>Day 24: Ceftaroline changed to vancomycin plus rifampin due to rash<br>Day 65: right knee incision and drainage with spacer placement. Cultures cleared after removal of prosthesis<br>Day 193: Right total knee arthroplasty Doing well 2 months after knee replacement |
| 9<br>85/M | Osteomyelitis of metatarsal head<br>Idiopathic peripheral neuropathy. | Wound: day **1**<br>Metatarsal bone: day **8**<br>No positive blood cultures | Vancomycin (2) | 600 mg IV every 8 h on days 1–42 | During previous admission: Daptomycin IV 6 mg/kg q24 h for 6 weeks | CrCl = 63 mL/ min | Yes[f] (no initial surveillance culture but radiographic clearance. Subsequent amputation due to traumatic pressure ulcer- bone culture sterile) | Yes | *C. difficile* associated diarrhea | Day 6: left foot 2nd digit amputation<br>Day 42: Discharged home<br>Day 46: Last clinic follow-up 3 days after completion of 6-week course of antibiotics. No evidence of osteomyelitis |

**Table 1** Case summaries

| Patient Age (years)/ gender | Diagnoses | Positive cultures[a] | Antimicrobial MIC (mg/l)[b] | Ceftaroline dose and duration[a] | Prior and concurrent anti-MRSA Agents | Renal function (CrCl in ml/min) | Microbiological cure[c,d] | Clinical cure[e] | Adverse drug reactions | Patient outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| 10<br>36/M | Recurrent psoas abscess despite drainage and full course of vancomycin therapy<br>Vertebral osteomyelitis<br>HIV | Wound: day *1*<br>No subsequent cultures<br>No positive blood cultures | Vancomycin (1)<br>Clindamycin (≤0.25) | 800 mg IV every 12 h on days 3–44 | Vancomycin days 1–3<br>Clindamycin IV 600 mg day 1<br>Gentamicin IV days 3–8<br>Prior admission:Drainage of psoas abscess, vancomycin for 4 weeks, oral clindamycin for 3 weeks followed by co-trimoxazole suppression | CrCl = 110 mL/ min | Yes[g] (clinical and radiographic, no repeat surveillance cultures) | Yes | Day 3: eosinophilia (asymptomatic) | Days 1–8: psoas abscess drain placed<br>Day 9–44: Ceftaroline as an outpatient<br>Doing well 10-months post-treatment. Last CT abdomen/ pelvis on day 212 showed no evidence of left psoas abscess recurrence |

*AICD* implantable cardioverter defibrillator, *HIV* human immunodeficiency virus, *MRSA* methicillin-resistant *Staphylococcus aureus*, *TEE* transesophageal echocardiogram

[a] Day 1 is considered the first day of cultures positive for MRSA; numbers in italics indicate days of positive cultures before ceftaroline started; numbers in bold indicate dates of positive cultures while on ceftaroline

[b] Minimal inhibitory concentration (MIC) performed by Vitek unless otherwise noted; # indicates an *E* test

[c] Microbiological cure was defined as absence of the baseline pathogen. Eradication was presumed if an adequate source specimen was not available to culture, but the patient was assessed as a clinical cure per CANVAS 2 clinic trials criteria

[d] Days listed in parentheses indicate the first negative culture and thus the presumed date of microbiological cure. Several patients had multiple negative cultures, but only the first negative culture is listed

[e] Clinical cure was defined as resolution of all signs and symptoms of infection or improvement such that no further antimicrobial therapy was necessary. Clinical failure defined as inadequate response to study therapy, or indeterminate (unable to determine clinical outcome) per CANVAS 2 clinic trials criteria

[f] We consider patient 9 to be a clinical and microbiological cure after his initial toe amputation. Three months after discharge, he developed a second pressure ulceration of his toe stump; a second amputation was done at another VA hospital. The bone culture was sterile. We consider this to be a microbiological cure

[g] Patient 10 had a psoas abscess previously treated in December 2010 with percutaneous drainage and 4 weeks of vancomycin followed by 3 weeks of suppression with oral clindamycin. Clindamycin was switched to oral co-trimoxazole in February 2011 because of rash thought to be caused by clindamycin. Despite drainage and treatment with vancomycin followed by clindamycin and then co-trimoxazole suppression, his left psoas abscess recurred in the same location in April 2011. We thus consider him a failure of prior antimicrobial therapy (specifically, vancomycin)

persistent bacteremia. A TEE was not performed because he was on the palliative care service and had refused further testing. He received 5 days of vancomycin without clearance of bacteremia (vancomycin MIC, 2) before he was switched to ceftaroline. He achieved microbiological cure after 7 days of ceftaroline, but ultimately expired of metastatic prostate cancer.

Patient 2 was admitted to the hospital with MRSA sepsis and quickly intubated in the intensive care unit. He had a peripherally inserted central catheter (PICC) line previously placed for chemotherapy for his acute myelogenous leukemia (he was not currently on chemotherapy) and was found to have septic pulmonary emboli thought to be caused by right-sided endocarditis; he was too ill to undergo TEE. Patient 2 had a prior vancomycin allergy (severe hives) and thus was treated with a combination of linezolid (both for lung penetration and for toxin reduction), daptomycin, and gentamicin (for endocarditis) before being switched to ceftaroline. Patient 2 was clear of bacteremia on day 5, 3 days after starting ceftaroline. Patient 2 was discharged with both microbiological and clinical cure but died 5 months later of leukemia. Blood cultures drawn 1 month after completion of ceftaroline remained negative.

Patient 3 was admitted with MRSA bacteremia, septic arthritis, and presumed endocarditis (tethered posterior mitral valve on TEE) and pacemaker lead infection. His hip was aspirated; the culture grew MRSA. Despite 9 days of vancomycin he remained bacteremic. He was switched to daptomycin monotherapy. After 10 days of daptomycin monotherapy, he remained bacteremic and ceftaroline was added, with clearance of his bacteremia 2 days after initiation of ceftaroline. Patient 3 achieved both microbiological and clinical cure on ceftaroline and daptomycin but was ultimately placed on daptomycin monotherapy because of rash and eosinophilia attributed to ceftaroline. He was then transferred to an outside hospital for pacemaker lead removal and switched to vancomycin, but his bacteremia had cleared by then.

Patient 4 had a prior hemodialysis catheter MRSA infection treated with 6 weeks of vancomycin and line removal. During a recent hospitalization, he was noted to have MRSA bacteremia and was restarted on vancomycin for 4 days before leaving the hospital, against medical advice. On this admission for chest pain, he was again noted to have MRSA bacteremia and was started on vancomycin and clindamycin before being switched to ceftaroline when his MRSA isolate was noted to have an MIC of 2 (previously 0.5 and 1 on the last two admissions). Patient 4 achieved both microbiological and clinical cure with ceftaroline, but vancomycin was substituted for ease of administration at hemodialysis after clearance of active infection.

Patient 5, who had a prior automatic implantable cardioverter defibrillator (AICD) in place, was admitted with fevers and found to have MRSA bacteremia. He was presumed to have MRSA endocarditis, but a TEE was not done as he was not deemed to be a candidate for AICD removal or valve replacement for reasons of age and comorbidities. Patient 5 received 3 days of vancomycin with persistent bacteremia and was switched to ceftaroline on day 3 when his MRSA isolate was found to have an MIC of 2. Patient 5 had infected AICD leads and received only 4 days of ceftaroline before suffering a fatal cardiac arrest. We consider him to be a ceftaroline treatment failure, although we cannot exclude the possibility that his infection was actually responding to ceftaroline but the cardiac arrest occurred because of his underlying heart disease or failure to remove the infected AICD.

### Other deep-seated infections

Patients 6 and 7 had MRSA pneumonia treated with ceftaroline. Patient 6 received 7 days of vancomycin without clearance of his sputum culture followed by 8 days of ceftaroline for MRSA pneumonia before withdrawing to care on the palliative care service with other medical comorbidities (no repeat cultures were obtained to prove microbiological cure before withdrawal of care). It is unclear whether his pneumonia would have cleared with a longer course of ceftaroline, but we nevertheless defined him as a microbiological and clinical failure. Patient 7 had recurrent MRSA pneumonias, an empyema complicating rheumatoid lung disease, and a bronchopleural (BP) fistula that did not close despite multiple treatments. He originally developed a BP fistula as a complication from a chest tube that was placed for a pneumothorax which resulted from the spontaneous rupture of a pulmonary rheumatoid bleb. After development of the BP fistula, he had several episodes of MRSA empyema and had multiple thoracenteses as well as the placement of a pigtail catheter. He was also treated with talc pleurodesis. With each drainage, catheter placement, and pleurodesis, he received long courses of vancomycin (trough, 10–22 μg/ml), linezolid, co-trimoxazole, and minocycline. His medical co-morbidities disqualified him as a surgical candidate for thoracotomy. On this admission, his empyema was drained by thoracentesis and he was started on vancomycin before being switched to ceftaroline by the Infectious Diseases consult team 2 days later. The empyema was cured after two 4-week courses of ceftaroline. He was discharged on chronic minocycline suppression. Since discharge, he has undergone multiple chest imaging radiographic studies without recurrence of his empyema appearing 12 months after his course of ceftaroline, representing the first time his MRSA empyema has not recurred despite his ongoing untreatable BP fistula.

Patients 3 and 8 were treated for septic arthritis, one of a native joint and one of a prosthetic joint. Patient 3 was bacteremic (as already discussed) and had an infected hip joint, both of which were cured on ceftaroline. Patient 8 had an infected prosthetic knee and had failed a prior 6-week course of treatment with vancomycin and rifampin. She was originally deemed not to be a surgical candidate for reasons of medical comorbidities and was given ceftaroline for 19 days before developing eosinophilia, rash, and pruritus. Despite ceftaroline she continued to have positive joint fluid cultures for MRSA until the prosthetic joint was ultimately removed. Ultimately, her fluid and tissue cultures did clear after removal of her prosthesis. Nevertheless, given her infection did not clear while on ceftaroline (although this was likely inadequate source control), we considered her a failure of ceftaroline therapy.

Patients 9 and 10 were treated with ceftaroline for osteomyelitis. Patient 9 had a residual MRSA infection of the adjacent metatarsal head after amputation of an infected toe. After 6 weeks of daptomycin without response, he was changed to ceftaroline; he improved and a second amputation was performed 6 days later. Radiographic imaging and serum markers (sedimentation rate, C-reactive protein) normalized after this second amputation. He subsequently had an additional amputation for development of a pressure ulcer on his toe stump. Bone cultures from his last amputation were negative. He was thus deemed to be both a clinical and microbiological cure. Patient 10 had human immunodeficiency virus (HIV) and osteomyelitis of the first lumbar vertebra with an associated recurrent left psoas abscess. He was first diagnosed with a psoas abscess in 2008 that had extended from his vertebral osteomyelitis, which was treated intravenously and then orally with antibiotics at an outside hospital, but the exact treatment regimen is unknown. In December 2010, he presented to another VA hospital with recurrent left psoas abscess ($2.9 \times 3.6 \times 14$ cm in size). He was treated with percutaneous drainage with cultures positive for MRSA. The drain was removed after 2 weeks when computed tomography (CT) of the abdomen showed decreased size of abscess to 0.6 cm $\times$ 1 cm. He was treated with 4 weeks of vancomycin followed by oral clindamycin suppression (switched after 3 weeks to co-trimoxazole for 4 additional weeks because of rash that was attributed to clindamycin). In April 2011, he presented to our hospital with left flank pain and was found to have a left psoas abscess ($6 \times 4.2$ cm in maximal dimension on CT scan). He was empirically started on vancomycin, piperacillin-ticarcillin, and clindamycin by the admitting physician before being switched to ceftaroline on day 3 by the Infectious Diseases consult team. His abscess was drained at day 1 with cultures positive for MRSA. We consider him a vancomycin failure based on the recurrence of his abscess despite his prior long course of vancomycin and drainage of the abscess. During this admission, he was treated with ceftaroline for 6 weeks and achieved both microbiological and clinical cure with no recurrence on imaging 7 and 10 months later.

## Discussion

Some MRSA infections, especially endocarditis, are difficult to treat with currently available antibiotics. Ceftaroline is a promising new option for the treatment of MRSA endocarditis, complex bacteremias, and other deep-seated infections. The FDA-approved dosing for ABSSSI is 400–600 mg q12 h, but more severe infections and bone and joint infections may warrant higher doses and longer treatment durations. The efficacy of the drug directly correlates to the percentage of time serum drug concentration is greater than MIC ($\%T >$ MIC); $\%T >$ MIC for stasis, 1 log kill, and 2 log kill against *S. aureus* is 26 %, 33 %, and 45 %, respectively [13]. We aimed to exceed the minimal bactericidal concentration (MBC) for 80 % of the day by using q8 h dosing because the half-life is reported to be only 1.6 h after 1 dose and 2.7 h after 28 doses [12]. All our patient isolates had MICs $\leq$0.5 mg/l by *E* test, except for patient 10 who had an MIC of 0.75 mg/l but nevertheless cleared his bacteremia after 6 days of ceftaroline. The FDA has currently suggested a MIC $\leq$1 as susceptible for MRSA isolates in skin only [14]. Recommendations on breakpoints for deeper infections are not yet available, but a large study of in vitro susceptibility of 2,988 MRSA isolates showed that ceftaroline was active against all but 4 with an MIC of $\leq$1 mg/l. Four genetically related isolates (0.13 %) from a single center had MIC >2 mg/l, suggesting a small nosocomial outbreak [15].

As a cephalosporin, ceftaroline has a good safety profile without the serious toxicities that can be seen with other anti-MRSA antibiotics. The major adverse drug reactions that we observed were rash, and such led to early termination of ceftaroline. However, three patients developed *Clostridium difficile* infection.

In summary, although this series is small and uncontrolled, ceftaroline was effective and well tolerated in most cases. This series suggests the potential of ceftaroline for treating MRSA bacteremia, endocarditis, and other deep-seated infections. We think that large prospective trials are indicated to establish the role of ceftaroline in treatment of severe MRSA infections and to establish the optimal dose and duration of therapy.

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