

Two cases of refractory methicillin-susceptible staphylococcus aureus endocarditis responsive to ertapenem

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Persistent methicillin-sensitive staphylococcus aureus (MSSA) bacteremia is usually defined as persistent bacteremia despite 7 days of appropriate antibiotic therapy. While nafcillin, cefazolin, or oxacillin are excellent antimicrobial options, persistent MSSA is a commonly encountered phenomenon in clinical practice for which further guidelines on appropriate management are necessitated. Here we highlight two cases of MSSA bacteremia requiring salvage therapy with ertapenem.

CASE 1

A 63-year-old female with a history of sickle cell disease and prior placement of a port for intravenous access, presented with complaints of fever, significant malaise, and purulent drainage from her port for the past 7 days. She initially required intensive care for septic shock on presentation, requiring inotropic support, initiation of broad-spectrum vancomycin and cefepime, and endotracheal intubation for airway protection.

A computed tomography (CT) of the lungs revealed evidence of multifocal pneumonia. Due to concern for catheter-related bloodstream infection (CRBSI), she underwent immediate port removal. Subsequent investigations with blood, urine, and port-tip cultures revealed MSSA, with transthoracic echocardiography confirming the presence of a 0.7 cm vegetation over the aortic valve consistent with aortic valve endocarditis. Given the sensitivity to methicillin, antibiotics were de-escalated to nafcillin 12 g over 24 h. Despite remaining on nafcillin for 6 days, her subsequent blood cultures still remained positive for MSSA on 3 subsequent blood

cultures taken 48 h apart. Due to worsening leukocytosis, hypotension, and persistent bacteremia, the decision was made to initiate salvage therapy with the addition of ertapenem 1 g daily. Her subsequent pair of blood cultures, taken 6 h following initiation of ertapenem, was noted to be negative, with a subsequent blood culture 48 h thereafter remaining negative. She had a relatively uncomplicated course thereafter, successfully completing 8 weeks of therapy with cefazolin and ertapenem with no further complications and resolution of her aortic valve vegetation.

CASE 2

A 74-year-old male with a prior medical history of type 2 diabetes mellitus presented with complaints of fever and malaise for the past 3 days. On initial evaluation, he was hypotensive requiring initiation of inotropic support and intravenous fluid. Further evaluation with a CT chest revealed evidence of multiple cavitory lesions raising concern for septic emboli. A presumptive diagnosis of septic shock was made, and the patient was immediately started on vancomycin and piperacillin-tazobactam.

Subsequently obtained blood cultures revealed evidence of MSSA, with transthoracic echocardiography revealing an 8mm mitral valve vegetation, and a 5 mm pulmonic valve vegetation. A diagnosis of infective endocarditis was made and antibiotic coverage was de-escalated to nafcillin monotherapy at 12 g over 24 h. Cardiothoracic surgery was consulted with a plan for continued intravenous antibiotic therapy at that time. Serial blood cultures obtained at 48 h and 96 h of antibiotic therapy remain-

ned positive for MSSA. Given persistent bacteremia, the decision was made to initiate salvage therapy with ertapenem 1g daily. The subsequent pair of blood cultures taken 8 h following ertapenem initiation were negative. The patient gradually had improvement in leukocytosis, and symptoms of malaise and had an uneventful subsequent hospital course with the completion of 8 weeks of ertapenem and cefazolin. Subsequent transthoracic echocardiography revealed complete resolution of mitral and pulmonic valve vegetations, with mild residual stenosis of both valves.

While staphylococcus aureus is the most common bacteria implicated in acute bacterial endocarditis, it is prudent for physicians to be aware that MSSA far more commonly is associated with community acquired infective endocarditis than is methicillin-resistant staphylococcus aureus (MRSA).^[1] MSSA endocarditis in itself has a high morbidity and mortality if it is not detected at an early stage, with persistent MSSA conferring an even higher mortality index.^[2] While methicillin-resistance is typically perceived as a poor prognostic factor for staphylococcus aureus endocarditis, there is in fact no statistically significant difference between mortality between both MSSA and MRSA in endocarditis.^[3] MSSA is typically managed with either oxacillin, nafcillin or cefazolin monotherapy, with the former two being preferred due to a higher potency, microbial clearance rates, and an increased likelihood of cefazolin failure due to the inoculum effect.^[4] While much attention has been addressed towards refractory MRSA bacteremia in patients with endocarditis, the data for persistent MSSA bacteremia is certainly more scarce. While some modest data exists on salvage therapy with rifampin and short course daptomycin for MRSA endocarditis, there exists no benefit for rifampin in MSSA endocarditis, and daptomycin has been shown to only show mild benefit for right-sided endocarditis.^[4]

Due to the increased mortality conferred by persistent MSSA, we believe physicians should first consider a lower threshold for the consideration of treatment failure by 2–4 days. While cefazolin and nafcillin/oxacillin are both appropriate initial choices for MSSA bacteremia, our case highlights the rapid microbial clearance induced with the addition of ertapenem. Ertapenem and cefazolin are believed

to have a synergistic effect leading to interleukin 1-beta production that is believed to augment the inflammatory response.^[3,5,6,7] This production of interleukin 1-beta is believed to be driven mostly by ertapenem, highlighting a potential immunomodulatory role for this antibiotic in MSSA endocarditis. Further studies are needed on the synergistic effects of ertapenem on nafcillin/oxacillin, however the immunomodulatory properties of ertapenem likely persist and will sustain this benefit. In our report, we aim to highlight two separate cases showing the importance of the addition of ertapenem for MSSA salvage therapy. We therefore propose that patients who present in septic shock on arrival may benefit from the immediate initiation of dual MSSA therapy with ertapenem and either an anti-staphylococcal penicillin, or cefazolin based on a higher likelihood of persistent MSSA bacteremia. Furthermore, early initiation of ertapenem following the first persistently positive blood culture needs to be investigated as the standard of practice for refractory MSSA bacteremia. We postulate that for patients with concomitant pseudomonas bacteremia, meropenem instead of ertapenem will have an equal, but efficacious effect for management persistent MSSA bacteremia.

This report serves to highlight an effective antimicrobial option of ertapenem for the therapy of persistent MSSA bacteremia in elderly patients with endocarditis, who otherwise may not tolerate surgical management, and is a viable future area of investigation.

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