Combination Therapy With Vancomycin and Ceftaroline for Refractory Methicillin-resistant *Staphylococcus aureus* Bacteremia: A Case Series

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ABSTRACT

Purpose: Although vancomycin has been the mainstay of therapy for methicillin-resistant *Staphylococcus aureus* (MRSA) infections, its effectiveness has been challenged. Combination therapy may be used for patients with persistent MRSA bacteremia refractory to initial therapy. Studies have reported in vitro synergy between vancomycin and ceftaroline; however, clinical experience with this therapy is limited. Here, we report our experience with 5 cases of vancomycin-refractory MRSA bacteremia treated with the combination of vancomycin and ceftaroline.

Methods: Between January 2014 and August 2016, 5 patients were identified who received vancomycin and ceftaroline combination therapy due to persistent bacteremia or deterioration of their clinical status on vancomycin alone (despite a vancomycin MIC within the susceptible range).

Findings: Five patients presented with MRSA bacteremia secondary to endocarditis (n = 2), epidural abscess (n = 2), or left iliopsoas abscess (n = 1). Four of the 5 patients experienced microbiologic cure, and 1 patient transitioned to palliative care.

Implications: This case series serves to describe additional clinical experience with vancomycin and ceftaroline combination therapy. This combination may be considered when vancomycin monotherapy does not lead to microbiological and/or clinical improvement in patients with metastatic MRSA bacteremia. Additional studies are warranted to further define its role in salvage therapy for persistent MRSA bacteremia. (*Clin Ther*. 2017;39:212–218)

Key words: bacteremia, ceftaroline, MRSA, *Staphylococcus aureus*, synergy, vancomycin.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections pose a substantial clinical and economic burden on the health care system. Although vancomycin has been the mainstay of therapy for decades, its effectiveness has been challenged.[1–4] For MRSA infections, treatment failure with vancomycin was reported for isolates within the susceptible range (MIC ≤ 2 μg/mL).[5–7] Alternatives to vancomycin such as linezolid, daptomycin, and ceftaroline have indicated noninferiority to vancomycin for the treatment of MRSA infections, but none have established superiority.[8,9] In addition, MRSA isolates with increased vancomycin MICs were correlated with reduced daptomycin susceptibility, and exposure to vancomycin can select for higher daptomycin MICs.[10–12] For cases of persistent MRSA bacteremia or vancomycin-intermediate *S aureus* (VISA) infections combination antibiotic therapy may be an option. In vitro studies have reported synergy between vancomycin and ceftaroline that may be greater than other β-lactam antibiotics.[13,14]

Ceftaroline is an attractive option for combination therapy because it possesses anti-MRSA activity, may enhance neutrophil killing, and may reduce bacterial virulence, even in subinhibitory ceftaroline concentrations.[14–17] Notably, evidence suggests that

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vancomycin and ceftaroline possess greater bactericidal activity than ceftaroline alone, the combination of either vancomycin and oxacillin, or daptomycin and ceftaroline.[13,17] To date, only one case report describing vancomycin and ceftaroline combination therapy for MRSA bacteremia has been published.[17] Here, we report our experience with 5 cases of vancomycin-refractory MRSA bacteremia treated with the combination of vancomycin and ceftaroline. (Figure 1)

Case 1

A 66-year-old woman presented with 4 days of lower back pain and bilateral lower extremity radiculopathy. She required emergent surgical decompression after a magnetic resonance image (MRI) revealed cauda equina syndrome with an L3 sacral epidural abscess. Blood tests revealed leukocytosis (22.7×10^9 cells/L). Four blood cultures and the epidural abscess fluid culture grew MRSA. Vancomycin 1000 mg (15 mg/kg) every 12 hours was initiated (trough concentration range, 13–15 μg/mL). Repeat blood cultures drawn daily until hospital day 9 continued to be positive for MRSA (MIC ≤ 0.5 μg/mL days 1–5, 1 μg/mL days 6–9). (Table 1)

On day 10, ceftaroline 600 mg IV every 8 hours (E-test MIC = 0.38 μg/mL) was added, and a repeat blood culture drawn in less than 24 hours was negative for growth. Vancomycin was stopped on hospital day 22 because of worsening renal function, and the patient was discharged the same day. The patient had received the combination vancomycin and ceftaroline for 13 days, and ceftaroline monotherapy was continued for 14 days after discharge. At 2-week follow-up to the infectious disease clinic, the patient had completed therapy and was free of bacteremia.

Case 2

A 42-year-old man with a past medical history of IV drug use presented with chest pain, back pain, and

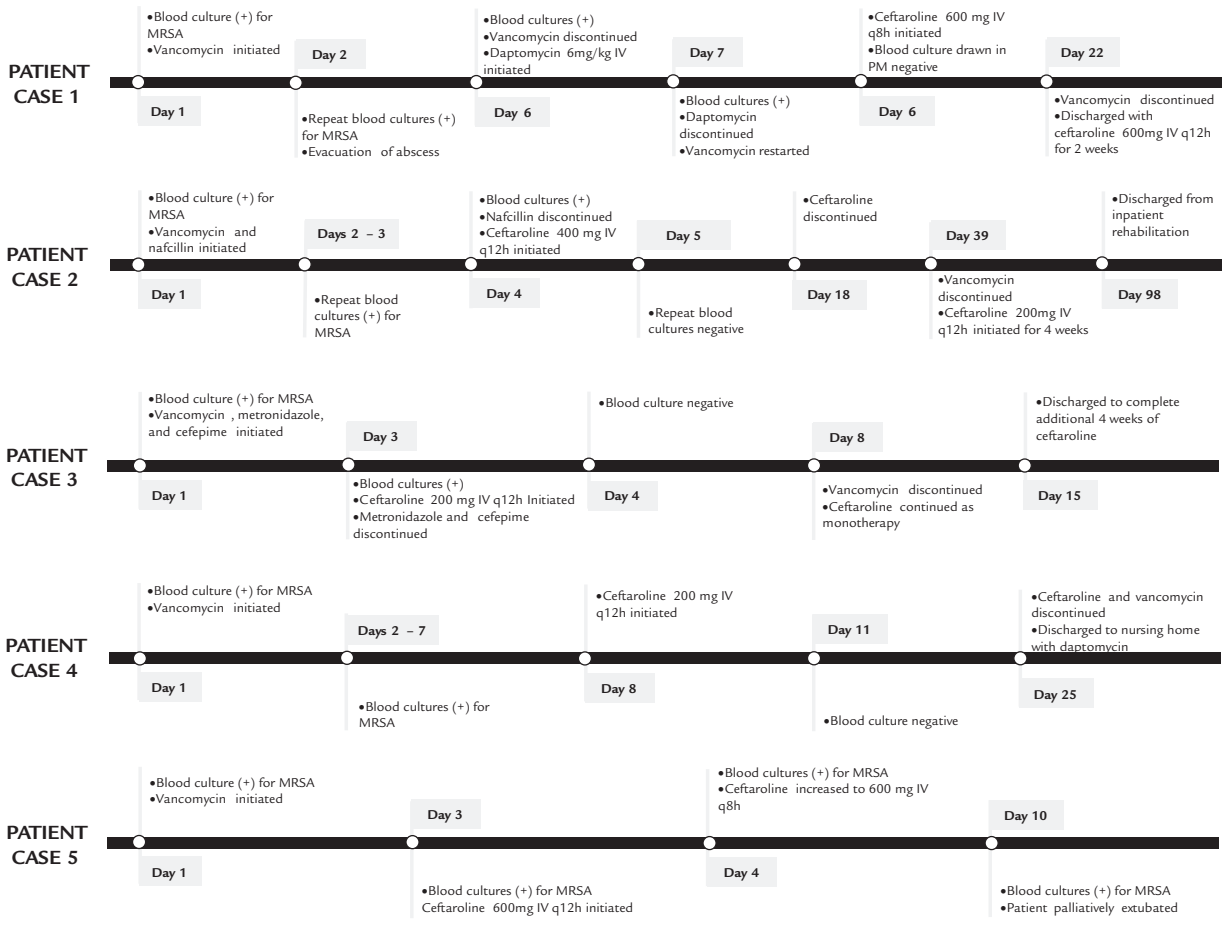

Figure 1. Timeline of hospital course.