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LETTER TO THE EDITOR

Salvage therapy with intravenous fosfomycin plus ceftriaxone for necrotizing fasciitis caused by penicillin-nonsusceptible *Streptococcus pneumoniae*

KEYWORDS
ceftriaxone;
fosfomycin;
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To the Editor,

Necrotizing fasciitis (NF) is rarely caused by *Streptococcus pneumoniae*, and is associated with high morbidity and mortality. Herein, we describe a diabetic patient who presented with NF of an upper extremity and from whom *S. pneumoniae* was isolated via pus and blood; the clinical condition responded to surgery and antibiotic combinations of ceftriaxone and fosfomycin.

A 62-year-old diabetic man presented with progressively painful swelling of his left shoulder and the upper arm for 7 days. One week before admission, he had fallen on his left shoulder, and received an intramuscular injection of ibuprofen for pain relief. On admission, he was afebrile (35.5°C), with a pulse rate of 70 beats/min, blood pressure of 94/79 mmHg, and respiratory rate of 20 breaths/min. Upon examination, his left shoulder and upper arm was warm, erythematic and painful, with ruptured bullae and thin skin covering the left shoulder. Laboratory studies showed a white blood cell count of 52,700/mm^3, and creatinine of 3.7 mg/dL. The diagnosis of NF of the left shoulder and upper arm was made. Intravenous ceftazidime (1 g every 8 hours) and minocycline (200 mg loading dose and 100 mg every 12 hours) were administered. Then he immediately received debridement and fasciotomy of the shoulder and upper arm. A Gram stain of pus revealed encapsulated Gram-positive diplococci. The empiric antibiotics were shifted to ceftriaxone (1 g every 12 h) and fosfomycin (2 g every 6 hours), and this combination therapy was used for a total of 14 days. The culture of blood and tissue were all positive for *S. pneumoniae*. Antibiotic susceptibility testing of the isolate exhibited minimal inhibitory concentration (MIC) to penicillin of 4.0 μg/mL; ceftriaxone, 0.5 μg/mL; fosfomycin, 4.0 μg/mL; and vancomycin, 1 μg/mL. The *S. pneumoniae* isolate belonged to serotype 23F, which was determined by latex agglutination (Pneumotest-Latex; Statens Serum Institut, Copenhagen, Denmark). The patient's NF was improved with ceftriaxone/fosfomycin combination therapy and a total of four surgical debridement sessions.

NF is not uncommon in Taiwan but is rarely caused by *S. pneumoniae*. The majority of the reported cases had underlying immunocompromising conditions, such as diabetes mellitus, recent use of nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol abuse, liver cirrhosis, postrenal transplantation status, rheumatoid arthritis with immunosuppressant use, systemic lupus erythematosus with immunosuppressant use, and cardiovascular disease.[1–5] In this case, the patient had two predisposing factors, diabetes mellitus and recent NSAID use.

The antibiotic regimens for streptococcal NF in previously reported articles were diverse.[1–5] In this study, we performed time-killing studies to evaluate the antibacterial effect of combination regimens with fosfomycin and ceftriaxone. The MIC of fosfomycin was assessed by E test, and ceftriaxone was by microbroth dilution. The combination of 2× MICs of both fosfomycin and ceftriaxone led to a >100-

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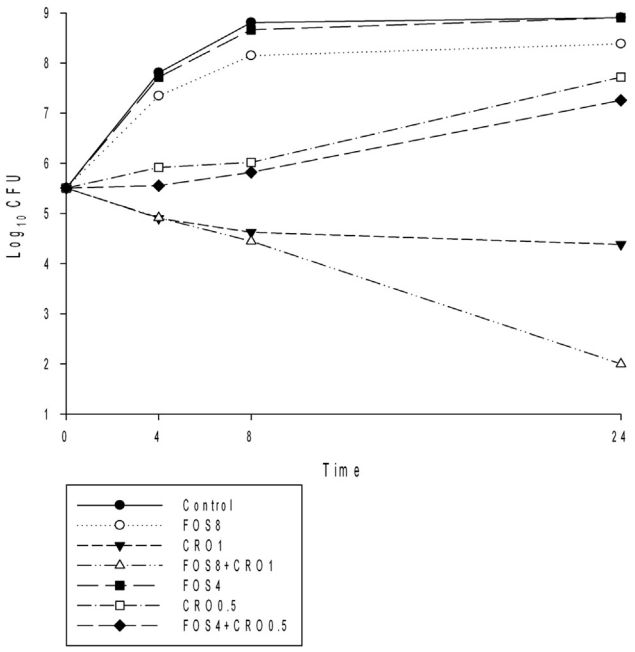

Figure 1. Time-killing curves for 2 × 10^5 CFU/mL *Streptococcus pneumoniae* cocultivated with 1× and/or 2× MIC of ceftriaxone alone or in combination with 1× and/or 2× MIC of fosfomycin for 24 hours. CFU = colony-forming unit; MIC = minimal inhibitory concentration.

fold decrease in CFU/mL compared with either monotherapy with 2× or 1× MIC of fosfomycin or ceftriaxone or a combination of both 1× MIC fosfomycin and ceftriaxone. Therefore, the synergistic effect of combination of fosfomycin and ceftriaxone was observed (Fig. 1).

In conclusion, NF can be caused by penicillin nonsusceptible serotype 23F *S. pneumoniae* in immunocompromised hosts; however, surgical intervention with antibiotic combination therapy of fosfomycin and ceftriaxone can be one of treatment choice.

Conflicts of interest

None to declare.

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