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CASE REPORT

Tigecycline therapy for bacteremia and aortitis caused by *Salmonella enterica* serotype Choleraesuis: A case report

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Non-typhoid *Salmonella* species represent a significant cause of aortitis. Few antimicrobial agents can be used when the patient is allergic or intolerable to cephalosporins or fluoroquinolones. Here, we report a case of bacteremia and aortitis caused by *Salmonella enterica* serotype Choleraesuis. This patient was cured by initial parenteral tigecycline and subsequent oral ciprofloxacin without surgical intervention.

Introduction

Non-typhoid *Salmonella* species are important human food-borne pathogens and can cause extra-intestinal infections, such as bacteremia, septic arthritis, osteomyelitis and mycotic aneurysms.[1] Ampicillin, trimethoprim-sulfamethoxazole, chloramphenicol, ceftriaxone and ciprofloxacin have been reported to be active *in vitro* and *in vivo* against *Salmonella* species.[2] In developed countries, there is increasing resistance to third-generation cephalosporins and fluoroquinolones among non-typhoid *Salmonella* isolates,[3] thereby making the selection of appropriate antimicrobial therapy more difficult. Most antibiotics that are active *in vitro* cannot cure *Salmonella* infections, due to poor intracellular penetration.[2] New antibiotics like tigecycline that possess good extracellular and intracellular antibacterial activity against *Salmonella* isolates are urgently needed.[4—7]

Tigecycline has been reported to be active *in vitro* against *Salmonella* species and to reach significant

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intracellular concentrations.[4–6] A recent study comparing the *in vitro* and *in vivo* intracellular killing effects of tigecycline with those of ceftriaxone against clinical non-typhoid *Salmonella* isolates has been published.[7] Tigecycline exhibited sustained intracellular killing activity and resulted in better survival rates of mice with peritonitis due to multidrug-resistant *Salmonella* isolates when compared to ceftriaxone, suggesting a potential use of tigecycline for human systemic *Salmonella* infections. However, pharmacokinetic evaluations of the parenteral administration of tigecycline demonstrated low serum levels which were regarded as insufficient to exhibit bactericidal activity against intracellular pathogens.[8,9] Here, we present a case of Salmonella enterica serotype Choleraesuis *(S* Choleraesuis) bacteremia and infective aortitis which were cured by initial parenteral tigecycline and subsequent long-term oral ciprofloxacin therapy without surgical intervention.

Case report

A 65-year old, non-insulin-dependent retired farmer was hospitalized because of fever and chills for more than two weeks. He had a body weight of 60 kg and was well until 3 days prior to admission to a regional hospital. Parenteral cefazolin was ineffective and intermittent fever persisted. A general skin rash over the limbs and trunk and mild dyspnea developed under cefazolin therapy. Blood cultures grew *S* Choleraesuis resistant to ampicillin, chloramphenicol, and trimethoprim/sulfamethoxazole, but susceptible to ceftriaxone and ciprofloxacin. Abdominal pain radiating to the back and tenderness over the lower abdomen were reported by the patient. An abdominal computed tomography (CT) scan disclosed infrarenal infective aortitis, a paraaortic abscess and a suspected mycotic aneurysm (Fig. 1A). Pus obtained by CT-guided percutaneous aspiration of the paraaortic abscess grew *S* Choleraesuis with the same antibiogram as the blood isolate. Based on the suspicion of a probable *Salmonella* mycotic aneurysm, the patient was transferred to the emergency department (ED) of a medical center for further evaluation and management.

After admission, a chest film showed increased patchy density over the bilateral lower lungs. Laboratory studies revealed leukocytosis (17,500 cells/μL), bandemia, a high serum level of C-reactive protein (CRP, 150 mg/L) and a high erythrocyte sedimentation rate (ESR, 120 mm/h). Ciprofloxacin was prescribed, due to a suspected allergy to cephalosporins. However, severe abdominal cramping and discomfort occurred during the first infusion of ciprofloxacin. Therefore, tigecycline was administered parenterally at a loading dose of 100 mg and subsequently 50 mg every 12 hours. Because of exacerbated back pain, a spinal magnetic resonance imaging scan was performed. The images revealed a soft-tissue mass surrounding the aorta at the levels of T10-L1, lumbar spondylosis with L4-L5 disc protrusion and moderate spinal stenosis. Conservative medical treatment was suggested by the cardiovascular surgeon.

Blood cultures collected at the ED still grew *S* Choleraesuis. The minimal inhibitory concentration (MIC) of tigecycline, as determined by the broth microdilution method, was 0.5 μg/mL. The patient's fever abated and his clinical symptoms resolved. Blood cultures after 5 days of tigecycline therapy were negative for growth and tigecycline treatment was continued for 28 days. The CT scan after one month of tigecycline therapy showed obvious shrinkage of the paraaortic abscess (Fig. 1B). Thereafter, oral ciprofloxacin at a dose of 500 mg was given every 12 hours and was tolerated well. After long-term antimicrobial therapy for four months, an abdominal CT scan revealed minimal fatty strands at the level of the infrarenal aorta (Fig. 1C). Follow-up serum studies disclosed normalization of serum CRP and ESR values.

Discussion

A review of the literature revealed that overall mortality from aortitis caused by *Salmonella* can be as high as 60%. Of patients treated non-surgically, 96% would die while 63% of patients managed by a combined medical and surgical approach would survive.[10] This highlights the essential role of surgical interventions for source control in infected aortitis. Traditionally, ceftriaxone and ciprofloxacin are the standard regimens for the treatment of *Salmonella* infections.[3,7] There has been at least one report indicative of increasing fluoroquinolone resistance in bacteremic isolates

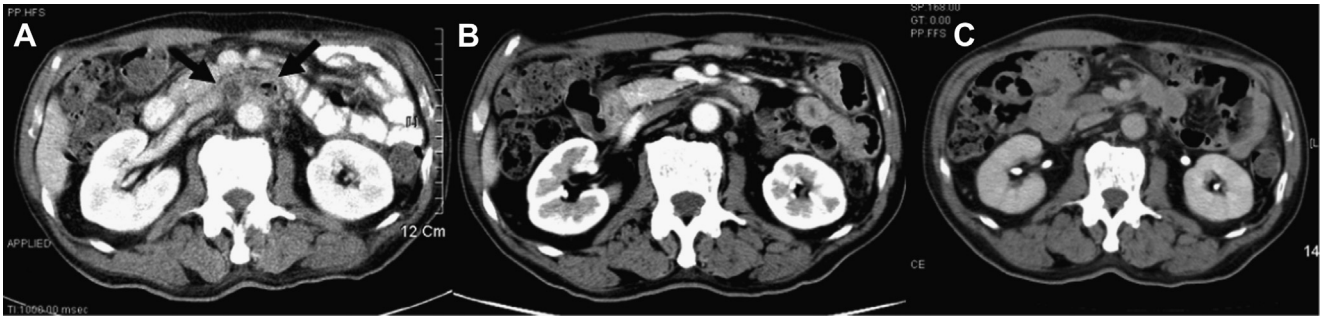

Figure 1. (A) A computed tomography scan with contrast enhancement revealed a mild irregular contour with wall thickening in the infrarenal abdominal aorta measuring 2.8 cm × 3.0 cm in size with surrounding amorphous-enhanced soft-tissue mass at levels T10-L1 (arrows). These characteristics are compatible with a paraaortic abscess and infective aortitis, as well as a suspected mycotic aneurysm. After tigecycline therapy for one month (B) and oral ciprofloxacin therapy for four months (C), there were minimal fatty strands at the infra-renal portion of the abdominal aorta. No additional Paraaortic abscess was found.

of S Choleraesuis in southern Taiwan.[11] In this case, cephalosporin allergy and gastrointestinal intolerance to ciprofloxacin prohibited their use. Imipenem reportedly cured two adults with relapsing infections due to ciprofloxacin-resistant and cefotaxime-resistant *Salmonella* isolates,[12,13] and may represent one of the treatment alternatives for human *Salmonella* infections. However, there is a lack of *ex vivo* or animal data supporting the use of carbapenem therapy for invasive *Salmonella* infections. In such a clinical setting, tigecycline, which is a glycylcycline that is effective *in vitro* with good tissue penetration, is a potential choice for the treatment of invasive human *Salmonella* infections.[4,7] Tigecycline uptake is rapid and yields high concentrations within polymorphic neutrophils and intracellular drug concentration is 20—30 times higher than extracellular concentration.[6] However, the use of tigecycline to treat bacteremia is questionable for patients in whom the MICs of the causative pathogen approach known serum tigecycline concentrations.[14]

In a recent review, tigecycline was demonstrated to be effective, safe and well tolerated in the treatment of secondary bacteremia associated with complicated intra-abdominal infections, skin and soft-tissue infections, and community-acquired pneumonia. The reported cure rates were similar to those observed for comparative standard therapy.[15] Lefort et al.[16] reported the potential of tigecycline therapy in a rabbit model of enterococcal endocarditis but there is no prior clinical experience with using tigecycline for the treatment of vascular infections or bacteremia caused by *Salmonella*. This is the first case of *Salmonella* bacteremia with aortitis to be successfully managed by initial tigecycline therapy and subsequent ciprofloxacin therapy without surgical intervention. Although the potential limitations of tigecycline therapy in treating bloodstream infections must be considered, the maximum serum level following a standard dosing of tigecycline in healthy subjects was 0.82 μg/mL, which was higher than the tigecycline MIC of the etiological isolate.[5]

In conclusion, our clinical experience indicates that tigecycline may be an effective treatment for bacteremia and vascular infections caused by S Choleraesuis.

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