

Outpatient Parenteral Antimicrobial Therapy With Ceftolozane/Tazobactam via Continuous Infusion for Multidrug-Resistant *Pseudomonas aeruginosa* Osteomyelitis

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We present a case of *Pseudomonas aeruginosa* osteomyelitis treated with surgery and antibiotic therapy with ceftolozane-tazobactam in continuous infusion at home using an elastomeric pump. We discuss the use of ceftolozane-tazobactam in continuous infusion administered at home as an effective alternative for the treatment of multidrug-resistant *Pseudomonas aeruginosa* osteomyelitis.

Keywords. ceftolozane-tazobactam; continuous infusion; elastomeric pumps; multidrug resistant; osteomyelitis; *Pseudomonas aeruginosa*.

Multidrug-resistant *Pseudomonas aeruginosa* infections are a growing problem. In many cases, it is essential to use the parenteral route for antibiotic treatment. Outpatient parenteral antimicrobial treatment (OPAT) is an alternative for these infections but generally requires several injections per day, and elastomeric pumps are a good alternative. In reference to an article published in your journal recently by Jones, Huelfer, and Bland [1], we present a case of *Pseudomonas aeruginosa* osteomyelitis treated with surgery and antibiotic therapy with ceftolozane-tazobactam in continuous infusion at home using an elastomeric pump.

CASE REPORT

An 88-year-old woman with a history of obesity, type 2 diabetes mellitus, and peripheral vascular disease presented with an ulcer on the fourth right toe with unfavorable evolution despite local cures and treatment with amoxicillin clavulanate. Surgical intervention was performed with closed transphalangeal amputation of the fourth toe. During follow-up, the surgical wound presented purulent exudate with erythema, edema, and local heat extended to the thigh accompanied by fever. On physical examination,

the patient's blood pressure was 140/80 mmHg, heart rate was 85 bpm, and temperature was 37.8°C. *Pseudomonas aeruginosa* nonsusceptible to all antibiotics except amikacin (minimal inhibitory concentration [MIC], 4 µg/mL), colistin (MIC, <0.5 µg/mL), and ceftolozane-tazobactam (MIC, 1 µg/mL) was isolated in wound exudate culture (antimicrobial susceptibility results are summarized in Table 1). The VITEK 2 automatic system was used for microorganism identification and susceptibility testing. Right foot magnetic resonance imaging showed a marked increase in fluid-sensitive sequences in intraosseous signal in the remnant of the proximal phalanx of the fourth toe and in the head of the fourth metatarsal, which extended to the diaphysis with joint effusion in relation to septic arthritis and osteomyelitis. Antibiotic therapy with ceftolozane-tazobactam was started with 1 bolus of 1000 mg/500 mg followed by continuous infusion (1500 mg ceftolozane and 750 mg tazobactam per day, adjusted according to renal function: glomerular filtration rate 40 mL/min) using an elastomeric pump with a volume of 240 mL and a flow rate of 10 mL per hour in the outpatient setting. Change of the pump was carried out at the patient's home by a nurse from the Hospital at Home Department. Local cures were also performed with povidone-iodine and topical colistin. The patient presented improvement with resolution of erythema, edema, and local heat in the right lower limb and disappearance of the purulent exudate. Surgical cleaning was performed with exeresis of the remnant bone of the fourth proximal phalanx and head of the metatarsal. In intraoperative cultures *Pseudomonas aeruginosa* was isolated with the same sensitivity pattern. Antibiotic treatment was administered for 4 weeks before surgery and 2 weeks after it. The patient had no adverse effects. The evolution was favorable, without inflammatory signs in the surgical wound and with adequate ambulation.

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Table 1. Antimicrobial Susceptibility Results

Antibiotic	MIC, µg/mL
Ceftolozane-tazobactam	1
Piperacillin-tazobactam	≥128
Aztreonam	16
Cefepime	8
Ceftazidime	16
Ciprofloxacin	≥4
Colistin	≤0.5
Imipenem	≥16
Meropenem	8
Amikacin	4
Tobramycin	≥16
Gentamicin	≥16

Abbreviation: MIC, minimal inhibitory concentration.

DISCUSSION

Pseudomonas aeruginosa is a nonfermenting gram-negative bacillus with intrinsic resistance to several antibiotics and develops acquired resistance frequently. About 14% of the isolates of *Pseudomonas aeruginosa* in the United States are multiresistant [2]. In Europe, 30.8% of *Pseudomonas aeruginosa* isolates were resistant to at least 1 antibiotic in 2017. Resistance to 2 or more antimicrobial groups was 18.3%, and resistance to 3 or more antimicrobial groups was 13.3% [3]. In this situation, it becomes necessary to develop new antibiotics. Ceftolozane-tazobactam is the combination of a potent antipseudomonal beta-lactam and a beta-lactamase inhibitor. This combination maintains good activity against *Pseudomonas aeruginosa* despite being resistant to other antibiotics. It is approved for use in intraabdominal infection and urinary infection at a dose of 1.5 g every 8 hours [4, 5] and in hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia at a dose of 3 g every 8 hours [6]. In the literature, a case series included 4 patients with multidrug-resistant *Pseudomonas aeruginosa* osteomyelitis treated with ceftolozane-tazobactam. Two patients were disease-free 6 months after therapy was discontinued, 1 required an additional curative surgical procedure, and another developed an adverse reaction that was probably related to the antibiotic [7]. Another case series included 4 patients with osteomyelitis and 3 with skin and soft tissue infection caused by extensively drug-resistant *Pseudomonas aeruginosa*. Six patients (85.7%) achieved clinical cure, and 1 developed infection recurrence [8].

There are 2 other published cases of multidrug-resistant *Pseudomonas aeruginosa* osteomyelitis treated with ceftolozane-tazobactam successfully [9, 10].

Ceftolozane-tazobactam can be administered in continuous infusion, and it is stable for up to 24 hours at room temperature, allowing for potential administration as a continuous infusion by elastomeric pumps. In a study published recently, 7 patients were treated with ceftolozane-tazobactam in continuous infusion in the outpatient setting, and 6 of 7 patients had symptom resolution [1].

In summary, ceftolozane-tazobactam in continuous infusion administered at home could be an effective alternative for the treatment of multidrug-resistant *Pseudomonas aeruginosa* osteomyelitis.

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Patient consent. Patient consent was obtained. The work has been approved, and it conforms to ethical standards.

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