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# Successful treatment of *Pseudomonas aeruginosa* osteomyelitis with antibiotic monotherapy of limited duration

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## KEYWORDS

*Pseudomonas aeruginosa*;  
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**Summary** *Objectives:* The aim of this study was to present a 15-year experience and provide a comprehensive analysis of a large cohort of patients with *Pseudomonas aeruginosa* osteomyelitis. *Methods:* We reviewed the medical records of patients admitted to a large French university hospital for *P. aeruginosa* osteomyelitis over a 15-year period. Patient outcome was assessed at follow-up after at least six months.

*Results:* Sixty-seven patients were included, comprising 57% with chronic osteomyelitis. Polymicrobial infection was predominant (63%), and an infected device was involved in 39% patients. The overall treatment success rate was 79.1%. All but one patient were treated with a combination of surgery and antibiotic therapy. The antibiotic treatment had a mean duration of 45 days (range, 21–90 days). Single-antibiotic therapy was preferred in nearly all cases. Treatment failure was reported for 14 (21%) patients and was due to the persistence of *P. aeruginosa* in four cases. No significant risk factor for treatment failure was identified, especially when treatment strategies were compared.

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**Conclusions:** We advocate optimal surgical debridement combined with initial parenteral antibiotics for a maximum of 15 days, followed by an oral fluoroquinolone. Total treatment duration should not exceed six weeks, and antibiotic treatment with two-drug combinations does not seem necessary.

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## Introduction

Osteomyelitis remains a major therapeutic challenge, and chronic osteomyelitis which persists for several weeks is often associated with a high rate of relapse despite apparently successful treatment. Relapses may prompt clinicians to use prolonged and multiple antibiotic therapies,<sup>1,2</sup> which may promote the spread of multidrug-resistant (MDR) bacteria, especially in the case of Gram-negative bacilli.<sup>3,4</sup> Prolonged treatment may also trigger side effects, e.g. the ototoxicity and nephrotoxicity of aminoglycosides.<sup>5</sup>

*Pseudomonas aeruginosa* is an under-reported pathogen in osteomyelitis.<sup>6–8</sup> It was found to be involved in only 3.6% cases of osteoarticular infections in a French study<sup>9</sup> and most studies focusing on *P. aeruginosa* osteomyelitis are limited to small case series<sup>1,2,10–21</sup> and individual case reports. These studies present heterogeneous data and often provide only few details regarding the duration of infection, the presence of prostheses or internal devices, the initial surgical treatment or the antimicrobial susceptibility test results. They also provide insufficient follow-up data in most cases. Although rare, *P. aeruginosa* osteomyelitis is of particular concern because of the natural antibiotic resistance profile of the causative pathogen<sup>22</sup> and its ability to develop additional resistance during the course of antibiotic treatment.<sup>4,22,23</sup> *P. aeruginosa* bone infection might be associated with a greater risk of treatment failure,<sup>6,21,24</sup> as well as higher recurrence and amputation rates, resulting in a poorer prognosis than infections caused by other bacteria.<sup>6,25</sup> Tice et al. report a significantly higher (more than a two-fold) rate of recurrence for *P. aeruginosa* as compared to *Staphylococcus aureus* osteomyelitis.<sup>25</sup> Similarly, Seghrouchni et al. reported a tendency (although nonsignificant) to lower remission rates for *P. aeruginosa* as compared to *S. aureus*-infected patients (60% vs 79%).<sup>26</sup> These observations might encourage antibiotic treatment of *P. aeruginosa* osteomyelitis with two-drug combinations.<sup>2,14</sup>

In this retrospective cohort study we present our 15-year experience and provide a comprehensive analysis of a large cohort of patients with *P. aeruginosa* osteomyelitis. We advocate single-drug antibiotic therapy for six weeks, which we consider to be efficient, with early change to oral antibiotics whenever possible.

## Patients and methods

### Study design and patient population

This study was conducted in an 830-bed teaching hospital in Paris, France. All patients whose bone biopsies were positive for *P. aeruginosa* between January, 2000 and April,

2015 were identified using the laboratory middleware system (SirWeb; i2a, Pérols Cedex, France). Databases containing prospectively registered clinical information and microbiological data were reviewed using a patient information system (DxCare; Medasys, Gif sur Yvette, France). Patients who presented with mono- or poly-microbial *P. aeruginosa* osteomyelitis were included in this study. Exclusion criteria were age under 18, pregnancy, uncertain diagnosis of persistent osteomyelitis after surgical excision (i.e. in patients who underwent amputation if no biopsy was made on the preserved limb section), files without sufficient clinical information, absence of antibiotic treatment and follow-up less than six months from termination of drug administration. All clinical, laboratory and radiological data were collected during hospitalization and follow-up visits.

### Definitions

Osteomyelitis in this study was defined as an infection with at least one bone sample (obtained by bone aspiration or biopsy during surgery before initiation of antibiotic treatment) positive for *P. aeruginosa* with compatible histologic, clinical, biological and radiological features.<sup>27</sup> Osteomyelitis was considered as “chronic” when it persisted for more than six weeks. Treatment failure was defined as the persistence or recurrence of osteomyelitis with the initial strain or the reinfection with another pathogen, the necessity for re-operation for any cause or the necessity to introduce a new antibiotic therapy for a local recurrence. Cure was defined as the complete resolution of clinical, biological and radiological symptoms related to osteomyelitis, with no relapse during the entire follow-up period. *P. aeruginosa* eradication was not systematically assessed in all patients since no bone sampling was performed when complete cure was achieved.

### Microbiologic analysis

Routine aerobic and anaerobic cultures, including those in enrichment broths, were performed with all bone samples collected during initial surgery. *P. aeruginosa* isolates were identified using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) (Microflex-Bruker Daltonics, Bremen, Germany). Antimicrobial susceptibility testing was performed using the disk diffusion method on Mueller-Hinton agar (Bio-Rad, Marnes-La-Coquette, France) and interpreted according to the French Society of Microbiology (CA-SFM) clinical breakpoints between 2000 and 2014 ([http://www.sfm-microbiologie.org/page/page/showpage/page\\_id/105.html](http://www.sfm-microbiologie.org/page/page/showpage/page_id/105.html)) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) ([http://www.eucast.org/clinical\\_breakpoints/](http://www.eucast.org/clinical_breakpoints/)) clinical breakpoints in 2015.

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