Intraperitoneal meropenem for peritoneal dialysis peritonitis with *Serratia marcescens* immediately on commencing dialysis

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Abstract

A 67-year-old man developed *Serratia marcescens* peritonitis within a week of commencing peritoneal dialysis. Dialysate cultures isolated multidrug-resistant *S. marcescens*, which was treated with intraperitoneal meropenem. This unusual case highlights the problem of multidrug-resistant peritoneal dialysis infections and the potential viability of intraperitoneal meropenem as ambulatory peritonitis therapy. New Microbes and New Infections © 2016 The Authors. Published by Elsevier Ltd on behalf of European Society of Clinical Microbiology and Infectious Diseases.

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Proportionally, non-*Pseudomonas* Gram-negative organisms account for approximately 20–30% of all peritonitis episodes complicating peritoneal dialysis (PD) [1]. These infections are typically more clinically severe and are associated with worse outcomes, including a higher risk of hospitalization and death [1,2]. Intraperitoneal (ip) antibiotic administration is favoured over the intravenous (iv) route [3]; however, the rise of multidrug-resistant organisms makes antibiotic choice increasingly complex with few guideline recommendations beyond aminoglycosides or third-generation cephalosporins.

We present the case of a patient who developed *Serratia marcescens* peritonitis just days after commencing PD. This case highlights that multidrug-resistant Gram-negative infections may present at any time point in therapy and that ip administration of meropenem is a viable alternative for the treatment of susceptible organisms.

A 67-year-old man with end-stage renal disease resulting from immunoglobulin A nephropathy presented with PD peritonitis 3 days after commencing nocturnal automated PD. Significantly, he had no known bowel or structural urinary tract pathology; nor did he have a history of recent hospitalization beyond outpatient-based PD training. A Tenckhoff catheter had been percutaneously placed without complications approximately 10 weeks before therapy commencement.

After only two overnight dialysis sessions, nonspecific abdominal pain was noted, followed by the development of turbid PD effluent. Empirical antibiotic therapy with ip cephazolin 1.5 g and gentamicin 0.6 mg/kg was initiated, in line with hospital protocol. Peritoneal effluent white cell count was elevated, and cultures isolated *S. marcescens* with an inducible β-lactamase in two separate samples (Fig. 1).

In the setting of significant reluctance to administer prolonged gentamicin and logistical difficulties for the patient in undertaking timely therapeutic drug monitoring, the antibiotic prescription was changed to ip meropenem 1 g daily with the intent of self-administration at home for a total 21-day course. Surveillance PD effluent confirmed microbiologic clearance, and PD has since continued uneventfully. Ip meropenem was well tolerated and easily self-administered at home.

In PD patients in Australia and New Zealand, peritonitis accounts for approximately 30% of technique failures and 21% of infectious deaths [4].

S. marcescens, a Gram-negative, rod-shaped *Enterobacteriaceae,* is an uncommon human pathogen associated with

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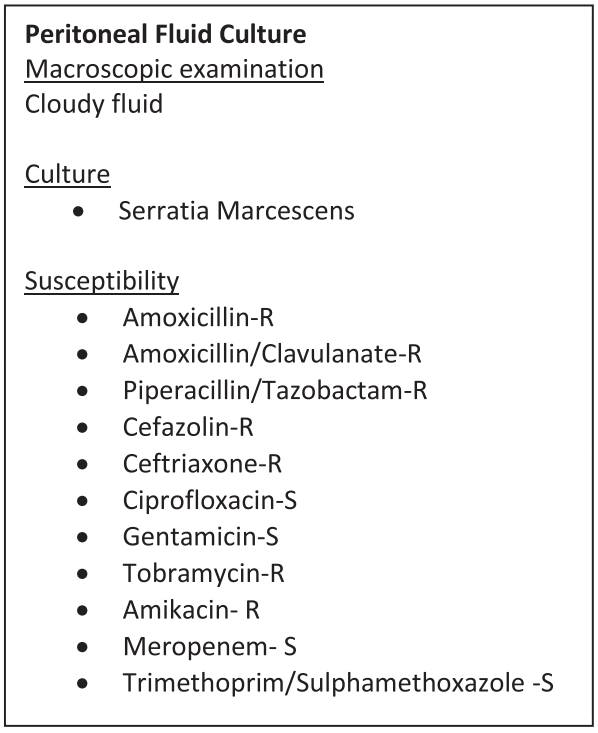

FIG. 1. Microbiology results from patient's peritoneal fluid. R, resistant; S, sensitive.

nosocomial infections, including catheter-associated bacteraemia, urinary tract infections and wound infections [5]. It is a relatively rare cause of peritonitis, contributing to approximately 3% of peritonitis episodes in Australia in 2003–2006 [4]. *S. marcescens* is notoriously difficult to treat because of an intrinsic antimicrobial resistance profile, and it is associated with worse outcomes compared to other Gram-negative organisms [1,6].

A number of predisposing factors have been proposed to be associated with Gram-negative peritonitis, including prior administration of antimicrobial agents, immunosuppression, diabetes, renal failure, steroid use, underlying gastrointestinal pathology and malignancy [4]. In our patient, the only evident risk factors were renal failure and exposure to the hospital environment during PD training. Although the median time from first PD treatment to first peritonitis in Australia is approximately 20 months [7], this case is somewhat unusual in that the patient had undertaken <5 days of therapy before manifestation of peritonitis, strengthening the case for nosocomial acquisition.

Data on the use of ip meropenem in humans remain limited to case reports, typically in association with *Pseudomonas* spp. infections [8]. No reference is made to the appropriateness or efficacy of ip meropenem in the latest iteration of the International Society for Peritoneal Dialysis (ISPD) guidelines for PD-associated infections. Despite poor stability demonstrated in the setting of elevated temperature and continuous iv infusions [9], the stability of meropenem over 6 hours in a 2.5% PD solution has been demonstrated [10]. Plasma area under the curve over 24 hours appears to approximate that of the iv route [11], though specific ip levels with respect to PD peritonitis–relevant bactericidal concentrations have not been reported. Particular concerns of drug intolerance during ip administration have not been raised, and the entire treatment course in our patient was well tolerated. Although it is a microbiologically inappropriate choice as a first-line agent, ip meropenem represents an attractive proposition for multidrug-resistant Gram-negative PD peritonitis. Administration properties are conducive to self-delivered therapy in the ambulatory environment without the logistical burdens of frequent therapeutic drug level monitoring.

This case represents an unusually rapid onset of PD peritonitis with a multidrug-resistant organism almost immediately after commencing dialysis and demonstrates the feasibility of ip meropenem in ambulatory PD peritonitis management. As practical experience with ip meropenem accumulates, this practice may merit discussion in the next iteration of the ISPD infection guidelines.

Conflict of Interest

None declared.

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