Peritoneal Dialysis-Related Peritonitis With Carbapenem-Resistant *Klebsiella pneumoniae* and Vancomycin-Resistant *Enterococcus faecium*

To the Editor—The rapid global dissemination of carbapenem-resistant *Enterobacterales* (CRE) and vancomycin-resistant *Enterococcus* (VRE) presents a major clinical challenge [1]. Treatment options for these organisms are limited, and there are few data regarding peritoneal dialysis (PD)-related intra-abdominal infections [2, 3]. Thus, we wish to share our recent experience in managing a patient with polymicrobial PD-related peritonitis involving New-Delhi metallo-beta-lactamase-1 (NDM-1)-producing *Klebsiella pneumoniae* and *vanB* VRE treated successfully with intravenous (IV) tigecycline.

A 69-year-old man recently commenced PD for end-stage renal failure secondary to antiglomerular basement membrane (anti-GBM) disease. His medical history was significant for previous autologous stem cell transplant for multiple myeloma and ischemic heart disease. He was initially admitted for management of thrombotic microangiopathy (TMA) complicating his anti-GBM disease, requiring immunosuppression with IV methylprednisolone, rituximab, and plasma exchange.

One week into admission, the patient developed severe abdominal pain with guarding. The peritoneal effluent was cloudy; however, he remained afebrile and the Tenckhoff catheter site was not infected. White cell count was 4.75×10^6/L and C-reactive protein was raised at 192 mg/L. The peritoneal fluid demonstrated an elevated polymorph count of 9260×10^6/L, and Gram-positive cocci (GPC) were noted on microscopy. A computed tomography scan of the abdomen demonstrated no evidence of bowel perforation or colitis. The patient was commenced on intraperitoneal (IP) cefazolin and received a single dose of IP gentamicin 0.6 mg/kg on day 1, as per institutional guidelines. An initial loading dose of 20 mg/kg IP cefazolin was given and continued at 125 mg/L per exchange until removal of the Tenckhoff catheter. A single dose of IP vancomycin 30 mg/kg was administered on the second day. Blood cultures returned positive for Gram-negative bacilli and IV piperacillin/tazobactam 4.5 g q8h was commenced. Serial sampling of peritoneal fluid demonstrated down-trending polymorph count; however, Gram-stain demonstrated persistence of GPC in peritoneal fluid at day 4. The initial peritoneal fluid cultures returned positive for *K pneumoniae*, *Enterococcus faecalis*, *Escherichia coli*, and mixed anaerobes with susceptibilities outlined in Table 1. The blood culture returned positive for *Bacteroides* species. Peritoneal cultures from the second and third day grew *E faecium* and *Candida albicans*.

The Tenckhoff catheter was removed due to ongoing positivity of peritoneal

Table 1. Antibiotic Susceptibilities of Organisms Cultured From Peritoneal Fluid

Antibiotic(s)	Minimum Inhibitory Concentration (mg/L) and Susceptibility[a]				
	Klebsiella pneumoniae	*Escherichia coli*	*Enterococcus faecium*	*Enterococcus faecalis*	*Candida albicans*
Ampicillin	≥32 (R)	≥32 (R)	≥32 (R)	≤2 (S)	
Amoxicillin-clavulanate	≥32 (R)	4 (S)			
Cefazolin	≥64 (R)	≤4 (S)			
Ceftriaxone	≥64 (R)	≤1 (S)			
Ceftazidime-avibactam	≥256 (R)				
Meropenem	≥16 (R)	≤0.25 (S)			
Aztreonam	0.25 (S)				
Ciprofloxacin	1 (R)	≥4 (R)			
Trimethoprim-sulfamethoxazole	2 (S)	≥16 (R)			
Gentamicin	≤1 (S)	≤1 (S)			
Tigecycline	1 (S)	0.25 (S)	≤0.12 (S)	≤0.12 (S)	
Colistin	0.5 (S)				
Fosfomycin	≥256 (no interpretation)				
Teicoplanin			≤0.5 (S)	≤0.5 (S)	
Vancomycin			≥32 (R)	1 (S)	
Linezolid			2 (S)	2 (S)	
Fluconazole					0.50 (S)
Caspofungin					0.06 (S)

Abbreviations: R, resistant; S, susceptible.

[a]Interpretation according to the Clinical and Laboratory Standards Institute clinical breakpoint values when available [4]. Interpretation for tigecycline was determined using the US Food and Drug Administration interpretive criteria [5].

fluid cultures and recurrence of abdominal pain on day 4. The *E coli*, *E faecalis*, and *C albicans* isolates were susceptible to multiple antimicrobials, but the *K pneumoniae* and *E faecium* isolates were resistant to meropenem (mean inhibitory concentration [MIC] ≥16 mg/L) and vancomycin (MIC ≥32 mg/L), respectively. Molecular testing indicated the presence of $bla_{\text{NDM-1}}$ in *K pneumoniae* and *vanB* in *E faecium*. Piperacillin/tazobactam was changed to IV tigecycline (100-mg load then 50 mg twice-daily), IV metronidazole 500 mg q8h, and oral fluconazole 400 mg thrice weekly (after dialysis). There was complete resolution of symptoms after commencement of the treatment regimen and no relapse. Unfortunately, after recovery from peritonitis, the patient developed treatment-refractory TMA and died 6 weeks after his initial presentation due to progressive anti-GBM disease.

Peritonitis is a common and potentially fatal complication of PD, with a reported incidence of 0.6 cases per patient year and mortality rate >20% for polymicrobial and fungal peritonitis [6]. Recommended empiric treatment for PD-related peritonitis includes (1) IP vancomycin or a first-generation cephalosporin and (2) a third-generation cephalosporin or aminoglycoside [7]. Our case highlights the risk of treatment failure with this regimen when multidrug-resistant or fungal organisms are isolated. $Bla_{\text{NDM-1}}$ was identified in our patient and renders all beta-lactams besides aztreonam inactive (including novel beta-lactam/beta-lactamase inhibitor combinations) [8]. Due to additional resistance genes, high rates of aztreonam and aminoglycoside resistance have also been noted in $bla_{\text{NDM-1}}$-carrying isolates [8, 9]. In contrast, tigecycline and colistin usually retain activity [8, 9]. In our case, tigecycline had the added advantage of activity against VRE.

There is a paucity of data on treatment of CRE or VRE in PD-related peritonitis [3, 6] and no published reports of IV tigecycline use in PD-related peritonitis as monotherapy. Although use of tigecycline has been limited by early reports of higher mortality than comparator antibiotics [10], it remains an important alternative when other antimicrobials are unavailable or have caused toxicity. Our case demonstrates that tigecycline remains a viable option for the treatment of nonbacteremic infections, including PD-related peritonitis with difficult-to-treat organisms such as CRE and VRE. The role of novel antimicrobials in this setting remains to be determined, but several agents such as plazomicin, eravacycline, omadacycline, and cefiderocol represent promising additions to the armamentarium [9].

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