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Clinical Report

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Daptomycin for a complicated urinary tract infection with vancomycin-resistant *Enterococcus faecium* in a renal transplant recipient

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Abstract
There is an increasing prevalence of urinary tract infection (UTI) caused by multiresistant gram-negative enteric bacilli such as extended-spectrum beta-lactamase as well as Gram-positive enterococci whose vancomycin-resistance can be as high as 25%. We report on a 68-year-old Caucasian female with a UTI caused by a vancomycin-resistant *Enterococcus faecium*, only tested to be susceptible to gentamycin, linezolid and daptomycin. Within a day after administration of the bactericidal daptomycin clinical and laboratory signs of infection regressed and graft function recovered. Our case suggests that daptomycin might be an effective alternative for UTI caused by vancomycin-resistant enterococci.

Keywords: renal transplant recipient; urinary tract infection; vancomycin-resistant entorococci

Background

Daptomycin is licensed in the USA and Europe for the treatment of complicated skin and soft tissue infections caused by gram-positive organisms, including both susceptible and resistant strains of *Staphylococcus aureus*, at a dose of 4 mg/kg daily. Additionally, it had been licensed for the treatment of various infections due to susceptible organisms, including serious and life-threatening Gram-positive infections, vancomycin-resistant enterococcal (VRE) infections and endocarditis with associated bacteraemia at 6 mg/kg once daily. Several studies also established dosing recommendations in patients undergoing various modes of renal replacement therapy [1–5]. Daptomycin is not only primarily (78%) excreted unchanged in the urine but also shows a favourable *in vitro* activity against Gram-positive uropathogens [6], making it an ideal candidate to treat severe urinary tract infection (UTI). Despite the rising prevalence of vancomycin-resistant enterococci in patients with complicated UTI [7], there is a paucity of clinical data on daptomycin in this clinical situation. Here, we now report the first case of successful UTI treatment caused by VRE using daptomycin in a renal transplant recipient with a complex medical history.

Case report

A 68-year old Caucasian female was admitted to the emergency room of our tertiary care hospital with rapidly progressing fever and hypotension. Upon arrival the malnourished patient (height 158 cm; weight, 46 kg; body mass index 18.4 kg/m^2) had a blood pressure of 88/56 mmHg and a heart rate of 110/min. She presented with nausea and dizziness, but was conscious (Glasgow Coma Scale 13). The remainder of the physical examination showed no significant pathological findings. Her past medical history was significant for kidney transplantation about 6 months prior to the admission due to underlying hypertensive kidney disease. She suffered from leucoencephalopathy as well as liver function impairment due to cirrhosis after longstanding alcohol abuse until 6 years prior to admission. Laboratory analysis was remarkable for increased inflammatory parameters [white blood count 22 000/μL, C reactive protein (CRP) 356 mg/L]. The patient had acute kidney injury of the renal graft. Her serum creatinine was 238 μmol/L when compared with the last available outpatient creatinine of 99 μmol/L 7 days before. Liver function test showed an increase in aspartate aminotransferase (143 U/L, upper limit 31 U/L) and alanine aminotransferase (124 IU/L, upper limit 34 IU/L). International normalized ratio was 1.25 indicating deteriorating liver function as well. Urinary sediment was positive for leucocytes (>20/view field) and erythrocytes (11–20/view field) without the presence of any casts. After transfer to our unit the initial antibiotic therapy was switched from meropenem to daptomycin (first dose 10 mg/kg body weight followed by 7.7 mg/kg doses). This was deemed to be prudent as the patient's last UTI, 4 months prior to this admission, was caused by a vancomycin-resistant *Enterococcus faecium*, tested to be

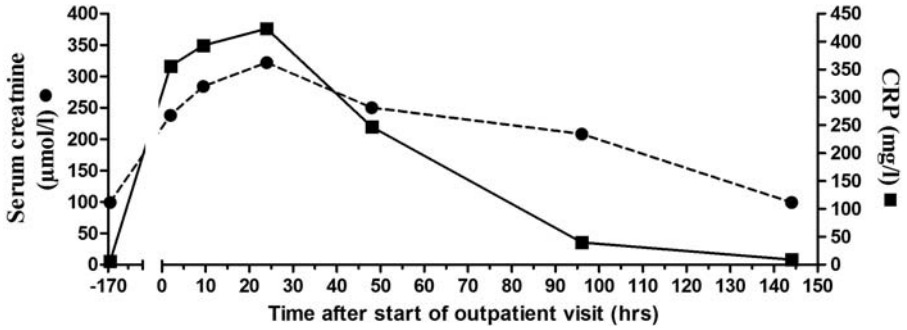

Fig. 1. Serum creatinine and CRP levels of a renal transplant patient at last outpatient visit as well as during the hospital course/treatment of severe UTI with daptomycin.

susceptible only to gentamycin and linezolid. Although we wanted to avoid the former one due to its nephrotoxicity, especially in the state of acute kidney injury, the latter one was deemed inappropriate due to the impaired liver function, as the liver plays an important role in the elimination of the drug [7]. In another culture, persistence of a vancomycin-resistant *E. faecium* was confirmed (minimum inhibitory concentration: vancomycin 8.0 mg/L; linezolid 0.5 mg/L). Unfortunately, daptomycin was not tested in this resistogram as, at that time, it was not part of the routine test panel. Over the subsequent 12 h the patient improved remarkably. The peak CRP declined rapidly and function of the renal graft improved over the 5-day therapy (Figure 1). No adverse effects such as elevation of creatine phosphokinase were seen.

Discussion

UTI is the most common infection following renal transplantation, accounting for about half of all infectious complications in this patient population [8]. In the first month after transplantation, it contributes substantially to the bacteraemia-associated mortality of kidney allograft recipients. But even less severe UTI may worsen graft survival. Resistance to multiple antibiotics, including vancomycin, has increased in prevalence, particularly in infections involving *E. faecium* [9], where the rate of vancomycin-resistance can be as high 10% in North America and 7% in Europe, varying in European countries [10]. Especially in patients with impaired renal function and concomitant hepatic dysfunction the management of UTIs caused by *Enterococcus* spp. has become challenging because of the limited therapeutic options available that almost exclusively consist of nephrotoxic or hepatically eliminated drugs. Our case as well as previous anecdotal reports suggest that daptomycin might be an effective alternative for UTI caused by vancomycin-resistant enterococci as it is neither harmful for the kidney nor cleared by the liver.

Conflict of interest statement. J.T.K. has received funds for speaking at symposia organized on behalf of Novartis Germany and has also received funds for research from Novartis Germany. All other authors have nothing to declare.

References

1. Cardone KE, Lodise TP, Patel N *et al*. Pharmacokinetics and pharmacodynamics of intravenous daptomycin during continuous ambulatory peritoneal dialysis. *Clin J Am Soc Nephrol* 2011; 6: 1081–1088
2. Kielstein JT, Eugbers C, Bode-Boeger SM *et al*. Dosing of daptomycin in intensive care unit patients with acute kidney injury undergoing extended dialysis—a pharmacokinetic study. *Nephrol Dial Transplant* 2010; 25: 1537–1541
3. Mueller BA, Crompton JA, Donovan BJ *et al*. Safety of daptomycin in patients receiving hemodialysis. *Pharmacotherapy* 2011; 31: 665–672
4. Salama NN, Segal JH, Churchwell MD *et al*. Single-dose daptomycin pharmacokinetics in chronic haemodialysis patients. *Nephrol Dial Transplant* 2010; 25: 1279–1284
5. Vilay AM, Grio M, Depestel DD *et al*. Daptomycin pharmacokinetics in critically ill patients receiving continuous venovenous hemodialysis. *Crit Care Med* 2011; 39: 19–25
6. Wagenlehner FM, Lehn N, Witte W *et al*. In vitro activity of daptomycin versus linezolid and vancomycin against gram-positive uropathogens and ampicillin against enterococci, causing complicated urinary tract infections. *Chemotherapy* 2005; 51: 64–69
7. Heintz BH, Halilovic J, Christensen CL. Vancomycin-resistant enterococcal urinary tract infections. *Pharmacotherapy* 2010; 30: 1136–1149
8. de Souza RM, Olsburgh J. Urinary tract infection in the renal transplant patient. *Nat Clin Pract Nephrol* 2008; 4: 252–264
9. Swaminathan S, Alangaden GJ. Treatment of resistant enterococcal urinary tract infections. *Curr Infect Dis Rep* 2010; 12: 455–464
10. Deshpande LM, Fritsche TR, Moet GJ *et al*. Antimicrobial resistance and molecular epidemiology of vancomycin-resistant enterococci from North America and Europe: a report from the SENTRY antimicrobial surveillance program. *Diagn Microbiol Infect Dis* 2007; 58: 163–170

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