# Successful treatment of *Leuconostoc* bacteremia in a neutropenic patient with tigecycline

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## Abstract

*Leuconostoc lactis* is a recognised cause of infection in immunocompromised hosts. It is intrinsically resistant to multiple antibiotics and treatment options may be limited. We report a case of safe and effective use of tigecycline in the treatment of *Leuconostoc* catheter-related line sepsis in a neutropenic patient. To our knowledge, this is the first reported case of successful use of tigecycline for *Leuconostoc* bacteremia.

## Case Report

A 52-year-old woman with granulocytic sarcoma affecting the anterior cranial fossa and frontal sinus was commenced on ADE (cytarabine, daunorubicin and etoposide) and Mylotarg (gemtuzumab) through a peripherally inserted central catheter (PICC) line as part of the AML 17 trial (*http://aml17.cardiff.ac.uk/aml17/Default.aspx*). She was known to have a beta-lactam allergy manifest as an erythematous rash.

On day 9 of chemotherapy, meropenem was empirically started for febrile neutropenia as per fever and neutropenia guidelines.[1] Her fever resolved after 48 hours and meropenem was stopped after 7 days. On day 18 of chemotherapy she was still neutropenic and developed further fevers to 39°C. Her PICC insertion site appeared erythematous with an associated blister. Meropenem was restarted in addition to teicoplanin. She remained febrile over the next three days and caspofungin was started in view of high-resolution computed topography (HRCT) chest findings compatible with possible fungal infection and a positive initial serum galactomannan assay (although the repeat specimen was negative). After 10 days of treatment she developed a rash and continued to spike temperatures. Meropenem was therefore replaced with ciprofloxacin as it was thought to be responsible for the rash. All cultures including multiple blood cultures and PICC line site swabs were culture negative.

On day 31 of chemotherapy she was still febrile and blood cultures from peripheral veins and the PICC line taken on day 30 yielded gram-positive cocci in pairs and chains after 24 and 11 hours' culture respectively. The isolate was identified as *Leuconostoc lactis* using the BD Phoenix identification (Becton, Dickinson and Company, USA) and API® rapid ID 32 Strep systems (bioMérieux, France). Mean inhibitory concentrations (MICs) determined by E-test (AB Biodisk, Sweden) were: penicillin 0.5 mg/L, vancomycin >256 mg/L, teicoplanin 256 mg/L, ciprofloxacin 1.0 mg/L, tigecycline 0.064 mg/L, linezolid 1.5 mg/L and daptomycin 0.064 mg/L. On day 32 of chemotherapy, ciprofloxacin and teicoplanin were changed to intravenous linezolid and the PICC was removed. The next day therapy was changed to tigecycline (50 mg IV q12h) because of concerns over myelotoxicity (anaemia and thrombocytopenia) associated with linezolid.[2] Daptomycin was unavailable in the hospital formulary and ampicillin was not used due to concerns over beta-lactam allergy and a borderline penicillin E-test MIC. Culture of the PICC tip yielded no significant growth. The patient continued to have low-grade fevers over the next four days, despite a negative transthoracic echocardiogram. On the fourth day of treatment, however, her fever resolved and she was discharged from hospital after completing 8 days of tigecycline, to which she had no adverse effects. She remained asymptomatic with sterile blood cultures and successfully continued her chemotherapy.

## Discussion

*Leuconostoc* spp. are catalase-negative, gram-positive, facultatively anaerobic coccobacilli. They are environmental organisms often found on plants, dairy products, vegetables, wine and occasionally in human vaginal and stool samples.[3] Although an uncommon human pathogen, cases of bacteremia, endocarditis, pneumonia, meningitis, osteomyelitis, peritonitis, brain and liver abscesses have been described.[4-12]

*Leuconostoc spp.* and other gram-positive antimicrobial-resistant organisms are increasingly recognised as important pathogens in neutropenic patients probably due, in addition to immunosuppression, to the use of indwelling intravascular devices, antibiotic prophylaxis and evolution of chemotherapeutic agents.[13] Infection with *Leuconostoc* may cause fever, intravenous catheter-related sepsis, bacteremia, abdominal pain, gastroenteritis, colitis or meningitis in this group of patients.[7]

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Other reported risk factors for infection include a history of surgery and prior vancomycin therapy.[7,14] Common portals of entry described include intravascular catheters or the gastrointestinal tract.[15,16] Removal of intravenous catheters alone has been shown to be curative in some patients without the need for antimicrobial therapy.[7]

There are no standardised criteria for interpreting the antimicrobial susceptibility testing of *Leuconostoc spp.* - therapy should be guided by the MIC of the isolate. *Leuconostoc* spp. are intrinsically resistant to glycopeptides, owing to the production of peptidoglycan precursors ending in D-Ala-D-Lac, but are usually susceptible to penicillin, ampicillin, aminoglycosides, clindamycin, minocycline and macrolides.[17] In addition, linezolid and daptomycin have been used successfully to treat *Leuconostoc* bacteremia, although linezolid MICs of *Leuconostoc* spp. are usually higher when compared with those of streptococci.[3,18] Moderate susceptibility is seen with cephalosporins, chloramphenicol, tetracycline and doxycycline.[3] Although the organism has been shown to be resistant to cefoxitin, it is susceptible to cefotaxime *in vitro*.[19] This may have been an alternative therapeutic option in our patient.

Tigecycline, a glycylcycline, is a broad spectrum synthetic derivative of minocycline which has a broad spectrum of activity against various gram-positive and gram-negative bacteria including multidrug-resistant strains, anaerobic bacteria and atypical organisms. It has proven to be useful in the treatment of hospi-

tal-acquired infections caused by vancomycin-intermediate and vancomycin-resistant enterococci (VRE), meticillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamase (ESBL)-producing *Enterobacteriaceae*, multidrug-resistant *Acinetobacter baumanii* and penicillin-resistant *Streptococcus pneumoniae*.[20,21]

In the UK, its licensed indications are complicated intra-abdominal and complicated skin and soft tissue infection.[22,23] It is also licensed for the treatment of community-acquired pneumonia in the US.[24]

## Conclusions

Although tigecycline has been demonstrated to be a safe and effective second-line option in microbiologically documented infections in neutropenic patients, there have been no trials to determine whether tigecycline is effective in neutropenic bacteremia and there are also theoretical concerns surrounding low serum concentrations (due to a large volume of distribution) and its mostly bacteriostatic activity.[25] It is for this reason that tigecycline is not generally recommended for primary bacteremia but it is used for secondary bacteremia associated with complicated skin and soft tissue infections, intra-abdominal infections and community-acquired pneumonia.[26] Despite these concerns, here we report the first successful use of tigecycline in the treatment of *Leuconostoc* bacteremia in a neutropenic patient.

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