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Case report

Unusual carbapenem resistant but ceftriaxone and cefepime susceptible *Klebsiella oxytoca* isolated from a blood culture: Case report and whole-genome sequencing investigation

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**ABSTRACT**

A carbapenem resistant but ceftriaxone and cefepime susceptible *Klebsiella oxytoca* was isolated from the blood of a patient with polymicrobial bacteremia after 2 weeks of ertapenem treatment. Whole-genome sequencing identified no carbapenemase gene nor plasmid, but only *blaOXY-2-8* gene with a mutation in the promoter that’s been reported to increase its expression. Two other specific carbapenem resistance mechanisms including mutated porin genes and the AcrAB-ToLC efflux system genes were also identified. Clinicians need to be aware of such unusual antibiogram and should not assume carbapenems are always broader spectrum antibiotics than expanded-spectrum cephalosporins.

**Introduction**

*Klebsiella oxytoca* is associated with blood stream, intra-abdominal and urinary tract infections. The rise of carbapenem resistant *Klebsiella oxytoca* (CRKO) has become part of the urgent threat of carbapenem resistant Enterobacteriaceae (CRE) epidemic, and most CRKO carry plasmid-mediated carbapenemase genes that are highly transmissible [1–4]. Here we report a case of bacteremia with an unusual CRKO that is susceptible to ceftriaxone and cefepime.

**Case report**

A patient with history of recent tricuspid valve endocarditis with septic pulmonary emboli, as well as a large, obstructing staghorn calculus developed polymicrobial bacteraemia including *Escherichia coli* and ESBL *Klebsiella pneumoniae* five days after suffering an iatrogenic ureteral perforation during a failed percutaneous nephrolithotomy (day 0). Empiric vancomycin and piperacillin-tazobactam were initiated and changed to ertapenem monotherapy when blood culture identification and susceptibilities were available. Subsequent blood cultures grew vancomycin resistant *Enterococcus faecium* (days 11, 13), which prompted addition of daptomycin. After 2 weeks of ertapenem, the patient continued to be clinically septic, and ertapenem was switched to meropenem to broaden coverage. Three days after changing to meropenem (day 25), blood cultures grew CRKO, *Stenotrophomonas maltophilia*, and *Enterococcus faecalis*. Amikacin was added to cover the CRKO, trimethoprim-sulfamethoxazole was started for the *Stenotrophomonas maltophilia*, and daptomycin and meropenem were continued. The CRKO isolate had an unusual antibiogram (Table 1), as it was resistant to cefazolin, piperacillin-tazobactam, ertapenem and meropenem, and intermediate to imipenem but susceptible to aztreonam and most 3rd and 4th generation cephalosporins including ceftriaxone, ceftazidime, and cefepime except cefotaxime (resistant) and cefotolozane/tazobactam (intermediate). It was susceptible to cefazidime/avibactam. Due to this susceptibility pattern, meropenem was switched to cefepime on day 29, after which no Enterobacteriaceae has been isolated to date. The patient didn’t have recent travel history.

**Investigation**

To investigate the carbapenem resistance mechanism of this CRKO isolate, the modified carbapenem inactivation method (CIM) [5] and
excluding K1[11]residual carbapenemase activities of chromosomal OXY-2 enzymes in institutions S23G, D38A, N134T, and A239T. Several reports have shown single-nucleotide polymorphisms (SNPs) resulting in amino acid sub-overexpression of the gene and > 100 fold increase in enzyme activity. S. Yang et al.

More studies are undergoing to verify the residual carbapenemase activity of CRKO without a plasmid, or carbapenemase or non-OXY-related ESBL genes. Overexpression of both blaOXY-2,8 and the AcrAB-ToIC efflux system, as well as loss of function in key porins, most likely contributed to carbapenem resistance in this isolate. The unusual antibiogram of this isolate (i.e. resistant to carbapenems but susceptible to cephalosporins and ceftriaxone) led to the change of treatment regimen from meropenem to cefepime, which treated the CRKO bloodstream infection.

The CRKO was isolated from an inpatient in a cardiac rehabilitation unit. New Microbiol 2015;38(July (3)):387–92.


Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing; twenty-seventh informational supplement; M100-S27, CLSI; 2017.

Pollett S, Miller S, Hindler J, Uslan D, Carvalho M, Humphries RM. Phenotypic and molecular characteristics of carbapenem-resistant Enterobacteriaceae in a health care facility.


