

EV0444

ePoster Viewing

Resistance mechanisms

Effectivity of a double-carbapenem regimen for the treatment of a KPC-producing *Klebsiella pneumoniae* infection in an immunocompromised patient.

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Background: Infections due to carbapenemase-producing *Klebsiella pneumoniae* (CPKP) are increasingly reported. CPKP usually co-expresses additional resistance determinants that confer resistance to several antibiotic families other than betalactams. This situation represents an important threat to public health since therapeutic options against these infections are limited. Double-carbapenem regimen (DCR) has been suggested as alternative to treat extensively drug-resistant (XDR) CPKP. In the present report we present a sepsis caused by an XDR CPKP after allogeneic hematopoietic stem cell transplantation (allo-HSCT). *In vivo* and *in vitro* synergistic activity of DCR is demonstrated.

Material/Methods: A 36-year-old Spanish woman with acute myeloid leukemia was admitted in August 2015 to receive an allo-HSCT, after conditioning chemotherapy regimen. She developed neutropenic fever (ANC=0cells/mm³) and mucositis. Piperacillin-tazobactam (PTZ) was initiated. On post allo-HSCT day 6, she remained febrile and reported dysuria. Blood cultures (BC) were negative, whereas urine culture (UC) grew CPKP. PTZ was replaced by amikacin and tygeciline empirically 24 hours later, due to persisting fever. Afterwards the patient developed hypotension and chills. CPKP was then isolated from a BC and later from a rectal screening.

Results: Genetic characterization of the CPKP revealed that it was a KPC-3 producing isolate, belonging to ST258. The antimicrobial susceptibility study showed that the isolate was resistant to all betalactams (MICs for ertapenem and meropenem of 256 and 128µg/ml, respectively), ciprofloxacin (MIC≥32 µg/ml) and fosfomycin (MIC≥128 µg/ml), and susceptible to gentamycin (MIC=2 µg/ml) and colistin (MIC=0.064µg/ml). Tygeciline showed an intermediate MIC (1.5µg/ml). *In vitro* synergy of carbapenems was evaluated by Etest, microdilution checkerboard, and time-kill methods. The fractional inhibitory concentration index was calculated for all these methods and was found as synergistic for ertapenem+meropenem and ertapenem+imipenem combinations.

Clinical progression: As patient was considered to be at a high risk of potential antibiotic-induced nephrotoxicity (hemodynamic instability, neutropenia, early after allo-HSCT and use of other nephrotoxic drugs), colistin was avoided. Due to a lack of alternative regimens, DCR was started following previous therapeutic approaches. Ertapenem (1g every 24h) followed one hour later by high dose of meropenem (2g every 8h, in 3h extended infusion) was given during 14 days, with no adverse

effects. The patient became afebrile in less than 48h and UC and BC underwent negative. The patient achieved clinical and microbiologic success and was discharged 2 weeks later.

Conclusions: CPKP bloodstream infections generally have a poor outcome, with a high mortality in immunocompromised patients and high treatment failure rates. We present a case of successful DCR therapy with ertapenem and meropenem of a septic allo-HSCT patient. As far as we know, this is the first reported case of the successful use of a DCR in a neutropenic patient.