SUCCESSFUL OUTCOME OF EXTRA-DRUG RESISTANT KLEBSIELLA PNEUMONIAE BLOODSTREAM INFECTION TREATMENT WITH CEFTAZIDIME-AVIBACTAM

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Background

Emergence of extensively drug resistant (XDR) *Klebsiella pneumoniae* is a major public threat and especially for pediatric patients. Therapeutic treatment options for these bacteria are extremely limited to ≤2 antimicrobial agents (including colistin) for which few or no efficacy/safety data exist.[1-2] Ceftazidime/avibactam is a newly developed antimicrobial agent with activity against KPC producing Enterobacteriaceae. [1-2]

Aim

The aim of this study was to describe the successful treatment outcome of an XDR *K. pneumoniae* bloodstream infection in a 2.5-year old girl using ceftazidime-avibactam.

Case presentation

A 2.5-year old girl admitted to Pediatric Intensive Care Unit (PICU) for cerebral injury as a result of car crushing. She was intubated and had a central venous catheter (CVC) in place.

On day 15 of hospitalization she suffered from bacteremia due to *Klebsiella pneumoniae* resistant to all antimicrobials except colistin, of which MIC of the isolate was, however, high (3 mg/l according to microdilution method). Meropenem and colistin (300,000 IU per day q 8h) were initially started and ertapenem, tigecycline and amikacin were subsequently added to the antimicrobial regimen. Blood cultures became negative.

However, 15 days later, (**day 30**) the patient, while in therapy, deteriorated again with high fever. C-reactive protein was elevated (max 313 mg/l). Blood cultures were obtained again and grew *K. pneumoniae*, which had the same resistant phenotype:

References

1) Shirley, Drugs, 2018:675, 2) Bradley, ECCMID, 2018 (#O1123)

Antimicrobial susceptibility test and Treatment

Antimicrobial (Vitek2)	MIC (mg/l)	Interpretation	Antimicrobial (Vitek2)	MIC (mg/l)	Interpretation
Ampicillin/Sulbactam	≥32	Resistant	Ciprofloxacin	≥ 4	Resistant
Cefoxitin	≥64	Resistant	Levofloxacin	≥ 8	Resistant
Ceftazidime	≥64	Resistant	Piperacillin/tazobactam	≥128	Resistant
Ceftriaxone	≥64	Resistant	Fosfomycin	64	Resistant
Cefepime	≥64	Resistant	Trimethoprime/ sulfomethoxazole	≥ 320	Resistant
Aztreonam	≥64	Resistant	Tigecycline	≥ 8	Resistant
Meropenem	≥16	Resistant	Amikacin	≥ 64	Resistant
Imipenem	≥16	Resistant	Gentamicin	≥ 16	Resistant

Colistin (broth microdilution method)	MIC >2 and ≤ 4 mg/l (EUCAST BP, ≤ 2mg/l)
Chloramphenicol (disc diffusion method)	Resistant (no inhibition)
Phenotypic tests for KPC-carbapenemase and Metallo beta-lactamase production	Positive for KPC production, negative for MBL-production
Ceftazidime-avibactam (disc diffusion method)	Susceptible (21mm, BP for Enterobacteriaceae)

After special ethics approval, **ceftazidime/avibactam** was administered to the patient at the dose of 62.5mg/kg/dose q8h. Blood cultures became negative after 2d and the patient improved clinically. Ceftazidime/avibactam was given for a total of 32 days without any related significant adverse event.

Learning points / Discussion

Treatment of bloodstream infections caused by XDR-*Enerobacrteriaceae* in children is challenging.

In XDR *K. pneumoniae* isolates, borderline colistin and fosfomycin resistance further narrows currently available antimicrobial options especially for children.

Double carbapenem treatment was used in combination with colistin for the first episode of *XDR K. pneumoniae,* but was found to be insufficient for the second episode.

Administration of ceftazidime/avibactam in this child with in vitro susceptibility and phenotypic confirmation of KPC production, resulted in microbiological eradication and clinical cure.

Ceftazidime/avibactam given at the dose of 62.5 mg/kg/dose q8h (according to currently clinical trials in children) seems to be efficacious against in vitro susceptible XDR-*Enterobacteriaceae* with no significant adverse effects.