



Case report

Successful treatment of KPC-MDR septic shock with ceftazidime-avibactam in a pediatric critically ill patient

Maria Vargas^{a,*}, Antonio Riccardo Buonomo^b, Pasquale Buonanno^a, Carmine Iacovazzo^a, Giuseppe Servillo^a

^a Department of Neurosciences, Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy

^b Department of Clinical Medicine and Surgery – Section of Infectious Diseases, University of Naples Federico II, Naples, Italy



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ABSTRACT

Ceftazidime-avibactam is a combination agent consisting of the β -lactamase inhibitor avibactam and the broad-spectrum cephalosporin ceftazidime. There are no published case reports or studies evaluating the use of CAZ-AVI in pediatric critically ill patients. We report a case of a successful treatment of septic shock due to *Klebsiella pneumoniae* (KP) in a 14-years-old boy (body weight 50 kg) admitted in intensive care unit (ICU).

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Introduction

Infections due to multi-drug resistant (MDR) gram-negative bacteria showed a significant morbidity and mortality in adult patients and required prompt effective antimicrobial therapy [1]. Ceftazidime-avibactam is a combination agent consisting of the β -lactamase inhibitor avibactam and the broad-spectrum cephalosporin ceftazidime [2]. Ceftazidime-avibactam was approved by the United States Food and Drug Administration (US FDA) for treatment of complicated intra-abdominal infection as well as complicated urinary tract infections, including pyelonephritis and hospital-acquired pneumonia, including ventilator-associated pneumonia [3]. Ceftazidime-avibactam (CAZ-AVI) was also approved in Europe for the treatment of adult nosocomial pneumonia [4]. However, the safety and effectiveness of CAZ-AVI in pediatric patients aged less than 18 years with hospital or ventilator acquired pneumonia have not been established [4]. Pediatric studies to address treatment options for MDR Gram-negative pathogens are needed; the recent INFORM Surveillance program (USA 2011–2015) reported a highly in vitro-activity of ceftazidime/avibactam against *Klebsiella pneumoniae* isolated from pediatric patients [5]. Actually there are no published case reports or studies evaluating the use of CAZ-AVI in pediatric critically ill patients. We report a case of a successful treatment of

septic shock due to *Klebsiella pneumoniae* (KP) in a 14-years-old boy (body weight 50 kg) admitted in intensive care unit (ICU).

Case report

A 14years-old boy, without comorbidities, was admitted in our university hospital ICU after a cardiac arrest occurred 3 days before. He was first admitted to an ICU of a peripheral hospital where he was sedated, intubated and put under mechanical ventilation. After 48 h of mechanical ventilation, he was moved to our hospital because his serious clinical condition required a major tertiary hospital.

At admission he was sedated, paralyzed and intubated, febrile (38 °C) and hemodynamically supported with high doses of inotropes and vasopressors. The APACHE II score was 29, the SOFA score was 12 while the SAPS II 59. His laboratory tests showed a white blood count (WBC) of 27,440 mCL, a lactate level of 3.5 mmol/L, a C-reactive protein (CRP) of 37 mg/L (normal value) and procalcitonin (PCT) of 25.99 ng/mL.

We suddenly performed blood and urine cultures, rectal swabs and a bronchial alveolar lavage. The bronchoscopy showed a diffuse hyperemic friable mucosa in both lungs while the bronchial alveolar lavage removed a large amounts of purulent secretions. He started an empiric intravenous antibiotic therapy with meropenem 1 g every 8 h and linezolid 600 mg every 12 h. We received a negative rectal swab 24 h after the admission. Four days later his clinical condition was not improved; he was still febrile (38.5 °C), hemodynamically instable under the continuous infusion of high doses of inotropes and vasopressors and his laboratory tests showed a CRP of 89 mg/L and

* Corresponding author at: Department of Neurosciences, Reproductive and Odontostomatological Sciences, University of Naples "Federico II", Via Pansini, 80100, Naples, Italy.

E-mail address: vargas.maria82@gmail.com (M. Vargas).

PCT of 6.7 ng/mL. The metabolic acidosis worsened with the lactate levels were still above the normal range (6 mmol/L). The APACHE II score was 22, the SOFA score was 14 while the SAPS II 48. He was still in respiratory failure with severe hypoxia ($\text{PaO}_2/\text{FiO}_2$ ratio = 97) and his HRCT showed the presence pleural effusion, parenchymal lesions and areas of diffuse consolidation in both lungs. We received the blood cultures and bronchial alveolar lavage positive for KP - multidrug resistant (MDR). The isolated bacteria was resistant to all the tested antibiotics except for colistin and then a susceptibility test (E-test) for CAZ-AVI was performed. The E-test of CAZ-AVI showed a MIC value of 1 mg/L and the E-test of Colistin that showed a MIC of 0.5 mg/L. According to his clinical conditions, his laboratory tests and radiologic findings, we performed a diagnosis of septic shock due to *Klebsiella pneumoniae*. Therefore, we decided to add CAZ-AVI 2.5 g every 8 h for 14 days to the antibiotic therapy with a close monitoring of renal function. Two days later the fever disappeared and he became hemodynamically stable. His laboratory tests showed a significant improvement of CRP (34 mg/L), PCT (0.19 ng/mL) and WBC (10,230 mL). During the therapy no renal impairment or adverse events occurred. At the discharge the patient had still a negative rectal swab for carbapenemase producing bacteria. No recurrence of infections was reported 20 weeks after the ICU discharge.

Discussion

CAZ-AVI demonstrated clinical efficacy in treatment of complicated intra-abdominal and urinary tract infections in adult patients [6,7]. Limited data existed about the use of CAZ-AVI in pediatric patients and even less in critically ill pediatric patients. Those patients have a wide interindividual pharmacokinetic variability due to size age and organ functions [8]. Many factors influenced the pharmacokinetics in critically ill pediatric patients such as cardiovascular system, organ dysfunction and organ support [8]. Indeed, current antibiotic regimens for critically ill neonate and pediatric patients are frequently suboptimal due to a poor understanding of altered pharmacokinetic properties [9]. Dosage individualization seems to be a key issue to optimize drug treatment in these specific populations [8]. To our knowledge this is the first case reporting the successful treatment with CAZ-AVI of *Klebsiella Pneumoniae* (KP)-MDR septic shock in a pediatric critically ill patient. A recent phase I study assessed the pharmacokinetics profile, safety, and tolerability of a single dose of CAZ-AVI in hospitalized pediatric patients with confirmed or suspected infections while we reported the use of CAZ-AVI in a pediatric critically ill patient with septic shock due to KP-MDR infection [10]. In this case, the use of CAZ-AVI was driven by the susceptibility tests performed on blood and respiratory tract cultures even if with an off-label drug prescription due to the patient age. A multidisciplinary approach including infectious disease and microbiology specialists associated with a close

control of infective parameters and organ functions may allow us to use this antibiotic in critically ill pediatric patients. However, future studies are needed to assess the safety profile of CAZ-AVI in a cohort of pediatric critically ill patients.

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Declaration of Competing Interest

The authors have no conflict of interest.

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