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CASE REPORT

Managing Drug-resistant *Acinetobacter baumannii* Infection in Premature Infants

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Acinetobacter baumannii is a major pathogen in neonatal intensive care units, particularly affecting extremely premature infants and posing challenges due to its extensively drug-resistant (XDR) or pan-drug-resistant (PDR) profiles. This report describes the successful treatment of two extremely premature neonates with severe, XDR/PDR *A. baumannii* infections using combination therapy of colistin, tigecycline, and cefoperazone/sulbactam. The first case involved a 26-week gestation neonate with ventilator-associated pneumonia unresponsive to initial therapy. The infant was successfully extubated after a tailored regimen. The second case, a 26-week neonate with XDR *A. baumannii* bacteremia and septic shock, presented with complications including necrotizing enterocolitis. Despite these challenges, the infant recovered fully after the combination therapy, with no long-term sequelae observed. These findings emphasize the potential of combination therapy as a life-saving intervention for critically ill neonates with multidrug-resistant *A. baumannii* infections, highlighting the need for further research to refine therapeutic strategies in this vulnerable population.

Key words: *Acinetobacter baumannii*, sepsis, drug resistance, extremely premature infants

INTRODUCTION

Acinetobacter baumannii (*A. baumannii*) is a growing concern, causing extensively drug-resistant (XDR) and healthcare-associated sepsis, particularly in neonates admitted to neonatal intensive care units (NICUs). Carbapenem-resistant *A. baumannii* (CR-AB) poses a significant challenge, especially for extremely premature infants. CR-AB is a key component of both XDR-AB and pan-drug-resistant *A. baumannii* (PDR-AB) infections, increasingly observed in this population. XDR refers to bacteria that are susceptible to only one or two classes of antibiotics, while PDR denotes bacteria that are resistant to all classes of antibiotics.[1] The incidence of XDR-AB infections among neonates in East Asia was higher than in other areas.[2] Limited therapeutic options due to resistance and the complexity of the neonatal immune system make managing XDR-AB infections in neonates challenging. Previous research demonstrates that timely colistin administration significantly reduces mortality in XDR-AB-infected premature infants.[3] Studies also highlight isolates from high-risk areas exhibiting XDR-AB colonization, with susceptibility limited to colistin and tigecycline.[3] *In vitro* experiments and animal studies, along with clinical reports, support the efficacy of combined drug therapy for XDR-AB infections.[4-6] Mortality risk factors in neonates with XDR-AB sepsis include umbilical vein catheters, absolute neutrophil count <1500/μL, platelet count <100,000/μL, and delayed initiation of adequate antibiotics.[3] Herein, we address the successful treatment of two extremely premature infants with severe XDR-AB/PDR-AB infection.

CASE REPORTS

This retrospective study involved extremely premature infants diagnosed with XDR-AB/PDR-AB infections admitted

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to the NICU at a tertiary care hospital between May 2022 and June 2023. The local ethics committee approved the study protocol (IRB#202315135). Written informed consent was obtained from all parents. Antimicrobial susceptibility testing results of *A. baumannii* from these two cases are shown in Table 1.

Case 1

A 900-gram extremely premature infant (26 4/7 weeks) delivered via cesarean section due to oligohydramnios and premature rupture of membranes received endotracheal intubation for respiratory distress. Meropenem was administered for ventilator-associated pneumonia 4 days later. Tracheal aspiration culture revealed XDR-AB, prompting aerosolized colistin. However, a follow-up chest X-ray revealed atelectasis in the left upper lung field. Despite a 1-week course of aerosolized colistin and intravenous meropenem, the infant's condition did not improve, with elevated C-reactive protein and leukocytosis. Tigecycline (2.5 mg/kg/day every 12 h) replaced meropenem, leading to gradual respiratory improvement and successful ventilator weaning. The patient was discharged thereafter under fair conditions without oxygen dependence.

Case 2

An 855-g extremely premature infant (26 3/7 weeks) delivered via cesarean section due to premature rupture of membranes developed VAP and septic shock due to XDR-AB one week after birth. Central venous catheter tip culture yielded XDR-AB and coagulase-negative staphylococci. The

Table 1: Susceptibility of the five *Acinetobacter baumannii* isolates

Antibiotics	Case 1: Tracheal aspiration	Case 1: Tracheal aspiration	Case 2: UVC tip	Case 2: Tracheal aspiration	Case 2: Blood	Case 2: Blood
Hospital day	Day 4	Day 18	Day 6	Day 16	Day 37	Day 40
Ampicillin	Resistant (≥32)	Resistant (≥32)	Resistant (≥32)	Resistant (≥32)	Resistant (≥32)	Resistant (≥32)
Cefazolin	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)
Gentamicin	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)
Amikacin	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)
TMP-SMZ	Resistant (≥320)	Resistant (≥320)	Resistant (160)	Resistant (≥320)	Resistant (160)	Resistant (160)
Piperacillin/ tazobactam	Resistant (≥128)	Resistant (≥128)	Resistant (≥128)	Resistant (≥128)	Resistant (≥128)	Resistant (≥128)
Ceftazidime	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)
Ceftriaxone	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)
Imipenem	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)	Resistant (≥16)
Ciprofloxacin	Resistant (≥4)	Resistant (≥4)	Resistant (≥4)	Resistant (≥4)	Resistant (≥4)	Resistant (≥4)
Cefepime	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)
Tigecycline	Susceptible (2)	Susceptible (2)	Susceptible (1)	Resistant (≥8)	Susceptible (2)	Susceptible (2)
Levofloxacin	Resistant (≥8)	Resistant (≥8)	Intermediate (≥8)	Resistant (≥8)	Resistant (≥8)	Intermediate (4)
Colistin	Susceptible (≤0.5)	Intermediate (≤0.5)	Intermediate (1)	Intermediate (2)	Intermediate (≤0.5)	Intermediate (≤0.5)
Flomoxef	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)	Resistant (≥64)
Doripenem	Resistant (≥8)	Resistant (≥8)	Resistant (≥8)	Resistant (≥8)	Resistant (≥8)	Resistant (≥8)
Cefoperazone/ sulbactam	Intermediate (32)	Intermediate (32)	Susceptible (16)	Intermediate (32)	Intermediate (32)	Susceptible (16)
Antibiotic administration	Intravenous meropenem (40 mg/kg/day, administered every 12 h) and aerosolized colistin (3 mg CBA/kg per dose, administered every 12 h) for 1 week	Intravenous tigecycline (2.5 mg/kg/day, administered every 12 h) for 10 days	Intravenous tigecycline (1.5 mg/kg/day, administered every 12 h)	Aerosolized colistin (4 mg CBA/kg per dose, administered every 12 h) and intravenous meropenem (60 mg/kg/day, administered every 8 h) for 14 days	Intravenous colistin (5 mg/kg/day, administered every 12 h), tigecycline (3 mg/kg/day, administered every 12 h), and cefoperazone/sulbactam (80 mg/80 mg/kg/day, administered every 8 h) for 14 days	

Data are resistance status (minimum inhibitory concentration, in μg/mL) unless otherwise indicated. TMP-SMZ=Trimethoprim-sulfamethoxazole; UVC=Umbilical venous catheter; CBA=Colistin base activity

infant received a 14-day course of tigecycline, vancomycin, and meropenem. Soon after, the infant experienced frequent apnea and elevated transcutaneous CO2 levels. Sputum culture revealed PDR-AB, prompting aerosolized colistin and intravenous meropenem for 14 days. Thereafter, his general condition improved gradually. However, 3 days after this treatment course, the patient developed necrotizing enterocolitis with acute kidney injury (peak creatinine 1.1 mg/dL on hospital day 34, normalized by hospital day 37). Importantly, all cultures obtained on hospital day 34 were negative. Despite broad-spectrum antibiotics, the infant's condition worsened, with septic shock and bilateral lung infiltrates on chest X-ray. This clinical deterioration, coupled with the subsequent positive blood culture obtained on hospital day 37 confirmed a new episode of XDR-AB growth. Therefore, we administered triple therapy for 14 days, comprising intravenous colistin (5 mg/kg/day, administered every 12 h), tigecycline (3 mg/kg/day, administered every 12 h), and cefoperazone/sulbactam (80 mg/80 mg/kg/day, administered every 8 h). The infant's blood pressure and respiration improved gradually, followed by successful extubation and complete resolution of infection. Routine monitoring of renal, hepatic, and hematological parameters ensured safety throughout treatment. Similar to Wei *et al*.,[3] we observed no nephrotoxic effects. Case 2 experienced transient, reversible liver enzyme elevations, which were closely monitored and managed. Both patients were followed up for 6 months postdischarge without readmissions related to the initial infection or long-term sequelae.

DISCUSSION

The present report highlights the effectiveness of combined antibiotic therapy for critically ill, extremely premature infants with *A. baumannii* sepsis. Although previous studies have suggested colistin-carbapenem-based combination therapy for the treatment of CRAB bloodstream infection,[7] the therapeutic evidence for this approach remains limited.[8] Limited data exist on the safety and efficacy of colistin, tigecycline, and cefoperazone/sulbactam combination therapy in extremely premature infants. However, this case series suggests promising results for treating XDR-AB infections in this vulnerable population, warranting further investigation. Antimicrobial resistance is highly associated with improper antibiotic prescribing. The protracted, unwarranted use of broad-spectrum antimicrobial agents should be avoided. Nonetheless, these immunocompromised extremely premature neonates frequently require invasive interventions, which raises the risk of late-onset sepsis. The selection of appropriate drugs for the clinical management of XDR-AB or even PDR pathogens is extremely challenging. However, our cases demonstrated that premature infants simultaneously experienced multiple severe and critical infections, including XDR-AB ventilator-associated pneumonia and XDR-AB bacteremia. We used a combination therapy of colistin, tigecycline, and cefoperazone with sulbactam, which effectively controlled the severe infection and completely cured the two critically ill premature patients after a sufficient treatment period. The dosing decisions for colistin, tigecycline, and cefoperazone/sulbactam were informed by a comprehensive review of current guidelines and pharmacokinetic studies tailored to neonatal populations. Specifically, the GREAT guidelines provided foundational recommendations and additional neonatal pharmacokinetic data-guided adjustments for extremely premature infants.[7] Colistin was administered at 5 mg/kg/day in a divided regimen, aligning with neonatal studies indicating mean peak concentrations of 3.0 ± 0.7 μg/mL and supported by expert consensus.[9] Tigecycline dosing was adapted from pediatric recommendations to ensure effective systemic exposure against XDR-AB.[10] Cefoperazone/sulbactam, dosed at 80 mg/80 mg/kg/day in three divided doses, was selected based on β-lactam pharmacodynamics in neonates to optimize pathogen clearance.[11] These dosing strategies underscore the critical need for evidence-based refinements in this vulnerable demographic. In Case 1, a shift in colistin susceptibility interpretation from "susceptible" to "intermediate" was observed. This change reflects the adoption of updated Clinical and Laboratory Standards Institute interpretive criteria for polymyxins, which now recognize the limited clinical utility of polymyxin monotherapy against *Acinetobacter*.[12] Therefore, based on the antibiotic susceptibility testing results, antimicrobial therapy was escalated to tigecycline, which was interpreted as "susceptible." This treatment strategy successfully led to the resolution of the patient's infection.

CONCLUSION

We describe the uncommon and effective antimicrobial action of the combination of cefoperazone/sulbactam, colistin, and tigecycline against XDR-AB or even PDR-AB infections. This study demonstrates the potential efficacy of combination therapy for treating multidrug-resistant microbial infections in premature infants.

Ethical approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its amendments, it was approved by the Institutional Review Board (IRB) of Tri-Service General Hospital (IRB#202315135, approved on July 7, 2023).

Declaration of patient consent

The authors certify that they have obtained appropriate consent forms from the legal guardians of the patient(s). In the form, the guardians have given the consent for the images and other clinical information of the patient(s) to be reported in the journal. The guardians understand that the name(s) and initials of the patient(s) will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Morrison L, Zembower TR. Antimicrobial resistance. Gastrointest Endosc Clin N Am 2020;30:619-35.
2. Teerawattanapong N, Panich P, Kulpokin D, Na Ranong S, Kongpakwattana K, Saksinanon A, *et al*. A systematic review of the burden of multidrug-resistant healthcare-associated infections among intensive care unit patients in Southeast Asia: The rise of multidrug-resistant *Acinetobacter baumannii*. Infect Control Hosp Epidemiol 2018;39:525-33.
3. Wei HM, Hsu YL, Lin HC, Hsieh TH, Yen TY, Lin HC, *et al.* Multidrug-resistant *Acinetobacter baumannii* infection among neonates in a neonatal intensive care unit at a medical center in central Taiwan. J Microbiol Immunol Infect 2015;48:531-9.
4. Jean SS, Hsieh TC, Hsu CW, Lee WS, Bai KJ, Lam C. Comparison of the clinical efficacy between tigecycline plus extended-infusion imipenem and sulbactam plus imipenem against ventilator-associated pneumonia with pneumonic extensively drug-resistant *Acinetobacter baumannii* bacteremia, and correlation of clinical efficacy with in vitro synergy tests. J Microbiol Immunol Infect 2016;49:924-33.
5. Liang W, Liu XF, Huang J, Zhu DM, Li J, Zhang J. Activities of colistin- and minocycline-based combinations against extensive drug resistant *Acinetobacter baumannii* isolates from intensive care unit patients. BMC Infect Dis 2011;11:109.
6. Yang H, Chen G, Hu L, Liu Y, Cheng J, Li H, *et al. In vivo* activity of daptomycin/colistin combination therapy in a Galleria mellonella model of *Acinetobacter baumannii* infection. Int J Antimicrob Agents 2015;45:188-91.
7. Sy CL, Chen PY, Cheng CW, Huang LJ, Wang CH, Chang TH, *et al.* Recommendations and guidelines for the treatment of infections due to multidrug resistant organisms. J Microbiol Immunol Infect 2022;55:359-86.
8. Isler B, Doi Y, Bonomo RA, Paterson DL. New Treatment Options against Carbapenem-Resistant *Acinetobacter baumannii* Infections. Antimicrob Agents Chemother 2019;63:e01110-18.
9. Nakwan N, Usaha S, Chokephaibulkit K, Villani P, Regazzi M, Imberti R. Pharmacokinetics of Colistin Following a Single Dose of Intravenous Colistimethate Sodium in Critically Ill Neonates. Pediatr Infect Dis J 2016;35:1211-4.
10. Mastrolia MV, Galli L, De Martino M, Chiappini E. Use of tigecycline in pediatric clinical practice. Expert Rev Anti Infect Ther 2017;15:605-12.
11. Bosso JA, Chan GM, Matsen JM. Cefoperazone pharmacokinetics in preterm infants. Antimicrob Agents Chemother 1983;23:413-5.
12. Satlin MJ, Lewis JS, Weinstein MP, Patel J, Humphries RM, Kahlmeter G, *et al.* Clinical and laboratory standards institute and European committee on antimicrobial susceptibility testing position statements on polymyxin B and colistin clinical breakpoints. Clin Infect Dis 2020;71:e523-9.