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Aztreonam–Avibactam as Salvage Therapy in Carbapenem Resistant Klebsiella Pneumoniae Infection with Renal Failure and Neurological Risk

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ABSTRACT

We describe the first documented use of Aztreonam–Avibactam under compassionate use for treatment of Metallo-β-lactamase–producing Klebsiella pneumoniae infection in our country. The patient achieved full clinical and microbiological cure without recurrence, and no adverse events occurred. This case underscores the therapeutic potential of Aztreonam–Avibactam in managing multidrug-resistant Gram-negative infections with limited treatment options.

Keywords: Carbapenem Resistant-Klebsiella pneumonia; Aztreonam-avibactam; MBL-Klebsiella; XDR- Klebsiella

Key Messages: Aztreonam–avibactam can serve as a safe and effective salvage therapy for Metallo-β-lactamase–producing, carbapenem-resistant Klebsiella pneumoniae infections, even in patients with renal failure and neurological risk, offering a promising option where treatment choices are extremely limited.

INTRODUCTION

Antimicrobial resistance (AMR) is a major global threat, with carbapenem-resistant Enterobacterales (CRE) listed as critical priority pathogens by WHO. [1] Klebsiella pneumoniae ranks first, followed by E. coli. CRE infections are associated with high mortality, [2,3] limited therapeutic options, and rapid spread in ICUs. [4] Colistin, once a mainstay, has nephrotoxicity rates exceeding 36% and is now reserved as a last-line drug. [5] While ceftazidime–avibactam is effective against OXA-48 CRE, it fails against Metallo-β-lactamase (MBL) producers and carries seizure risk, especially in renal or neurological disease. [6] Aztreonam–avibactam, a novel fixed-dose combination, retains activity against MBL-producing Enterobacterales, offering a critical therapeutic option. We report its use in a patient with post–cardiac arrest VA-ECMO, complicated by neurological injury, renal failure, and carbapenem-resistant Klebsiella pneumoniae infection—clinical conditions where both Colistin and ceftazidime–avibactam posed high risk.

CASE HISTORY

A 24-year-old male with a three-day history of fever and two days of intermittent retrosternal chest pain suffered sudden unresponsiveness at home on 19 June 2025. He was brought to the emergency department approximately 15–20 minutes later, unresponsive and pulseless. Advanced cardiac life support was initiated, with return of spontaneous circulation achieved within 15 minutes. He was intubated, and ECG revealed accelerated junctional rhythm; echocardiography showed severe Left Ventricular (LV) dysfunction with regional wall motion abnormalities, consistent with acute anterior wall myocardial infarction complicated by cardiogenic shock (SCAI E→D).Risk assessment revealed a SAVE score of four (predicted survival 48%), VIS of 141, and markedly reduced cardiac power output (0.43). Informed consent was obtained for Veno-arterial extracorporeal membrane oxygenation (VA-ECMO), initiated at 13:30 via right femoral arterial (21 Fr) and left femoral venous (25 Fr) cannulation, with distal perfusion cannula placement. Coronary angiography revealed a critical LAD lesion, treated with IVUS-guided PCI. An intra-aortic balloon pump (IABP) was placed for LV unloading. Anticoagulation was maintained with heparin (ACT target 140–160 seconds), and haemoglobin was kept above 10 g/dL with transfusions. Over 48 hours, vasopressor requirements decreased and LV function improved.

On 21 June, the patient developed left lung collapse due to a mucopurulent plug requiring bronchoscopy. Multiplex Biofire film array panel revealed methicillin-resistant Staphylococcus aureus (mecA-positive) and Klebsiella pneumoniae producing CTX-M-type extended-spectrum β-

lactamase (ESBL). Antibiotics were escalated to Meropenem and vancomycin, later confirmed by cultures. He developed acute kidney injury with rhabdomyolysis and was initiated on continuous renal replacement therapy (CRRT).On 22 June consequent to improved hemodynamics, ECMO weaning was initiated and was successfully decannulated from ECMO on Day five of admission. Neurologically despite sedation was withheld he remained minimally responsive. MRI brain revealed hypoxic–ischemic encephalopathy (HIE) with bilateral frontoparietal and occipital cytotoxic oedema and multiple small acute infarcts. On 25 June, percutaneous tracheostomy was performed.

Shortly afterward, he developed new-onset fever, increasing oxygen requirements, and radiographic signs suggestive of ventilator-associated pneumonia (pVAP). Repeat ET aspirate cultures grew extensively drug-resistant (XDR)/Carbapenem resistant Klebsiella pneumoniae, which demonstrated in-vitro susceptibility only to the combination of ceftazidime-avibactam with aztreonam by elution method, and colistin. Given the known seizure risk associated with ceftazidime and the patient's documented HIE, the ceftazidime-avibactam and aztreonam combination was deemed unsafe. Colistin was initiated as a bridging option; however, the patient's renal function further worsened and continued to be febrile despite 72 hours of colistin indicating its clinical failure. Considering these limitations and clinical deterioration, a decision was made to initiate the novel β-lactam/β-lactamase inhibitor combination of aztreonam-avibactam under compassionate use. He was continued on intermittent haemodialysis and dose Aztreonam avibactam was adjusted as per creatinine clearance. [7]

Over subsequent days, the patient showed marked clinical improvement, including resolution of fever, progressive decrease in oxygen requirements, and improved ventilatory parameters. Repeat endotracheal cultures showed no growth, indicating successful microbiological cure. Tracheostomy was decannulated on 9thJuly; and he was discharged home on 14th July after 26 days of hospital stay. He didn't have any elevation of hepatic enzymes or diarrhea **(Figure 1) (Table 1)**

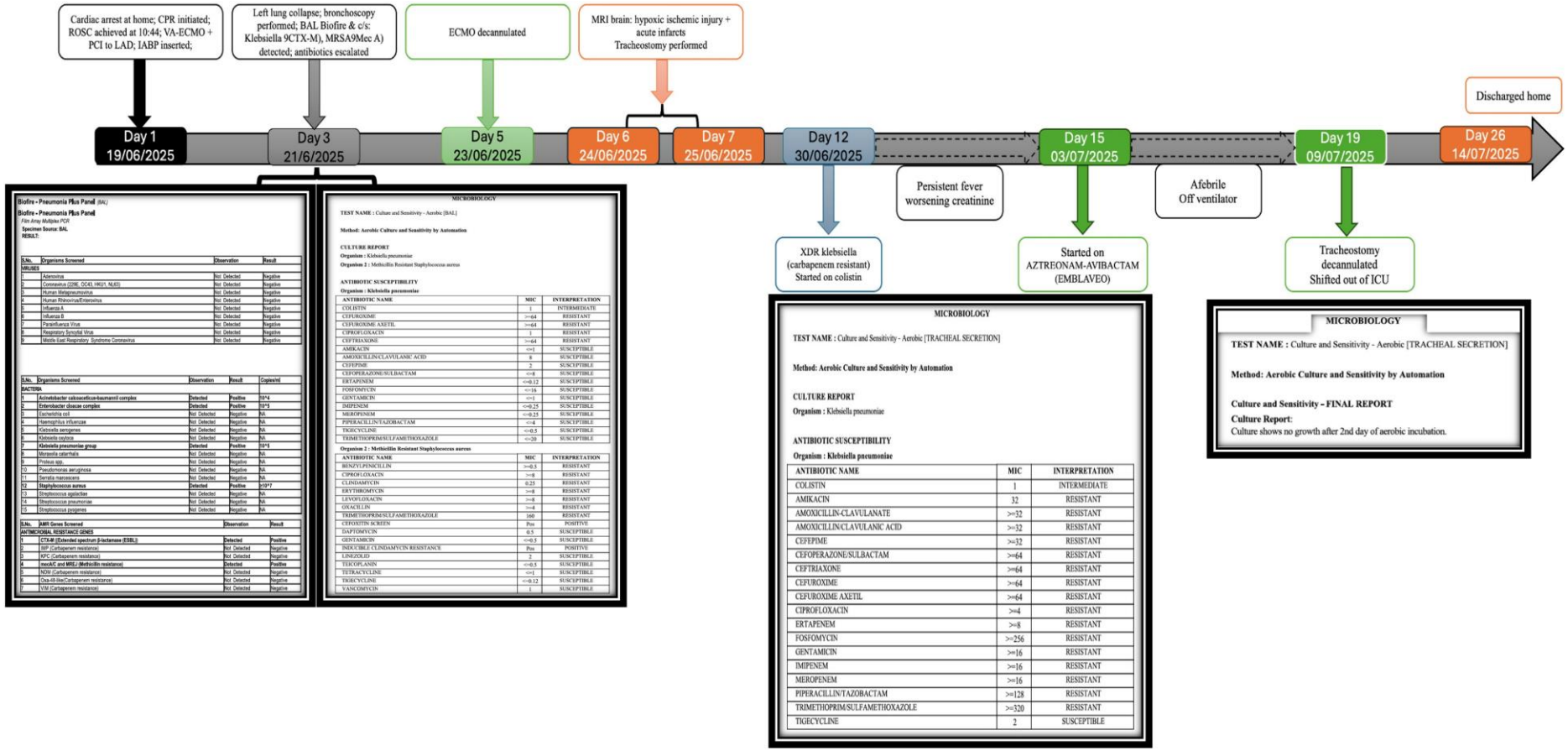

Figure 1: Timeline of Events

Table 1: Laboratory markers trend, CRP- C- reactive protein, PCT-Procalcitonin.

DATE	30/6	01/7	02/7	03/7	04/7	05/7	06/7	07/7	11/7	14/7
S.UREA (mg/dl)	140	128	185	157	90	151	130.9	98.9	87	106
Creatinine (mg/dl)	5.9	5.31	7.65	6.56	4.44	6.71	5.66	4.55	3.89	2.3
CRP (mg/L)	212			284			172	91		5
PCT (ng/dl)	4			4.5				1		
Total Bilirubin (mg/dl)	6.34						5.39		2.25	1.8
SGPT (U/L)	88								18	14
SGOT (U/L)	373								55	34

DISCUSSION

The rise of extensively drug-resistant (XDR) gram-negative pathogens, particularly Klebsiella pneumoniae producing Metallo-β-lactamases (MBLs), has posed significant therapeutic challenges in the critical care setting. Infections caused by MBL-producing Enterobacterales are particularly difficult to treat due to their resistance to nearly all β-lactams, including carbapenems, and often limited susceptibility to last-line agents such as colistin, which carries significant toxicity. The Infectious Diseases Society of America (IDSA) [8] currently recommends using a combination of ceftazidime-avibactam (CAZ-AVI) with aztreonam (ATM) for such infections .

Our patient developed pVAP due to XDR Klebsiella pneumoniae, susceptible only to colistin and the combination of CAZ-AVI plus aztreonam. However, the patient had suffered hypoxic-ischemic encephalopathy (HIE) post-cardiac arrest and was at high risk for seizures. Given that ceftazidime has been associated with neurotoxic adverse effects, including seizures, its use was avoided. Colistin was initiated but led to worsening renal function with signs of critical illness neuromyopathy (CINM), necessitating an alternative treatment strategy.

Aztreonam-avibactam (ATM–AVI), offers a novel and rational alternative. Avibactam, a non-β-lactam β-lactamase inhibitor, inactivates Amblers class A, C, and some class D β-lactamases, while aztreonam remains stable against MBLs. Their combined use provides broad-spectrum activity against MBL-producing Enterobacterales. Unlike the CAZ-AVI + ATM combination, Aztreonam avibactam simplifies

administration by providing optimized pharmacokinetic/pharmacodynamic (PK/PD) exposure and eliminates the risk of neurotoxicity associated with ceftazidime.

Although comprehensive real world clinical data on Aztreonam avibactam are still emerging, The ASSEMBLE trial [9] specifically targeted MBL-positive infections showed clinical cure rates of 42% for aztreonam-avibactam in comparison to best available therapy. 28-day all-cause mortality rates for aztreonam-avibactam and best available therapy were eight percent (8%) and 33%, respectively. Regarding the safety profile both the Rejuvenate [10] and Revisit trial [11] showed most common adverse effect being mild transaminitis followed by diarrhoea. Our patient didn't have either of them and had clinical and microbiological cure.

CONCLUSION

To the best of our knowledge, this is the first documented case of successful treatment with aztreonam–avibactam administered under compassionate use for a patient infected with metallo-β-lactamase–producing Klebsiella pneumoniae, with no adverse events reported during therapy.

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