



Background

- Acinetobacter baumannii* is a gram-negative, non-lactose fermenting coccobacilli isolated in many healthcare-associated infections and is one of the most resistant-prone pathogens [1]
- Given the various resistance pathways, combination therapies have been suggested, often including polymyxin B, high-dose ampicillin/sulbactam, and rifampin [2]
- Penicillins are well known for their potential to cause neurotoxic manifestations including encephalopathy, non-convulsive status epilepticus, myoclonus, and seizures [3,4]
- These toxicities are more commonly seen with increased doses, prolonged duration of therapy, and in the presence of impaired renal function [3,4]
- Similarly, several case reports have noted neurotoxic side effects associated with polymyxin use. However, the more notable neurologic toxicities include paresthesias and ataxia, with less frequent reports of convulsions and seizures [3,4]

Isolate1 (Final)
 Aerobic Blood Cult Vial
Acinetobacter baumannii complex
 Results read back and confirmed by Infection Control
 5/4/20
 Ceftazidime etest = 256 ug/mL Resistant
 Polymyxin B etest = 0.75 ug/mL Research use only
 Eravacycline = 17mm Research use only

Isolate
Acinetobacter baumannii

MIC (mcg/ml)		
Amp/Sulb	4	Resistant
Cefazolin	>=64	Resistant
Cefepime	>=64	Resistant
Ceftriaxone	>=64	Resistant
Ciprofloxacin	>=4	Resistant
Gentamicin	4	Susceptible
Pip/Tazo	>=128	Resistant
Tobramycin	4	Susceptible
Trim/Sulfa	>=320	Resistant
MIC (mcg/ml)		
Amikacin ETEST	256	Resistant
Meropenem ETEST	32	Resistant
Minocycline ETEST	32	Resistant

Figure 1: Susceptibility report from blood culture in Case 1

Patient Cases

We will now present 2 cases of patients who developed seizure-like activity while receiving combination therapy for resistant *Acinetobacter baumannii* infections.

Description	Case 1	Case 2
Gender	Male	Male
Age	56	69
PMH	Pre-diabetes Obesity	HTN DM HLD
Admitting diagnosis	COVID-19	COVID-19
Culture-organisms	Blood and Respiratory cultures – MDR A. <i>baumannii</i>	Respiratory culture – MDR A. <i>baumannii</i> , ESBL <i>Proteus mirabilis</i>
Electrolytes (mEq/L)	Na: 133 K: 3.6 Ca: 9.7 Cl: 97	Na: 135 K: 3.5 Ca: 9.7 Cl: 101
CBG (mg/dL)	167	191
Antibiotics on the day of suspected seizure	Ampicillin-Sulbactam and polymyxin	Ampicillin-sulbactam, rifampin, and polymyxin
Day of therapy	7	1
Concerning findings	Twitching episode	Seizure vs myoclonic movements
Medication given for seizure	Midazolam 2mg IVP	Midazolam infusion 10mg/h
EEG Done	Yes	No
Antibiotics readjusted	Discontinued	Amp/sulbactam frequency decreased
Other documented seizures	Possible seizure episode noted one day prior to described event	None
Naranjo Algorithm Score	4; possible adverse drug reaction (ADR)	3; possible adverse drug reaction (ADR)

Cases Continued

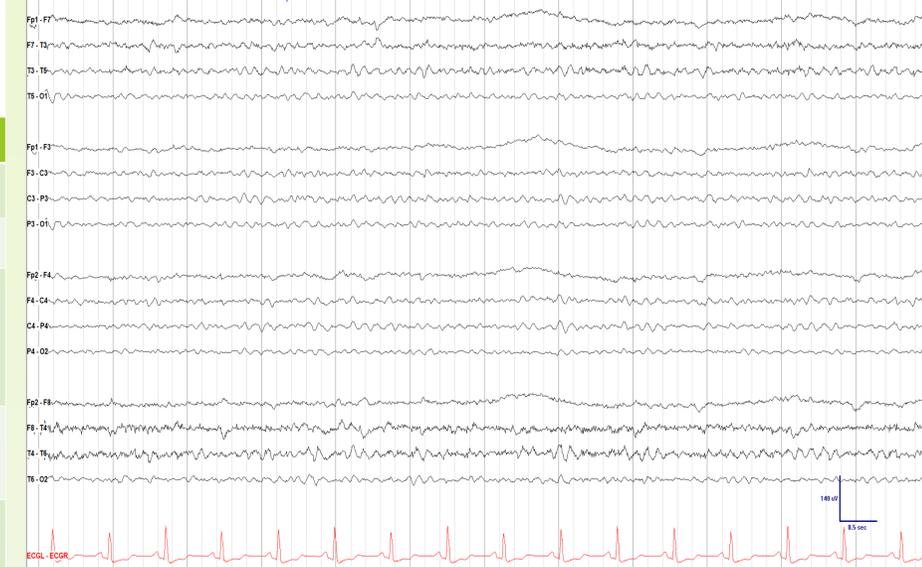


Figure 2: EEG report from Case 1: "Abnormal EEG due to slowing of the background and diffuse slowing which is indicative of a nonspecific diffuse disturbance of cerebral activity"

Discussion

- Neurologic toxicities can have significant implications and could sometimes be fatal; fortunately, both our patients had resolution of their events with minimal medical intervention required and no long-term sequelae
- Based on previously documented neurotoxicities of polymyxin and beta-lactams, the combined antimicrobials could have been possible contributing factors
- We used the Naranjo Algorithm to assess causality of the adverse drug reaction to the antimicrobials; scores of 4 and 3 respectively indicated a possible ADR
- In conclusion, combination therapy with polymyxin and high-dose ampicillin/sulbactam can result in neurotoxicity; therefore, patients must be monitored throughout therapy and adjustments must be considered if toxicities occur

References

- Peleg, A., Seifert, H. and Paterson, D., 2008. *Acinetobacter baumannii*: Emergence of a Successful Pathogen. *Clinical Microbiology Reviews*, 21(3), pp.538-582.
- Spellberg, B. and Bonomo, R., 2015. Combination Therapy for Extreme Drug-Resistant *Acinetobacter baumannii*. *Critical Care Medicine*, 43(6), pp.1332-1334.
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- Sutter, R., Ruegg, S. and Tschudin-Sutter, S., 2015. Seizures as adverse events of antibiotic drugs. *Neurology*, 85(15), pp.1332-1341.