CEFEPI ME INDUCED NEUROTOXICITY: A CASE REPORT.
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Introduction
- Cefepime is a fourth-generation cephalosporin with excellent activity against multi-drug-resistant gram-negative organisms and pseudomonas.
- Multiple side effects have been associated with cefepime, the most common of which are hematologic in nature. Cefepime is also predominantly excreted renally, so patients with renal impairment are at higher risk of side-effects.
- Rarely, it can also cause neurotoxicity, which has been well-described in the literature, with studies describing generalized tri-phasic waves (GTW) on Electro-Encephalography (EEG).
- This Cefepime induced neurotoxicity (CIN), is more common in elderly patients, patients with renal dysfunction and those with prior neurologic insults.

Case Presentation
- A 79-year-old female with a past medical of newly diagnosed small cell lung cancer with metastatic lesions to the brain and associated seizures presented to the hospital for evaluation of altered mental status.
- Initial Physical Examination was significant for frank confusion but no focal deficits or neurologic defects. She was subsequently found to have a urinary tract infection (UTI) and hyponatremia. Initial CT scan of her head was negative for acute processes.
- She was initially started on ceftriaxone for UTI treatment and her antibiotic regimen was eventually broadened to cefepime at 2 grams Q8 hours after she was noted to be increasingly febrile with consolidation on chest imaging.
- By day 4 on cefepime, she developed worsening encephalopathy, with worsened confusion and physical examination showing development of bilateral upper extremity myoclonus.
- An EEG was obtained which revealed no seizure activity but showed abnormal biphasic and triphasic waves.
- Cefepime was discontinued with a slow resolution of her encephalopathy by day 1 of discontinuation and eventual discharge. She was seen outpatient and was noted to be doing well.

DISCUSSION
- This represents a complex case of acute encephalopathy with multiple potential causes including infectious, malignancy, electrolyte, and medication-induced (Metabolic causes).
- Her encephalopathy was initially thought to be infection/electrolyte induced but worsened despite appropriate treatment. Development of a myoclonus prompted an EEG evaluation which revealed characteristic triphasic waves described as generalized periodic discharges.
- This patient has risk factors predisposing her to cefepime induced neurotoxicity, including her advanced age, metastatic disease, and electrolyte abnormalities. Her worsened encephalopathy was objectively caused by cefepime, given the high dose of cefepime (2 grams three times a day). Presence of myoclonus, treatment of alternative causes and rapid resolution with discontinuation of cefepime.
- This case serves as an excellent teaching case regarding differentials for acute encephalopathy. It also adequately shows unique identifiers for cefepime induced neurotoxicity including physical examination and EEG findings.

CIN
Background: Described in the literature as early as 1999 in a patient with ESRD who developed myoclonus and seizures and was found to have high cefepime levels.
Presentation: Presents mostly in patients with renal dysfunction, increased blood brain barrier (BBB) Permeability secondary to neurologic insult or CNS infection, and the elderly. Especially common with inappropriately dosed cefepime.
Pathophysiology: Mechanism is hypothesized to be secondary to GABA inhibition by cefepime, though not fully understood.
Differential diagnosis: Other causes of toxic/metabolic encephalopathy including electrolyte, infectious, other medications. CIN is typically a diagnosis of exclusion, but neurologic symptoms and EEG findings support a diagnosis of CIN.
Management: CIN is treated with cefepime discontinuation. Rarely dialysis is indicated for severe presentations, especially in patients with poor renal function. Convulsive seizures and non-convulsive status epilepticus require antiepileptics.

REFERENCES