Neurology Case

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CC: Abnormal Movements
73 y.o. F

- Transferred from an OSH for valve replacement for paravalvular leak with CHF, Group B Strep Bacteremia, and AKI requiring CRRT.
- Initially required pressors, but at time of consult, she is metabolically and hemodynamically stable
- Neurology consulted for 5 hours of encephalopathy with abnormal movements
PMH

- Mechanical AVR and MVR, 16 years prior, secondary to Rheumatic Heart Failure
- Afib
- CHF with AICD
- Pulmonary HTN
- Pacemaker
**Medications**

- Argatroban gtt (HIT)
- Risperidone
- Hydrocortisone
- Cefepime
- Levaquin
- Vancomycin
- Historical Review of medications did not reveal any additional significant meds
Vitals 24 hours: Afebrile, O2 93-100%, Pulse 71 – 110, BP: (96-121)/(50-61)

- General/Mental Status: Eyes Open, Follows Simple Commands, nonverbal, tracks around room
- CN: blinks to threat, PERRL, no nystagmus, symmetrical face, strong gag reflex, tongue midline
- Motor: Diffuse bilateral asynchronous tremor/myoclonic movements, moves all four extremities
- Sensory: withdraws to painful stimuli equally
- Reflexes: 1+ bilateral and symmetric. Negative Babinsky.
Where?

What?
Ddx: Myoclonus + Encephalopathy

- Metabolic: liver failure, renal failure, hyponatremia, hypoglycemia, Hashimoto's encephalopathy
- Medication Induced: opioids, anticonvulsants, TCAs, SSRI, antipsychotics, anesthetics, multiple antibiotics, ifosfamide
- Encephalitis
- Hypoxic/post-hypoxic
- Seizure
Hospital Course

- Basic labs stable
- CK wnl, risperidone held anyway. TSH wnl
- CT head unremarkable
- EEG: diffuse encephalopathy
- Could not obtain LP secondary to Argatroban/Hypotension

- Cefepime was held. Continued on Vanc, Levaquin, Zosyn
- Myoclonus/tremor resolved 3 days later, Encephalopathy improved
Hospital Course Continued

• Started again requiring pressors. Still afebrile.

• Hypotension worsened, required intubation. Zosyn changed to Meropenum. Micafungin added.

• Hypotension worsened to the point that CRRT had to be held. Electrolytes became unregulated. Family agreed to make her DNR. She coded and passed away.
Cefepime Neurotoxicity - Characteristics

- Altered Level of Consciousness, Myoclonus, Tremor, Seizure (Especially NCSE), Psychosis, Global Aphasia.
- All reports are with renal failure (though not all on dialysis)
- All reported are >50 yo
- Mean onset was 3-5 days (Range 1-10 days)
- Most are renally dosed
Cefepime Neurotoxicity - Seizure

• 1945: Epileptogenic activity of beta lactam antibiotics. Seizures in experimental animals after intraventricular injections of penicillin

• 2012 FDA safety announcement: dose adjust Cefepime in patients with renal impairment secondary to seizures, specifically NCSE. At this time, 60 cases were reported.

• One cases series suggests that NCSE is rare compared to other neurologic manifestations
Cefepime Neurotoxicity - Pathophysiology

• 4th generation cephalosporin; Broad Spectrum

• Normally, CSF concentration is low. It is not lipophilic, and there is active transport from CSF to back to the blood.

• In renal failure, there is inhibition of the active transport by accumulation of toxic organic acids which increases the CSF concentration

• Sepsis can also increase the permeability of the BBB

• Reduced clearance: 1/2 life normally 2-2.5 hours. If creatinine clearance is <10ml/min, half life is 13-22 hours
Cefepime Neurotoxicity - Pathophysicsology

• Build up of drug itself or metabolite: N-methylpyrrollidine metabolite

• Competitive antagonism of GABA by a portion of antibiotic molecule. May also decrease GABA release from nerve terminals

• Exact mechanism of neurotoxicity not completely understood
Cefepime Neurotoxicity - Treatment

- Low drug-protein binding, enables efficient removal of unbound fraction by hemodialysis
- 70% can be removed by dialysis
- Blood and dialysate flow determine characteristics of dialysis – difficult to determine individual pharmacokinetics
- Unclear evidence if intensive dialysis would decrease mortality/morbidity
Cefepime Neurotoxicity - Prognosis

- Not well known

- Some reports, early diagnosis = better prognosis

- Some studies suggest partial/complete recovery following withdraw

- One series, all patients died (range 1-42 days). Many of these patients had some improvement and then neurologic tableau

- Mortality of sepsis in ICU = 20-50% Even higher with renal failure
References


References


