

Cefepime Induced Neurotoxicity in an ICU Patient

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Introduction

Many antibiotics, especially beta-lactam containing medications, are known to be neurotoxic and can cause symptoms including encephalopathy, aphasia, myoclonus, seizures, and nonconvulsive status epilepticus [1]. Approximately 85% of the drug is excreted by the kidneys, and only a few cases of Cefepime-induced neurotoxicity have been reported in patients with impaired kidney function after dose adjustment [2]. This is a case of Cefepime-induced neurotoxicity that resolved with discontinuation and clearance of this drug by hemodialysis.

Case Report

A 69 year old female, with a past medical history of Coronary Artery Disease, Hypertension, Hyperlipidemia, End stage renal Failure, and depression, presented to the emergency department for management of dry gangrene. She lived alone at home and was able to perform all of her daily activities. She denied any history of alcohol or drug abuse. During her hospitalization, she did not receive any of her home medications. On admission, she was alert, awake and oriented, and had no complaints. Her white blood cell count was 4.9. Procalcitonin was not obtained. She received empiric antibiotic treatment including Cefepime, Metronidazole, and Vancomycin which were renally dosed as needed. On the first hospital day, she was evaluated by the Infectious Disease team. Metronidazole was discontinued at that time. Later the same day, she became disoriented to time and was noted to be anxious, requiring Lorazepam 1.5 mg, as well as 25 mg diphenhydramine for sleep. She was continued on Cefepime and Vancomycin. Over the next few days, she had a gradual decrease in mental status. During this time, she remained afebrile, and her infectious markers were normal, including CBC, ESR and CRP. On the fourth day, she was noted to have agitation and required 2 mg of Haloperidol. On the sixth day, she was found unresponsive, hypotensive, and seizing. She was intubated for airway protection, transferred to the ICU, and started on vasopressors for hypotension. For seizures patient was given 1 gm of Levetiracetam. However, seizures continued so she was started on a Midazolam drip, at which point seizures resolved.

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The differential diagnoses of her altered mental status were infection, neurological causes, and medications. Infectious causes were dismissed because her labs were normal. Most medications were eliminated as causes because she was not receiving any of her home medications during her hospital stay. Her home medication of sertraline was not suspected as a cause. Even though sertraline remains in the blood for a prolonged period of time, this medication is not effected by convention hemodialysis. Delirium was evaluated as a cause. However, confusion assessment method for ICU (CAM-ICU) was negative. Therefore, the suspected cause was an antibiotic.

The only medication she consistently received during the time of symptom progression was cefepime. By hospital day six, Cefepime was the suspected cause of her symptoms so the medication was discontinued.

On hospital day 7, a blood sample that had been drawn before hemodialysis on hospital day four revealed a serum cefepime concentration of 140ug/ml. The minimum inhibitory concentration for cefepime is 7 ug/ml. The patient had received her regular scheduled doses of cefepime on day 4 and 5. On day eight, serum cefepime concentration before and after hemodialysis, respectively was 19.3ug/ml and 2.1ug/ml. Upon stopping cefepime and enhancing elimination with hemodialysis, patient's symptoms began to improve. After hospitalized for 15 days, her mental status was at baseline, and she was discharged to a rehabilitation facility.

Discussion

Though many cases have reported on Cefepime induced neurotoxicity, time to diagnose is delayed because of low suspicion after dose adjustment in high risk patients. Risk factors include critical illness, chronic kidney disease, and dosing errors [3]. Cefepime induced neurotoxicity presents as confusion, aphasia, agitation, coma, myoclonus, seizure, and nonconvulsive status epilepticus. Neurotoxicity occurs at Cefepime levels of greater than 22mg/L,

altered mental status at levels greater than 48.1 mg/L, and seizures at levels greater than 60 mg/L [4].

Five major groups of antibiotics are known to cause neurotoxicity- Carbapenems, Fluroquinolones, Isoniazid, Metronidazole, and those containing beta-lactam rings, as the beta-lactam ring itself is known to be neurotoxic. Cefepime contains the neurotoxic beta-lactam ring [5].

Primary treatment of Cefepime-induced neurotoxicity is discontinuing the drug. Seizures are treated with either benzodiazepines or barbituates because other antiepileptics are ineffective. Dialysis is an effective treatment to remove 60-70% of the drug.

Conclusion

Risk factors for Cefepime induced neurotoxicity include critical illness, chronic kidney disease, and dosing errors [3]. In these high risk patients who develop unexplained neurologic symptoms, Cefepime should always be considered as possible etiology. Even with dose adjustment in renal impaired patients, Cefepime should be considered a cause for altered mental status, and serum levels should be checked promptly to prevent further neurologic consequences.

References

1. Fugate JE, Kalimullah EA, Hocker SE, Clark SL, Wijdicks EF, et al. (2013) Cefepime neurotoxicity in the intensive care unit: a cause of severe, underappreciated encephalopathy. *Crit Care* 17: R264.
2. Barbhaiya RH1, Knupp CA, Forgue ST, Matzke GR, Guay DR, et al. (1990) Pharmacokinetics of cefepime in subjects with renal insufficiency. *Clin Pharmacol Ther* 48: 268-276.
3. Garces EO, Andrade de Anzambuja MF, da Silva D, Bragatti JA, Jacoby T, et al. (2008) Renal failure is a risk factor for cefepime-induced encephalopathy. *J Nephrol* 21: 526-534.
4. Lamoth F, Buclin T, Pascual A, Vora S, Bolay S, et al. (2010) High cefepime plasma concentrations and neurological toxicity in febrile neutropenic patients with mild impairment of renal function. *Antimicrob Agents Chemother* 54: 4360-4367.
5. Grill MF, Maganti RK (2011) Neurotoxic effects associated with antibiotic use: management considerations. *Br J Clin Pharmacol* 72: 381-393.

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