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Case Report

CEFEPIME INDUCED ENCEPHALOPATHY: NATURAL COURSE AND SYMPTOMS OF TWO PATIENTS

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BACKGROUND

Intensive care units are breeding grounds for resistant organisms, necessitating early and aggressive anti-microbial therapy. Cefepime is a fourth generation cephalosporin known for its extended spectrum of activity against Gram-positive and Gram-negative bacteria, more so than any other drug in its class. Widespread utility can also be attributed to the fact it is an antipseudomonal agent; cefepime is carefully reserved to treat severe infections and cases with known multidrug resistance. A key characteristic that serves to differentiate cefepime among other cephalosporins is its ability to resist degradation by beta-lactamases; making cefepime a front-line agent for treating Enterobacteriaceae.

Cefepime is minimally metabolized by the liver and excreted nearly unchanged by the kidneys, making it imperative to renally dose. Illustrating its potency, the dosage must be cut in half as creatinine clearance approaches 11 mL/min.

Frequent adverse effects of cefepime include: positive Coombs test result without hemolysis (16%), rash (4%), elevated alanine aminotransferase (3%), fever/headache/pain (1%). Post marketing reports suggests that there is evidence for potential neurotoxicity, namely encephalopathy. Further reports have elucidated that the majority of severe encephalopathy cases have been in patients who necessitated renal adjustment of their doses (Jallon, *et al.*, 2000). However, the encephalopathy is reversible and symptomatology appears to resolve within 24-48 h of discontinuation, this underscores two things; first, that renal failure is a significant risk factor for cefepime-induced reversible encephalopathy and second, the importance of reducing dosages in renally impaired patients (Garces, *et al.*, 2008). Despite

case reports, the incidence and natural disease course of this side effect is under appreciated. Here we describe our experience in two separate patients, with resumption of cefepime therapy in one.

CASE 1

KR is a 62 year old male with a past medical history of hypertension and diabetes status post left nephrectomy in 2014 for renal cell carcinoma. In May of 2015 he presented with hyperglycemia, fevers, and generalized failure to thrive and was found to have an elevated white blood cell count and multiple liver abscesses. A drain was placed by interventional radiology, and the fluid grew out Acinetobacter and fungus. He recovered from this episode well, but represented later in the year.

He was transferred from an outside hospital in late December 2015 with suspicion of pneumonia and gram negative bacteremia. CT scan revealed erosive changes at T10-11 concerning for osteomyelitis, then confirmed on MRI. IR biopsy of T10-11 on 1/7/16 ultimately grew out Enterobacter. Infectious disease was consulted and he was discharged home on Cefepime.

Later that month, he re-presented with bilateral band like pain superior to the iliac crests and MRI revealed progression of the T10-T11 discitis and osteomyelitis. He also demonstrated myoclonic jerks effecting his head, neck, upper and lower extremities.

Due to the myoclonic jerking, infectious disease recommended discontinuing the cefepime. At that point they noted that myoclonus, "while rare, is a known adverse effect of this drug. The progression of the kidney dysfunction could have also increased the serum levels in his system." The drug was held and the patient went to dialysis, the next day his mental status and myoclonus were improved, but not yet resolved. However after two rounds of hemodialysis, the symptoms resolved and mental status returned to baseline. The patient was in an unfortunate situation at this point with limited treatment options for his osteomyelitis and diskitis, according to infectious disease he could be treated with cefepime, meropenem, or polymixin B; all three have serious side effects in the setting of renal dysfunction. It was then decided that the safest option was to restart cefepime, dosed for a creatinine clearance of <10. Per infectious disease recommendations cefepime was continued for 8 weeks while monitoring for appropriate renal dosing, and then discontinued without any further episodes of encephalopathy.

CASE 2

KC is a 49 year old female with a past medical history of hypertension, type 2 diabetes, hyperlipidemia, end stage renal disease status post a deceased donor kidney and pancreas transplant in 2003 on tacrolimus and also status post multiple percutaneous nephrostomy

tubes. She presented to us in October of 2016 after her nephrostomy tube dislodged at home as she repositioned herself on her couch. At presentation she reported that she had been experiencing some abdominal pain and about one week of fevers and chills. She had previously been admitted for a recent UTI with infectious disease consulted due to her history of multidrug resistant pseudomonas and enterococcus. Imaging revealed moderate hydronephrosis and therapy included placement of a percutaneous nephrostomy tube and infectious disease recommended initiating therapy with cefepime and ampicillin. Her hospital stay was uneventful until hospital day four when she told her nurse that she didn't understand what was going on. As the night progressed she had increasing difficulty answering questions, unable to rate or describe her pain, but still able to state yes when asked if she were uncomfortable. The night resident assessed the patient and with some encouragement she was able to name the president, day, month, year, town, and hospital. Nevertheless, a full set of vitals and labs were obtained including urinalysis, which was significant for 3+ blood and nothing else. It is also worth noting now that tacrolimus levels were routinely monitored and were within normal limits throughout the hospitalization. The following day the patient was even less communicative, labs remained normal, and she did respond to her nurse with a good amount of encouragement. However the following morning she became restless, tossing and turning in bed, completely unresponsive to the house staff. A CT head was obtained that was normal, arterial blood gas and all other routine labs were unremarkable, leading to a psychiatry consult. According to psychiatry there was no immediately obvious source of abnormality that would explain the episode of encephalopathy. They recommended a more extensive workup, with electroencephalogram and lumbar puncture, consideration for MRI. The same morning infectious diseases, who were still following the patient, recommended discontinuing cefepime as a possible cause of the encephalopathy. The antibiotic was discontinued and she improved significantly within one day, returning to baseline two days after the drug was stopped. She reported only minimal memory from the events, noting that the past few days all seemed "hazy".

DISCUSSION

Cefepime induced encephalopathy has been documented in the literature, particularly in patients with impaired kidney function. However, we believe that despite the case reports that exist in the literature, cefepime is still an underappreciated cause of altered mental status and the natural course cannot be completely appreciated without more cases. In the case of our patients, the recognition that cefepime was the offending agent allowed us to avoid invasive and expensive workups, including lumbar puncture, EEG, and MRI. Caution should be used when prescribing cefepime, especially in ICU patients who are already prone to mental status changes which may be dismissed as ICU delirium too quickly. Without signs of overt infection and in the presence of hemodynamic stability we recommend discontinuing cefepime before further workup of encephalopathy to conserve resources and limit invasive testing.

REFERENCES

1. Jallon, P., Fankhauser, L., Du Pasquier, R., Coeytaux, A., Picard, F., Hefft, S. and Assal, F. (2000). Severe but reversible encephalopathy associated with cefepime. ***Neurophysiol Clinique/Clin Neurophysiol***, 30(6), 383-386.

2. Garces, E. O., Azambuja, M. F. A. D., Silva, D. D., Bragatti, J. A., Jacoby, T. and Thome, F. S. (2008). Renal failure is a risk factor for cefepime-induced encephalopathy. **J Nephrol**, 21(4), 526-534.

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