中文題目: Cefepime 相關神經毒性發生在一位肺炎病人上

英文題目: Cefepime related neurotoxicity in a patient with pneumonia

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Background: Cefepime, a widely used 4th-generation cephalosporin for empirical use of hospital acquired pneumonia and neutropenic fever, has the risk of neurotoxicity even under appropriate dose. However, these events may not be easily identified due to patient's presentation. We report a patient with pneumonia suffered from consciousness change during Cefepime treatment.

Case presentation:

A 92-year-old female with a history of hypertension, left shoulder osteoarthritis status post operation, dementia, irritable bowel syndrome, mineral-corticoid insufficiency and late latent syphilis presented to our emergent department because of 1-day fever with cough and purulent sputum. She was treated as community acquired pneumonia initially and received FLOMOXEF plus Azithromycin as empirical antibiotics. Her baseline consciousness is clear with orientation to time, place and person. Fever and clinical symptoms became better on 6th day of hospitalization, but new onset fever developed on 8th day of hospitalization. After a series of examinations showed the progression of pneumonia and urinary tract infection, so we switched the antibiotics to cefepime (Dose: 2 gram every 12 hours) plus Daptomycin (250 minigram every day) to cover nosocomial pneumonia and Vancomycin-resistant Enterococci reported from urine culture. However, the patient presented disorientation with odd behavior on the 10th day of hospitalization, the 3rd day of cefepime use. Her consciousness became comatose status. Besides, frequent myoclonic jerk and limbs tremor were also noted. We discontinued Cefepime use and checked electrolytes and biochemistries data, which all showed in normal limit. Lumbar puncture was suggested but family refused due to too invasive, but previous data a month ago for neuro-syphilis survey showed no evidence of neuro-syphilis. Brain computed tomography (CT) and magnetic resonance imaging (MRI) and electroencephalography (EEG) were arranged. There was no brain lesions in CT or MRI, but EEG showed found epileptiform discharge so we prescribed anti-epileptic

drug with Levetiracetam for her. The patient got totally clear and well oriented without myoclonic jerk nor tremor on 15th day of hospitalization, the 5th day of discontinuation of Cefepime.

Discussion:

Cefepime related neurotoxicity is a serious event and need prompt discontinuation of using if clinically suspected. The common presentations of neurotoxicity are altered mental status, agitation, myoclonic jerk and seizure. The mechanism of neurotoxicity is probably related to inhibition of GABA-A receptors or inhibition of GABA neurotransmitter releasing. However, these presentations are common in critically ill patient and up to 15% of intensive care unit (ICU) patient may experience. As a result, early detection on presentation of neurotoxicity should be keeping in mind when clinicians using cefepime. Besides, Ayesha A. Appa and his colleagues showed that only 50% patient received correct cefepime dose in their study, so appropriate dose adjusted according to renal function is also important. The diagnosis of cefepime-related neurotoxicity is made by excluding other common etiologies of altered mental status. The EEG is also important as a diagnostic tool. Median onset time is 4 days after cefepime initiation and may recover 2 days after discontinuation. The managements include discontinuation of cefepime, anti-epileptic agents or hemodialysis.

Our report will remind clinical physicians again on the typical presentation, common risk factor and clinical course of cefepime related neurotoxicity. The most importantly is how to manage neurotoxicity. Another issue is how to prevent or, more precisely, predict the possibility of developing neurotoxicity. Common risk factor like old age, renal impairment (defined as glomerular filtration rate, GFR < 60 ml/min/1.73m2) and altered blood brain barrier. However, altered protein binding of cefepime caused by renal impairment or hypoalbuminemia, which may lead to unbound part of cefepime entering into the central nervous system.

Conclusion

Clinical physicians should be aware on cefepime related neurotoxicity when using on old age, renal impairment or risk of deficit of blood brain barrier patient. Further study on prediction scoring system may be the best way to prevent the event of neurotoxicity, and may need to become the standard operating procedures before clinicians starting the cefepime use.