Case Report

Cefepime Induced Encephalopathy Presented with Asymmetric Generalized Periodic Discharges in Electroencephalogram: A Case Report

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Cefepime-induced encephalopathy is not uncommon but easily ignored in clinical practice. The risk is higher in an elderly or patient with pre-existing renal dysfunction, especially when the cefepime dosage is not adjusted accordingly. In our case, the woman with recent right middle cerebral artery infarction had unexplainable consciousness disturbance after cefepime use for 3 days. Laboratory examination showed deteriorated of renal function, and electroencephalogram (EEG) showed asymmetric generalized periodic discharges (GPDs). After cessation of cefepime for 7 days, her consciousness recovered to baseline without other medical intervention, and EEG pattern resolved concomitantly. In conclusion, awareness of cefepime dosage adjustment in critically ill patient can reduce the risk of cefepime-induced encephalopathy, and EEG is helpful in early detection. Timely discontinuation of medication usually leads to full recovery of neurological symptoms.

Key words: cefepime-induced encephalopathy, generalized periodic discharges

Introduction

Cefepime, a broad spectrum fourth-generation cephalosporin, is frequently prescribed for infection control in critically ill patients. However, cefepime-induced neurotoxicity, manifesting as encephalopathy, myoclonus, and seizure, is often ignored by physicians. Early recognition can be achieved by characteristic findings in the electroencephalogram (EEG). Here, we presented a patient who had acute consciousness deterioration followed by cefepime use.

Case Report

An 81-year-old woman with hypertension and chronic kidney disease was admitted for

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suspecting acute right middle cerebral artery (MCA) infarction. Her condition stabilized in 2 weeks with clear consciousness and left hemiplegia. Brain magnetic resonance imaging (MRI) showed right MCA territory infarction with patent of large vessels in arteriogram (Fig. 1). Due to aspiration pneumonia and prolonged fever despite of ceftriaxone use, we shifted antibiotic to cefepime 4 g per day in divided dose. However, on the 3rd day of cefepime use, her consciousness acutely deteriorated and intermittent myoclonus over right limbs was observed. There were neither fever nor new focal neurologic deficits (ex. eyes deviation, pupil anisocoria, new onset limbs weakness). Laboratory examination revealed mild deterioration of renal function (creatinine: 1.1-1.6 mg/dL) without electrolyte imbalance or other metabolic disturbance. We had considered about repeat brain image study, but owing to without apparent evidence of new brain insult presented according to the neurological exam, we decided to discontinue cefepime first under the suspicion of cefepime induced encephalopathy. Initial electroencephalogram (EEG) revealed generalized periodic discharges (GPDs) in triphasic morphology, in the frequency of 2 Hz, and predominantly over the left hemisphere

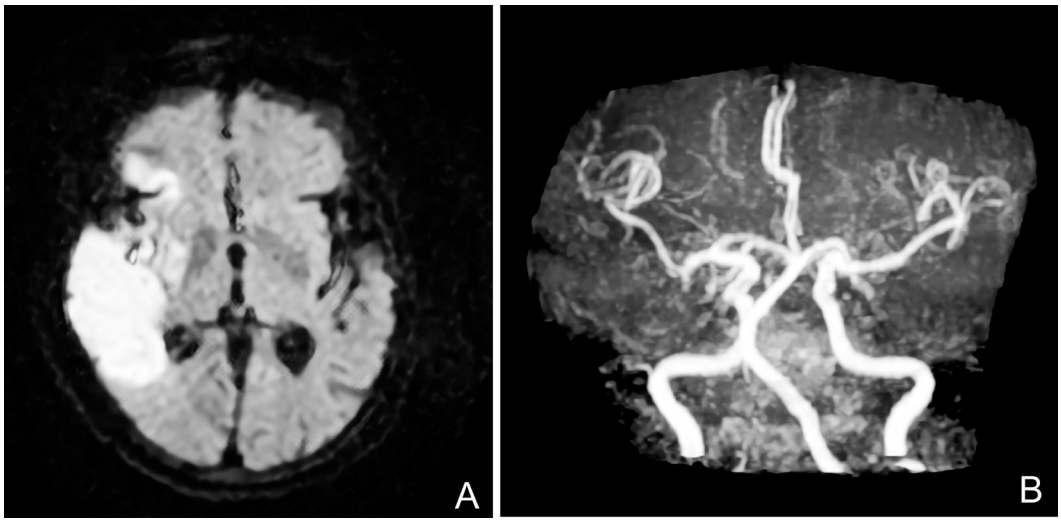

Fig. 1 Brain MRI showed right MCA territory acute infarction. (A) Right MCA acute infarction (B) Right MCA stenosis.

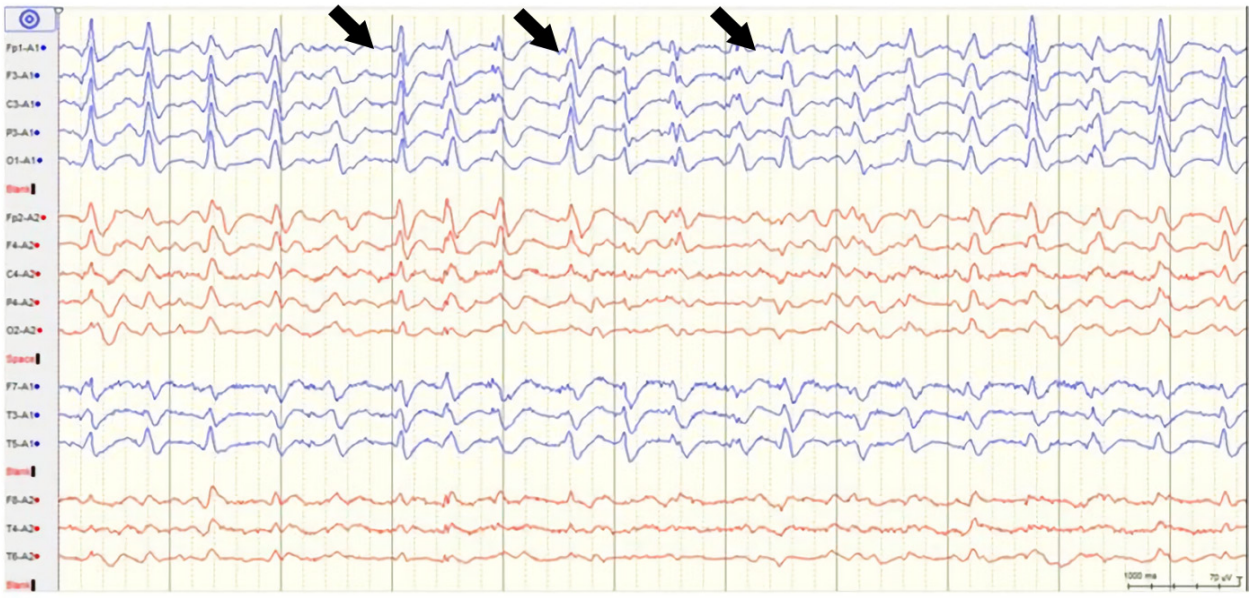

Fig. 2 Initial EEG after cefepime use for 3 days

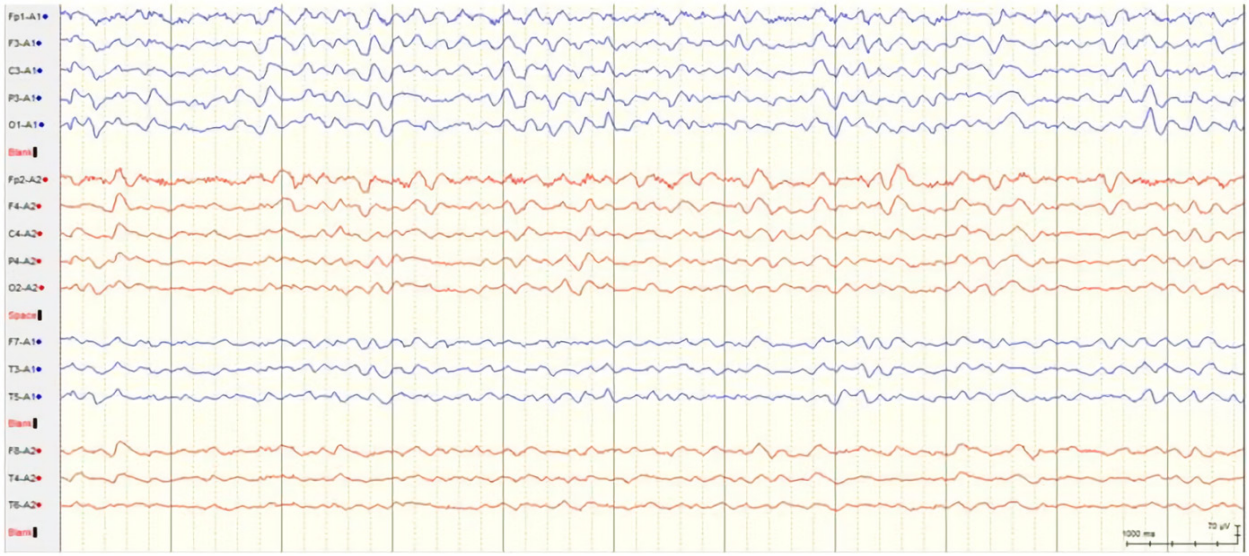

Fig. 3 Followed up EEG showed remission of periodic discharges

(Fig. 2). The possibility of non-convulsive status epilepticus was excluded by the absence of evolution in EEG frequency and amplitude, regional spreading, and reactivity to voice and pain stimulus. We simply discontinued cefepime without adding any anti-epileptic drugs. Her consciousness improved one week after cessation of cefepime, and follow-up EEG showed remission of GPDs (Fig. 3).

Discussion

Consciousness disturbance in critically ill patients is frequently encountered by physicians. Electrolyte disturbances, metabolic and infection-related encephalopathy are the most common etiologies. When managing patients with prolonged fever, we often choose broad-spectrum and highly cytotoxic antibiotics to cover nosocomial infection. However, the neurotoxicity of antibiotics is easily ignored and may lead to drug-induced encephalopathy.

Cefepime-induced encephalopathy is not uncommon. It typically manifests as impaired consciousness, myoclonus, and seizure.[1]

The critically ill patients with pre-existing renal dysfunction are particularly susceptible to cefepime induced neurotoxicity, especially when the cefepime dose is not adjusted accordingly.[2] The most acceptable management was discontinuation of cefepime or reduction of the dosage, which leads to clinical resolution of symptoms in most cases. Symptoms recovery typically occurs in a median of 2 days, emergent hemodialysis may hasten the recovery time.[3]

Early EEG may help us early identify cefepime-induced encephalopathy, which commonly shows characteristic GPDs. In previous reports, GPDs can present with varied morphology as slow-wave, spike-wave, or triphasic waves.[4] In clinical practice, it's sometimes difficult to define whether the periodic discharges (PDs) are presentations of non-convulsive status epilepticus (NCSE) or not. According to the consensus of EEG criteria of NCSE,[5] the periodic discharges are considered epileptogenic when the frequency is faster than 2.5 Hz. When the frequency is lower (between 0.5 – 2.5 Hz), additional conditions (ex: responsiveness to benzodiazepines (BZDs), subtle clinical phenomenon, or spatiotemporal evolution) must exist to meet the NCSE criteria. Nevertheless, empirical BZD injection may worsen consciousness and lead to respiratory insufficiency without invasive airway protection in comatose patients. As a result, it's challenging for physicians to decide whether to use anti-

epileptic agent or not, especially when overt clinical seizures are absent. In our experiences, continuously monitoring clinical presentations and following series of EEG may help us to adjust the management.

According to recent studies, PDs had been referred to acute neuronal destruction. Most experts regard PDs as a dynamic, unstable neurobiological status in between ictal-interictal continuum.[6] In our case, the PDs were more prominent over left hemisphere, which is contralateral to the infarction. The phenomenon may hint that PDs probably generated from neurons with preserved function. However, the mechanism of periodic discharge generation is not fully understood and further investigation is warranted.

In conclusion, cefepime-induced encephalopathy should be highly suspected if a patient presented with unexplainable consciousness deterioration after a period of cefepime use, especially with concomitant GPDs in EEG. Timely discontinuation of the medication usually leads to full recovery of clinical symptoms. When prescribing cefepime in elderly or patients with pre-existing renal dysfunction, we must adjust the dosage and closely monitor neurological condition.

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