ATYPICAL PRESENTATION OF CEFEPIME-INDUCED NEUROTOXICITY

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Introduction

Cefepime-induced neurotoxicity (CIN) is an increasingly recognized adverse drug reaction that occurs in up to 15% of critically ill patients receiving this fourth-generation cephalosporin[1]. Risk factors include renal dysfunction, excessive dosing, preexisting brain injury, and elevated serum concentrations[2]. We present a case of severe CIN with atypical presentation in a patient with chronic kidney disease, ultimately requiring prolonged intensive care

Case Summary

A 74-year-old male with a history of chronic kidney disease, congestive heart failure, diabetes mellitus, and hypertension presented to the emergency department with an acute onset of expressive aphasia. The patient was last known to be well at approximately noon of that day. On presentation, his speech was garbled, and he was only able to say "yes" and "okay." The patient was recently admitted for chronic diabetic left foot infection with osteomyelitis and was started on a six-week course of intravenous antibiotics, including cefepime, daptomycin, and metronidazole.

The next day, the patient's neurological status deteriorated significantly. His National Institutes of Health Stroke Scale (NIHSS) score changed from 6 to 13, and his speech continued to worsen. By the following day, he was completely unable to speak. Electroencephalography (EEG) revealed nonconvulsive status epilepticus. Given concern for cefepime-induced neurotoxicity in the setting of renal dysfunction, cefepime was discontinued, and the antibiotic regimen was changed to piperacillin-tazobactam. The patient was transferred to a higher level of care for continuous EEG monitoring.

Despite the discontinuation of cefepime, the patient's condition continued to deteriorate. He underwent a rapid sequence of intubation with mechanical ventilation. Weight-based loading and maintenance doses of levetiracetam (Keppra) were initiated. The patient developed worsening acute kidney injury refractory to diuretic challenges, requiring initiation of continuous renal replacement therapy (CRRT) approximately one week after presentation.

Case Summary

Following CRRT initiation and continued antiepileptic therapy, the status epilepticus eventually resolved. The patient experienced gross global deconditioning, diaphragm dysfunction, and ICU-associated weaknesses. MRI of the head revealed an area of restricted diffusion along the right posterior corpus callosum consistent with an acute ischemic infarct (Image 1).

Two weeks after admission, an attempt to extubate the patient failed due to increased work of breathing in the setting of profound neuromuscular weakness associated with his prolonged ICU course. The patient subsequently underwent tracheostomy and percutaneous endoscopic gastrostomy (PEG) tube placement. A tunneled dialysis catheter was placed shortly thereafter. The patient had difficulty tolerating intermittent hemodialysis, requiring significant vasopressor support. With worsening conditions and a poor prognosis, the patient's family decided to proceed with palliative care. The patient passed approximately three weeks after the initial presentation.

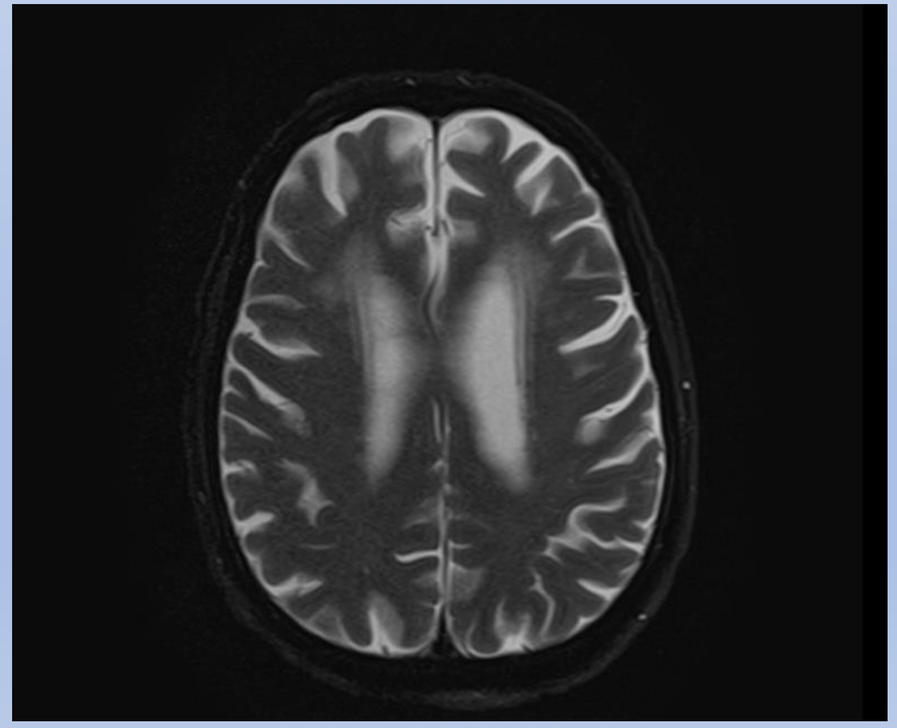

Image 1: Multiplanar multisequence MRI of the brain without contrast was performed. 3 mm focus restricted diffusion along the right posterior corpus callosum suspicious for acute infarct.

Discussion

Atypical Stroke-Like Presentation

- This case highlights CIN mimicking acute ischemic stroke—an increasingly recognized but underappreciated presentation
- Patient presented with isolated expressive aphasia and progressive neurological decline (NIHSS 6→13), leading to initial management as a cerebrovascular event with dual antiplatelet therapy rather than drug-induced neurotoxicity

Diagnostic Complexity

- This raises an important clinical question: Did CIN and true ischemic stroke coexist independently, or did the stroke develop secondary to prolonged status epilepticus and critical illness?

Conclusion

Cefepime-induced neurotoxicity can present with focal neurological deficits mimicking acute stroke, particularly aphasia. Clinicians should maintain a high index of suspicion for CIN in patients with risk factors who develop altered mental status, aphasia, or seizures while receiving cefepime. Early recognition, prompt discontinuation of the offending agent, and consideration of hemodialysis in severe cases are critical management strategies.

References

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