

Cephalosporin Induced Neurotoxicity-A Rare Cause of Acute Encephalopathy

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DIFFERENTIAL DIAGNOSES:

- Steroid induced psychosis
- Seizure like activity
- Toxic encephalopathy due to drug overdose/ toxins
- Metabolic encephalopathy due to sepsis/ infections etc.
- Acute delirium
- Posterior Reversible Encephalopathy Syndrome due to tacrolimus.

MECHANISM OF ACTION:

Upon crossing the BBB, cephalosporins may inhibit GABA release or competitively antagonize gamma-aminobutyric acid (GABA) A receptors; this resulting excitatory potential manifests as altered mentation.

TREATMENT:

- Antibiotic discontinuation
- Antibiotic-free interval with dose reduction
- Hemodialysis
- Benzodiazepine

CASE:

A 63 year old male with history of melanoma, marginal lymph zone lymphoma, recently treated for AML with stem cell transplant on 1/6/21, was hospitalized for diarrhea related to GI GVHD and sapovirus infection. He was treated with steroid taper along with tacrolimus for GVHD, and with nitazoxanide and immunoglobulins for sapovirus colitis and was started on IV cefepime for concern of sepsis secondary to pneumonia. He started displaying signs of confusion and expressive aphasia. He underwent bronchoscopy, BAL cultures grew *Stenotrophomonas* but he remained asymptomatic on room air. CT head and MRI brain did not show any acute abnormality. Neuro-oncology was consulted and EEG showed intermittent diffuse slowing, suggestive of widespread cerebral disturbance but no epileptiform discharges. Lumbar puncture CSF studies were negative for bacterial or viral meningitis. Despite being on broad spectrum antibiotics including cephalosporins, patient's mentation continued to deteriorate with dystonia, stereotypical movements, religious delusions, emotional lability. He was treated with IV benzodiazepine and haloperidol recommended by Psychiatry with concern for diagnosis of possible hyperactive catatonia. Cephalosporins were discontinued on 3/20/22 due to possible risk of contributing to encephalopathy. Patient showed marked improvement in mentation within 36 hours. The ultimate working diagnosis was cephalosporin induced toxicity.

CLINICAL AND IMAGING FINDINGS:

- Reduced consciousness
- Confusion
- Psychosis (hallucinations, delusions)
- Agitation
- Convulsion
- Tremor
- Delirium
- Coma
- Myoclonus
- Cerebellar toxicity
- Language dysfunction
- EEG: Tri-phasic waves/ Multi-focal sharp waves/ Non-convulsive status epilepticus / Generalized slowing/ Myoclonic status epilepticus

PREDISPOSING FACTORS:

- Older age group
- Reduced renal clearance
- Underlying neurological disease
- Increased inflammation of blood brain barrier
- Critically sick
- Supratherapeutic dosing

CITATIONS:

1. Payne LE, Gagnon DJ, Riker RR, et al. Cefepime-induced neurotoxicity: a systematic review. *Crit Care*. 2017;21(1):276. Published 2017 Nov 14. doi:10.1186/s13054-017-1856-1
2. Keerty D, Shareef NA, Ramsakal A, Haynes E, Syed M. Cefepime-Induced Encephalopathy. *Cureus*. 2021;13(2):e13125. Published 2021 Feb 4. doi:10.7759/cureus.13125