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Case Report

Cefepime Neurotoxicity in a Patient Undergoing Hemodialysis: A Case Report

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Abstract

Neurotoxicity is a rare complication of cephalosporin therapy. This side effect has been reported mainly in patients with renal insufficiency. Patients with chronic renal failure treated with cefepime can be more sensitive to neurotoxicity despite dose adjustment. We report a 65-year-old male patient who underwent hemodialysis treated with cefepime who experienced neurotoxicity while receiving adjusted dose cefepime.

Introduction

Cefepime is a widespectrum, fourth-generation cephalosporin. It has enhanced activity against certain gram-negative bacilli [1]. It is also active against the Enterobactericeae, that have a broad-spectrum, inducible, chromosal Amp C beta-lactamase (Enterobacter, indol-positive Proteus, Citrobacter and Serratia) [2]. Approximately 85 percent of the drug is excreted via the kidney, and adverse events in the Central Nervous System (CNS) related to encephalopathy have been reported in patients with decreased renal function [3]. The development of cefepime-induced encephalopathy seems to be related to the severity of impairment in glomerular filtration [4]. Neurotoxicity in patients with renal failure and treated with cefepime has been reported sporadically [3].

We present a patient with spondylodiscitis and chronic renal failure treated with cefepime in whom neurotoxicity arised as a side effect.

Case Report

A 65-year-old male patient who underwent hemodialysis for 9 months admitted to our clinic with a diagnosis of spondylodiscitis. Medical history revealed type II diabetes mellitus, hypertension, coronary artery disease and physiotherapy for back pain that lasted two months. During this therapy, he reportedly lost the ability of walking and felt severe pain while sitting. Lomber Magnetic Resonance İmaging (MRI) showed "infectious process through L2-L4 vertebrae and psoas muscle. Daptomisin 6 mg/kg/48 hours and cefepime 1 g/day were intravenously administered empirically. On the 9-10th days of treatment, patient experienced trembling in left hand, disorientation, insomnia and anxiety. Electroencephalogram (EEG) and brain MRI revealed normal findings (Figure 1). He was given valproic acid 500 mg twice a day with the diagnosis of myoclonus. Later, his mental functions as well as talking and eating worsened, and consequently delirium developed. Blood analysis showed Blood Urea Nitrogen (BUN) and creatinine, 68 mg/dL and 7,4 mg/dL (predialysis) respectively, aspartate aminotransferase (AST): 14 U/L, alanine aminotransferase (ALT): 11 U/L, sodium: 143 mm/L, potassium: 5.1 mm/L, clor: 100 mm/L. Therefore, cefepime was switched to ciprofloxacin due to its risk of neurotoxicity. Control cranial MRI and diffusion MRI tests revealed no discrete findings.The second EEG showed diffuse 5-6 cyc/s slow waves mixed with diffuse sharp waves (Figure 2), which were interpreted as heavily and diffuse cerebral disorder with epileptiform activity. Five days after discontinuation of cefepime treatment, his mental functions totally returned normal.

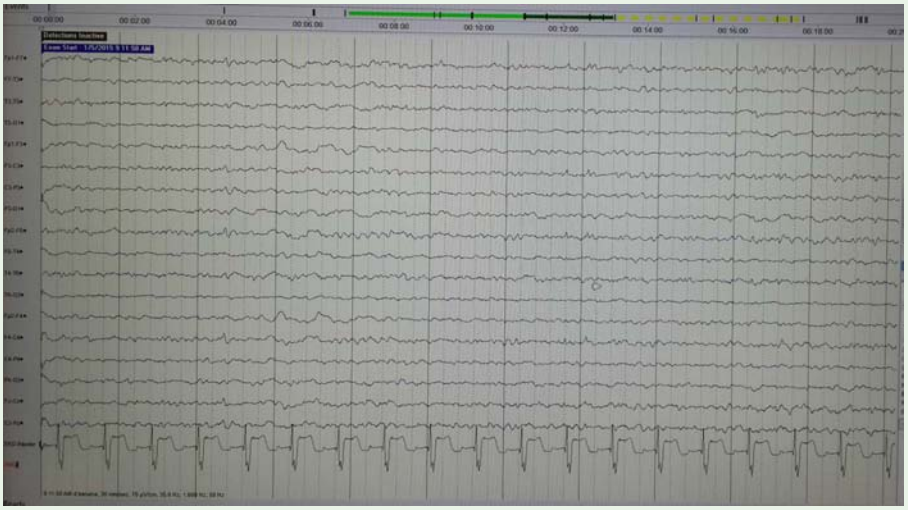

Figure 1: First EEG shows normal pattern before cefepime neurotoxicity developed.

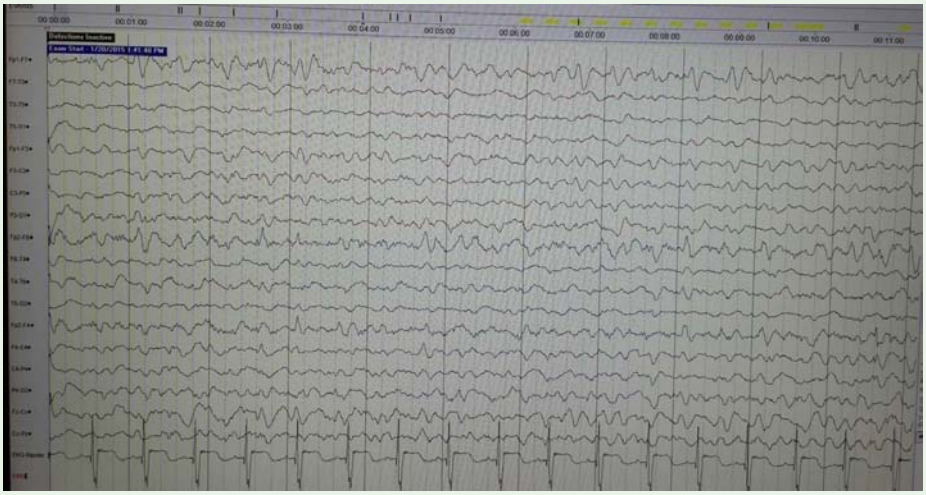

Figure 2: Second EEG shows the encephalopathy on the 10th day.

Discussion

Neurotoxicity is a rare complication of cephalosporin therapy. The underlying mechanisms have not been clearly understood. Decreased γ-amino butyric acid releasing from nerve terminals and subsequent increase dexcitatory neurotransmission, γ-amino butyric acid transporter system dysfunction, and induction of endotoxins along with there lease of tumor necrosis factor-alfa have all been proposed to explain the pathophysiology [5].

Cefepime is excreted mostly via glomerular filtration, and its neurotoxicity has been reported mainly in patients with renal insufficiency [6]. In June 2012, the United States Food and Drug Administration released a safety announcement reminding clinicians to adjust the dose of cefepime in patients with renal impairment because of the possibility of seizures [7]. In our patient, despite dose adjustment neurotoxicity arised. We think that this was due to metabolic encephalopathy induced by chronic uremia that made patient more sensitive to neurotoxicity.

Some previous studies reported that the time to onset of symptoms (e.g., decrease in consciousness, epilepsy, aphasia, convulsion, and coma) from the administration of cefepime was approximately 5 days (range 1-10 days) [6]. In our patient, the first symptom that can be relevant to cefepime neurotoxicity was myoclonus. Then impaired counsciousness and subsequently encephalopathy arised. In a retrospective study, it was found that the more common clinical manifestations of cefepime neurotoxicity included impaired consciousness, encephalopathy, and myoclonus [8]. The EEG was in normal limits when myoclonus occurred, that's why the treatment continued. However, when impairment in counsciousness and no other causative agent identified, neurotoxicity due to cefepime use was assumed as the second EEG revealed encephalopathy with diffuse sharp waves which strongly suggested cefepime-related neurolotoxical adverse events.

Diagnosis of cefepime neurotoxicity can be delayed due to multiple factors, including old age, severe infection, multiple

comorbidities and administration of multiple drugs. Unexpected neurological impairments should alert the physicians about possible cefepime neurotoxicty and when encountered, none of the other cephalosporins should be choosen instead.

In conclusion, patients with chronic renal failure treated with cefepime can be more sensitive to neurotoxicity despite dose adjustment.

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