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Case Report

Cefepime Induced Neurotoxicity Case Series (CIN)

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Abstract

Cefepime, classified as a fourth-generation cephalosporin, serves as a broad-spectrum antibiotic extensively used to treat infections caused by Gram-positive and Gram-negative bacteria. Our focus revolves around a case series involving five patients who initially sought hospitalization for unrelated conditions, but subsequently developed encephalopathy, all while being administered Cefepime. This antibiotic is recognized for its propensity to antagonize gamma-aminobutyric acid receptors, which hinders GABA release. Such effects are more pronounced in people with renal failure or impaired renal function due to increased central nervous system (CNS) penetration. Clinical manifestations include altered levels of consciousness, delirium, and occasionally seizures. The prompt cessation of Cefepime is crucial for treatment, with a notable improvement generally observed within 48 hours. This underscores the importance of vigilance in monitoring patients for potential neurological complications, particularly in those with renal dysfunction.

Keywords: Cefepime; Encephalopathy; Neurological Complications; Renal Dysfunction

Introduction

Cefepime obtained approval for use in the United States in 1996[1]with sanctioned applications for pneumonia, complicated urinary tract infections, skin and soft tissue infections, complicated intra-abdominal infections, and neutropenic fever. Within our hospital setting, Cefepime ranks as the third most frequently prescribed antibiotic in all indications, due to its notable activity against Pseudomonas and the proclivity to use piperacillin-tazobactam, which predisposes patients to acute kidney injury. Although cefepime-induced neurotoxicity (CIN) is recognized to occur in cases where Cefepime is administered without appropriate dose adjustment, it has also been observed in patients receiving the correct dosage. Consequently, the U.S. Food and Drug Administration (FDA) issued a safety advisory, recommending dose reduction for patients with renal dysfunction, specifically those with an estimated Glomerular filtration rate (GFR) less than 60 ml/min. CIN is typically reversible if early detection and discontinuation of Cefepime are achievable, which constitutes the definitive treatment. Rigorous monitoring, particularly through frequent neurologic examinations and evaluations of renal function becomes imperative, particularly in elderly individuals with compromised renal function or a history of previous central nervous system (CNS) injury. Through a comprehensive examination of cases, case series, and meta-analyses, we have detailed incidence, pathogenic mechanisms, risk factors, clinical manifestations, EEG abnormalities, and appropriate management strategies for CIN. Furthermore, a thorough analysis of all reported CIN cases has been conducted from multiple sources in the medical literature.

Methods

All of these cases were under admitted within the previous year and underwent a comparable diagnostic evaluation for encephalopathy. This evaluation included CT head, MRI brain, EEG, ammonia level, blood alcohol level, complete blood count (CBC), basic metabolic panel (BMP), arterial blood gas (ABG), thyroid stimulating hormone (TSH), urine analysis, blood culture, chest radiograph, and urine drug screen. They all presented to the hospital with symptoms that were not related to neurology.

Results

We present 5 cases of CIN in which the diagnosis was made after the exclusion of other common etiologies of altered mental status.

The predominant symptom observed in these patients was altered mental status/confusion, with all five patients exhibiting no renal impairment. Three out of the five patients showed EEG patterns indicative of diffuse slowing activity, consistent with toxic/metabolic encephalopathy, and exhibited a classic triphasic morphology.

All individuals witnessed a resolution of symptoms within 48 to 72 hours after stopping Cefepime. Both CT and MRI were negative for all patients, and urine drug tests, blood alcohol levels, and TSH values were all within normal ranges.

Discussion

We present a series of cases involving five patients who experienced Cefepime-induced toxicity. To our knowledge and based on our research, this marks the inaugural case series report featuring individuals with normal kidney functions. Neurotoxicity emerges as a relatively underreported and unrelated side effect of Cefepime in patients with normal kidney function. Although Cephalosporins are recognized for their potential to cause neurotoxicity, there is an elevated risk associated specifically with Cefepime[2].

Cefepime continues to be widely used in the treatment of infections caused by gram-positive and gram-negative bacteria. Its increased use is particularly evident in non-ICU settings, as highlighted in the report from our hospital pharmacy and the Pharmacy & Therapeutics (P&T) Committee.

Typically, only 10% of the serum Cefepime crosses the blood-brain barrier [3].However, due to inflammation-induced disruption of the blood-brain barrier and reduced protein binding capacity, there is an increased risk of elevated cefepime concentrations in the central nervous system (CNS). Therapeutic serum trough concentrations are generally identified within the range of 5 to 10 mcg/mL, but concentrations greater than 20 mcg/ml are associated with a substantial risk of neurotoxicity [4].

In conclusion, clinicians, including hospitalists and infectious disease specialists, should maintain a high index of suspicion for cefepime-induced neurotoxicity, even in patients with normal renal function. Risk factors include advanced patient age, liver disease, and preexisting neurological disorders [5].

Conflict of Interest: The authors declare that there are no conflicts of interest regarding the publication of this article.

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