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# CEFTRIAXONE INDUCED CHOREOATHETOSIS

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## ABSTRACT

Beta-lactam antibiotics are widely used for the treatment of various bacterial infections due to their broad spectrum of activity and favourable pharmacokinetic properties. In patients with impaired renal function, these antibiotics can lead to a range of neurological manifestations as a result of altered drug metabolism and pharmacokinetics. Here we present a case report of a 74-year-old woman with End stage Kidney disease who exhibited neurological symptoms after receiving intravenous ceftriaxone. It also underscores the importance of considering altered pharmacokinetics and potential neurological side effects when prescribing beta-lactam antibiotics in patients with impaired renal function. This case highlights the need to closely monitor patients for any neurological manifestations, particularly when using ceftriaxone, whichhas good central nervous system penetration and extended half-lives.

**KEYWORDS:** Choreoathetosis, Ceftriaxone, End Stage Kidney Disease.

## INTRODUCTION

Choreoathetosis (CAS) is the occurrence of involuntary movements characterised by a nonrhythmic throwing, flowing, and twisting movement disorder of one or more limbs. The development of choreoathetosis has been attributed to various etiologies, both neurological and systemic disorders, such as genetic and hereditary disorders, cerebrovascular diseases, systemic lupus erythematosus, connective tissue diseases, hyperthyroidism, hypoparathyroidism, post-streptococcal infection, focal cerebral infection, hyperglycemia, postanoxic and post-traumatic brain injury, etc.[1] Cases of drug-induced CAS have been rarely

reported till date. Apart from neuropsychiatric agents, significantly few other drugs have been related to itspresentation.

Ceftriaxone is a third generation semisynthetic cephalosporin with a very long half-life compared to other cephalosporins and is highly penetrable into the meninges, eyes and inner ear. It has a broad spectrum of activity against Gram-positive and Gram-negative aerobic, and some anaerobic, bacteria.[2] Due to its long half-life and easy penetration into the cerebrospinalfluid, ceftriaxone is often chosen to treat patients with end-stage kidney disease (ESKD).

Common adverse events attributed to ceftriaxone use are anaphylactic reactions, respiratory system disorders, immune system disorder, and gastrointestinal disorders, whereas nervous system involvement has rarely been mentioned.[3] Till date, 202926 Adverse drug reactions of Ceftriaxone have been globally reported to UMC,' Sweden through WHO program for international drug monitoring. Out of these only 5% are nervous system disorders and just 0.12% accounts for choreoathetosis.[4]

Hereby we describe a patient with ESKD complicated with choreoathetosis after the administration of ceftriaxone. Choreoathetosis disappeared without leaving any symptoms afterceftriaxone therapy was withdrawn.

## CASE REPORT

A 74 year old woman who is a known case of End Stage kidney disease with Type II diabetes mellitus, systemic hypertension, dyslipidemia, and status post right radical nephrectomy for renal oncocytoma. She was on conservative management for end–stage kidney disease. Her initial clinical presentation included altered sensorium, lethargy, and poor response. In addition to these findings, she had elevated white cell counts and C-reactive protein levels. She was also febrile with a temperature of 100$^{o}$F. She was administered IV. Ceftriaxone 1g twice daily for theprevention of bacterial infection. On the fifth day, her consciousness level suddenly deteriorated, and she developed choreoathetosis. It was characterised by truncal dyskinesia movements and choreiform movements of the bilateral lower limbs, primarily affecting the distal segments. The abnormal movements were not noticed during sleep. In addition to this, there were no significant findings in blood tests, blood culture and laboratory parameters. She was then suspected to have developed choreoathetosis due to Ceftriaxone therapy and hence it was discontinued. The patient's symptoms resolved rapidly upon

ceftriaxone withdrawal, suggesting a causal relationship with the reaction.

## DISCUSSION

Ceftriaxone is a widely used beta lactam antibiotic with a broad bactericidal spectrum. While itselimination half-life (T1/2) is 6–9 h in normal subjects, it prolongs to 16.6 hours in patients with ESKD, specifically in patients with creatinine clearance (CrCl) <5 mL/min/1.73 $m^2$.[5] Since it has a longer elimination half life and is not affected by hemodialysis, the administration of ceftriaxone is rational and practical to eradicate susceptible organisms in patients with severelyimpaired renal function.

Beta-lactam antibiotics, including ceftriaxone, have the ability to penetrate the blood-brain barrier and induce glutamate excess in the striatum and cerebral cortex. This disruption of neurotransmitter balance leads to neurological hyperexcitability disorders, which may manifest as a wide range of movement abnormalities and cognitive disturbances. Neurologic manifestations, such as myoclonus, asterixis, seizures and altered level of consciousness, may be induced in patients with impaired renal function receiving β-lactam antibiotics, which is due to drug accumulation because of altered pharmacokinetics. The underlying mechanisms of drug-induced choreoathetosis remains unclear, but impaired γ-butyric acid (GABA) modulation, cytokine release (i.e., TNF-α) regulated by bacterial endotoxin and the excess of glutamate, a neuroexcitotoxic neurotransmitter, have been hypothesised. Hence, the imbalance of excitatory and inhibitory motor control pathways within the striatum may cause the occurrence of involuntary movement disorder. Thus, glutamate exerts a significant influence on both cortical and subcortical striatal neurons, which leads to a variety of neurological disorders such as seizure, encephalopathy, in its marked excess within the brain.[6]

In the above case, the patient's symptoms were not noticed during sleep and neither seizure disorder nor central nervous system infection was likely. Furthermore, her symptoms resolved rapidly upon Ceftriaxone withdrawal, suggesting a causal relationship. The temporal relationship between the start of ceftriaxone therapy and the manifestation of choreoathetosis as well as the withdrawal of ceftriaxone and the disappearance of the symptom strongly indicated that ceftriaxone was a causative agent. The temporal relation of neurotoxicity associated with cephalosporins was reported to have a latency of 1–10 days after exposure and to resolve 2–7 days after withdrawal.[7] The severely impaired renal function alters the drug's pharmacokinetic profile leading to its accumulation that surpasses therapeutic level,

which is not seen in normal subjects. Hence, it's important to be mindful of this potential adverse reaction, especially in elderly patients with chronic kidney disease, even when they are prescribed the standard dosageof Ceftriaxone.[8]

On evaluation we could establish a 'probable' causal relationship between ceftriaxone and choreoathetosis using the WHO - UMC Causality Assessment Scale (Naranjo scale-5). The typeof ADR was evaluated according to Rawlins Thompson Classification and was found to be Type B. Severity was assessed using the modified Hartwig's Scale and Level 3 severity was found. According to WHO criteria, the seriousness of the reaction was revealed to be moderate, suggesting that it required therapeutic intervention and hospitalisation prolonged by 1 day but resolved in 24 h or change in drug therapy or specific treatment to prevent a further outcome.

Since this patient did not have a history of any such reaction due to ceftriaxone, this adverse drug reaction was unpreventable and our observation is supported by the Schumock and Thornton scale.

The clinicians thus need to be cautious when prescribing such antibiotics, especially those belonging to the beta lactam class and the potential for a class effect of beta-lactam antibiotics should be recognized.

## CONCLUSION

Our case report shows that even common antibiotics can sometimes cause unusual reactions, especially in patients with compromised renal function. This case serves as a reminder that even commonly prescribed antibiotics like ceftriaxone can lead to rare neurological complications in patients with ESRD. Healthcare providers should be vigilant for signs of neurotoxicity in this population and dose adjustments when necessary.

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## CONFLICT OF INTEREST

There are no conflicts of interest.

**ABBREVIATION**

CAS - Choreoathetosis

ESKD - End Stage Kidney Disease

UMC- Uppsala Monitoring Center

WHO-World Health Organization

GABA- Gamma Amino Butyric Acid

**REFERENCE**

1. Jankovic A, Lang AE: Diagnosis and assessment of Parkinson's disease and other movement disorders; in Daroff RB, Lankovic J, Mazziotta JC, Pomeroy SC (eds): Bradley's Neurology in Clinical Practices, ed 7. London, Elsevier, 2016; 223–249.
2. Richards DM, Heel RC, Brogden RN, Speight TM, Avery GS. Ceftriaxone: a review ofits antibacterial activity, pharmacological properties and therapeutic use. Drugs, Jun, 1984; 27: 469-527.
3. Sathirapanya P. Choreoathetosis is a possible adverse event of a commonly usedantibiotic. Case Reports in Neurology, Jul 11, 2017; 9(1): 81-5.
4. https://www.vigiaccess.org/
5. Losno Garcia R, Santivañez V, Battilana CA: Single-dose pharmacokinetics of ceftriaxone in patients with end-stage renal disease and hemodialysis. Chemotherapy, 1988; 34: 261–266.
6. Garcia, L., Santixañez, V., & Battilana, C. A. Single-dose pharmacokinetics ofceftriaxone in patients with end-stage renal disease and hemodialysis. Chemotherapy, 1988; 34(4): 261-266.
7. Roncon-Albuquerque R Jr, Pires I, Martins R, Real R, Sousa G, von Hafe P: Ceftriaxone-induced acute reversible encephalopathy in a patient treated for a urinary tract infection. Neth J Med., 2006; 67: 72–75.
8. Patel IH, Sugihara JG, Weinfeld RE, Wong EG, Siemsen AW, Berman SJ. Ceftriaxone pharmacokinetics in patients with various degrees of renal impairment. Antimicrobial agents and chemotherapy, Apr, 1984; 25(4): 438-42.