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Case Report

Cefixime induce non convulsive status epileptics: a neurotoxic effect

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ABSTRACT

Nonconvulsive status epileptics comprises a group of syndromes that display a great diversity regarding response to anticonvulsants ranging from virtually self-limiting variants to entirely refractory forms cephalosporins are thought to provoke seizure through inhibitory effects on gamma-aminobutyric acid (GABA) transmission and GABA receptors. Interference with GABA transmission result in pre-disposition towards excitatory neurotransmission, which can leads to seizures. Antibiotics can alter the serum concentration of anti-epileptic, resulting in seizures and anti-epileptic drugs toxicity.

Keywords: Cephalosporin and seizure, Neurotoxicity and seizure, Antiepileptic drugs

INTRODUCTION

Although non-convulsive status epileptics (NCSE) is known to be heterogeneous disorder with varied aetiology, the diagnosis of drug-induced NSCE has notably increased on recent years.[1] NCSE is a conditions in which electrographic seizure activity is prolonged and results in non-convulsive clinical symptoms, usually lasting >30 min.[2] Cefixime is a third-generation cephalosporin, commonly used in the treatment of serious gram-negative infections due to its broad antimicrobial spectrum, long half-life, and easy penetration into the cerebrospinal fluid.[3,4] Cephalosporins are thought to provoke seizures through inhibitory effects on gamma-aminobutyric acid (GABA) transmission.[5,6] Since GABA is the primary inhibitory neurotransmitter of the central nervous system, interference with GABA results in pre-disposition toward excitatory neurotransmission, which can lead to seizures.

CASE REPORT

A 56 years old male, epileptic patient resident of Yamuna Vihar, Delhi, presented to institute of human behavior and allied sciences, Dilshad garden, Delhi, with history of two episodes of generalized clonic tonic seizures in last 24 hrs. Patients was on oral anti-epileptic drug carbamazepine (900 mg/day) and levetiracetam (1250 mg/day) and was seizure free from last 6 months developed seizure followed the use of oral third

generation of antibiotic cefixime for acute pharyngitis. Patient has good compliance with no alteration in day to day activity.

On primary survey, airway, patent bilateral chest rise present, bilateral air entry equal, respiratory rate of 22/min, SPO2: 98% on room air. GCS, pupils 2 mm BERL, moving all four limb, no external injuries noted**.** The neurologic examination revealed change in mental status, and minimal response to noxious pain stimulation. There was no focal neurological sign, pathologic reflex, and neck stiffness.

Peripheries were cold and peripheral pulses well felt, CRT less than 2 sec, HR- 96/min, BP- 134/96 mm Hg. Blood sample collected and send to neuro biochemistry and neuro psychopharmacology lab for routine blood examination and therapeutic drug monitoring. Investigations revealed serum carbamazepine level (11 mg/l), serum levetiracetam level (19 mg/l), mild anemia (Hb: 11.3 g/dl), (TLC: 7.5×10^9 l), Normal liver and renal function tests. Urine routine and microscopy was normal. RBS random 112 mg/dl. Sr. calcium 9.1 mg/dl and sr. magnesium 1.6 meq/l. MRI brain showed symmetric area of prolongation and mild restricted diffusion seen in bilateral basal ganglia. The electroencephalograph (EEG) revealed continuous 2-3 Hz generalized sharp and wave (Figure 1). NCSE was diagnosed. He was than further treated with loading dose levetiracetam 500 mg and clonazepam 0.5 mg stat. He stayed on maintenance doses of levetiracetam (1250 mg/day) and carbamazepine (900 mg/day), clonazepam (1.5 mg/day). Repeated EEG revealed improved after anti-epileptic treatment (Fig. 2). As we discontinued cefixime, considering as a causative agent for NCSE, clinical symptoms improved 3 days after discontinuation of cefixime (1500 mg/day).

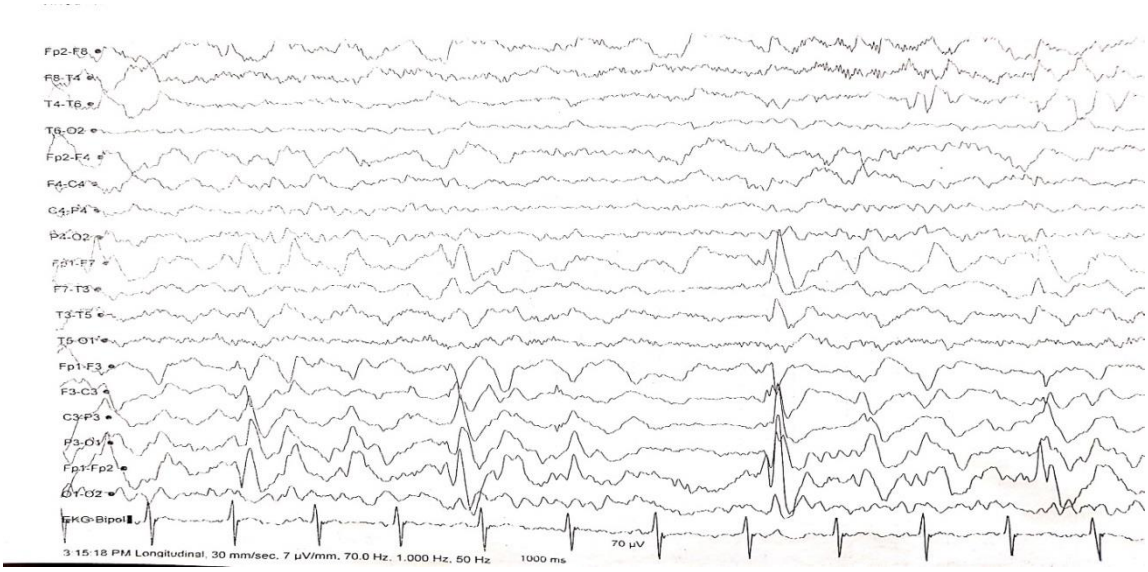

Figure 1: EEG (longitudinal bipolar montage) of a patient receiving cefixime shows diffuse slowing of the background, atypical triphasic waves, and multifocal sharp waves.

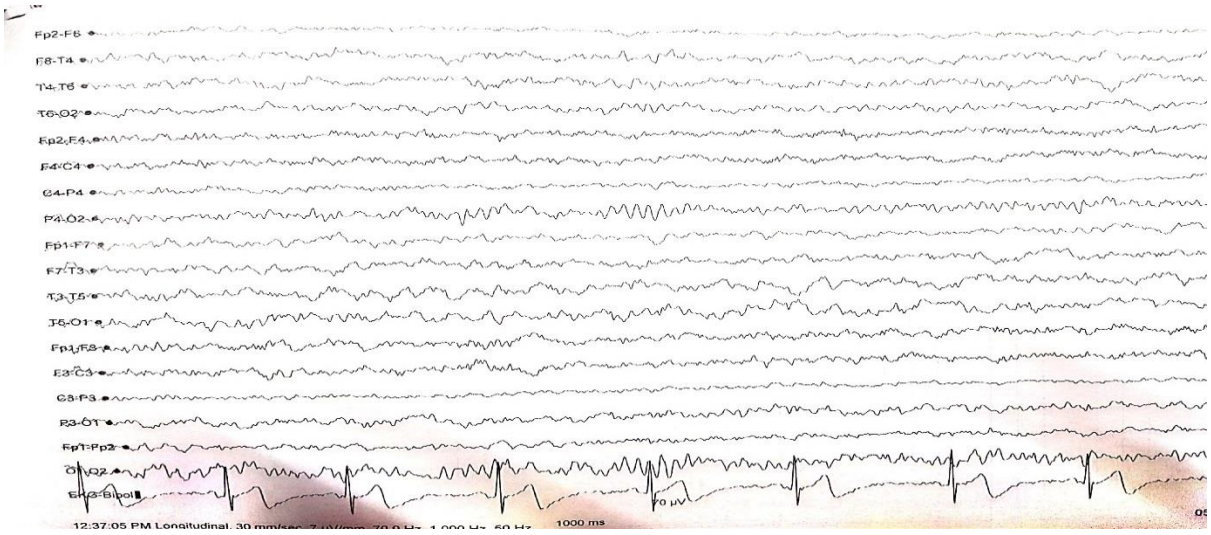

Figure 2: Normal EEG after one week of discontinuation of cefixime.

DISCUSSION

Present case report describes a case of seizure relapse in patient with well controlled seizure from last 6 months. Temporal relationship between the initiation of cefixime therapy and relapse of seizure, as well as withdrawal of cefixime and control of seizure strongly indicate that the ceftriaxone was the induction factor.

Beta (β) lactam antibiotics (i.e., penicillin's, cephalosporins, carbapenems and monobactams) are antibiotics widely used in clinical practice because of their higher antibacterial activity.[7, 8] The administration of β lactam antibiotics into cerebral ventricle's or subarachnoid space or directly to cerebral cortex of chicks, cats dogs, monkey and mice has been reported to induce a focal or generalized epileptic state initially characterized by spike and wave discharges which are followed by clear tonic-clonic or clonic seizures.[9,10]

The convulsant action of penicillin's and cephalosporins has been attributed to the inhibition of the GABA system.[11,12] The cephalosporins are a family of β-lactam antibiotics that contains the 7-amiocephalosporanic acid nucleus. They differ in their basic structure from the penicillin's in that they cephalosporins contain a six-membered dihydrothiazine ring fused to the β-lactam portion. The cephalosporins resemble penicillin's in their actions as both antibiotics and convulsant compounds.[7] Several investigator found that the ability of penicillin derivatives to produce a seizure is abolish by pencillinase.[13,14] Since the study support the idea that the β-lactam ring is an indispensable structural feature for epileptogenic activity cephalosporins.

CONCLUSION

Cephalosporins can cause seizures in epileptic and in non-epileptic patient. Cephalosporins attributed to inhibition of the GABA system, reduces threshold, increases severity of seizures and decreases the efficacy of clinically used anti-epileptic drugs.

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