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Case Report

Paediatrics Section

A Case Report of Fosphenytoin Induced Orofacial Dyskinesia in an 11-month-old Baby with Post-encephalitic Sequelae

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ABSTRACT

Fosphenytoin is used as an alternative phosphate ester prodrug to intravenous phenytoin for seizure treatment. Acute orofacial dyskinesia, secondary to phenytoin treatment is very uncommon. This case report gives the details of an 11-month-old baby girl, with post encephalitic sequelae, who developed orofacial dyskinesia during treatment with fosphenytoin. She was on fosphenytoin for the last 11 days. She presented with lip smacking movements on the 11th day of administration of fosphenytoin. At the time of presentation of orofacial dyskinesia, she found it difficult to keep her tongue inside her mouth and the involuntary movements subsided following the withdrawal of the drug. In this case, it was a probable cause of the relationship between the patient's symptoms and the use of fosphenytoin according to the causality assessment scales such as the Naranjo scale and the World Health Organisation (WHO) Uppsala Monitoring Centre causality assessment system. She had a score of six. Also, the reaction is not likely to be owing to coexisting diseases or drugs. Though fosphenytoin induced orofacial dyskinesia is infrequent, there is a need to consider the adverse effects of fosphenytoin as a differential diagnosis in all patients with a movement disorder in the course of fosphenytoin treatment.

Keywords: Anticonvulsant drug, Antiepileptic drug, Lip-smacking movement, Movement disorder

CASE REPORT

An 11-month-old baby girl was brought to the hospital with febrile status epilepticus and was admitted in the Paediatric Intensive Care Unit (PICU). The child was referred to the current hospital from a private clinic. She had a history of intermittent, high-grade fever since two days, one episode of vomiting and developed multiple episodes of Generalised Tonic Clonic Seizure (GTCS) since a day. The child had uprolling of eyes, tonic posturing of all limbs and urinary incontinence at the time of convulsions. Each episode of convulsions lasted for about three-five minutes and had post-ictal drowsiness of about 30 minutes. The child was developmentally normal, born at full term and breast feed for six months. There was no history of febrile convulsions and no family history of seizure disorder. Neurocutaneous markers were absent.

Vitals on admission were as follows: temperature 38.88° Celsius, pulse rate of 162 beats per minute, blood pressure of 90/80 mmHg, SPO_2 100%, Capillary Filling Time (CFT) less than three seconds and Capillary Blood Glucose (CBG) of 244 mg/dL. Seizure activity stopped after three anticonvulsant drugs were given; 1 mg stat dose of injection lorazepam, second dose of 0.5 mg lorazepam (0.05 mg/kg), three loading doses of fosphenytoin: first dose of 300 mg (30 mg/kg) followed by two subsequent doses of 150 mg (15 mg/kg) and one loading dose of phenobarbitone 200 mg (20 mg/kg). Also, the child was on oxygen therapy, maintenance fluids and injection paracetamol (100 mg if necessary). One stat dose of injection dexamethasone 1.5 mg and injection mannitol of 300 mg were administered due to the clinical suspicion of raised intracranial pressure. On examination the child was drowsy, Glasgow Coma Scale (GCS) of 9/15. Per abdomen examination revealed hepatosplenomegaly. In view of suspected meningitis, empirical injection ceftriaxone (1 g/day) was started.

On hospital day two, the child had no further episodes of convulsions, fever spikes were present and the sensorium was poor. Routine blood investigations revealed elevated neutrophils 78.4%, Erythrocyte Sedimentation Rate (ESR) of 50 mm in 1 hour and C-reactive protein of 44.3 mg/dL. Lumbar puncture revealed acellular sample with slightly elevated proteins 77 mg/dL and glucose 193 mg/dL. Computed tomography showed no abnormality. As the child's neurological state did not show significant improvement, parenteral acyclovir 100 mg, three times a day (10 mg/kg/dose) was started, suspecting viral encephalitis. The child was on maintenance dose of injection fosphenytoin 38 mg, two times a day (7.5 mg/kg/day) and injection phenobarbitone 25 mg, two times a day (5 mg/kg/day). Dengue Non-Structural Protein 1 (NS1) antigen test was negative.

As there were no further convulsions after day one, dose of fosphenytoin was reduced to 25 mg, two times a day (5 mg/kg/day) and phenobarbitone 15 mg, two times a day (3 mg/kg/day) on day three. Parenteral multivitamins were added to the therapy. On hospital day three (evening), the child again had one more episode of convulsion and the child was given supplemental oxygen, injection lorazepam 1 mg stat which resulted in cessation of convulsion after 40 seconds.

GCS (14/15) improved on day four and the child was started on nasogastric tube feeding. With a suspicion of metabolic disorder, Inborn Errors of Metabolism (IEM) cocktail was started. IEM screening was done and was found normal, hence IEM cocktail was discontinued. In view of persistent fever spikes, parenteral amikacin (40 mg, two times a day) was started.

Supervised breast feeding was started on day seven of admission and was shifted out of PICU to step down ICU as child's neurological state improved. Parenteral amikacin was stopped after the course. Child was readmitted in PICU due to an episode of convulsion, GTCS type, lasted for three-five minutes on the same day and conservative treatment with anticonvulsants were given. Neurologist opinion was taken. Electroencephalogram done was normal. MRI could not be done as child could not be sedated adequately for imaging.

On day 11, the patient developed lip-smacking movements as a symptom of orofacial dyskinesia [Video 1]. Fosphenytoin was stopped since it was suspected of inducing orofacial dyskinesia and treated only with oral phenobarbitone 5 mg/kg/day. Subsequently, the movement disorders gradually reduced and almost resolved. The final diagnosis was made as post-encephalitic sequelae based

on the presence of elevated proteins in CSF analysis, low cell count and clinical response to encephalitic treatment.

Child improved during the hospital stay, GCS was 15/15. Serial circumference monitoring was done and showed no increase in size. Examination of the child revealed inability to sit with support, partial head control. It was noticed that child was not fixating to light and mother's face. Ophthalmologist's opinion was taken and a suspicion of cortical blindness was entertained. Hearing assessment done showed normal bilateral pass of otoacoustic emission. Occupational therapy was given for three days.

On hospital day 21, the child was discharged. She was afebrile and convulsion free, on oral phenobarbitone (3 mg/kg/day). On follow-up evaluation, she remained stable with no recurrence of dyskinesia and a repeat MRI was done after one week and found to be normal. Also, the parents were advised to administer oral phenobarbitone to the child for a period of one year.

DISCUSSION

Orofacial dyskinesia is a movement disorder which is characterised by severe, involuntary, dystonic movements of the facial, oral and cervical musculature [1]. Drug induced dyskinesia is commonly seen with neuroleptics and antiparkinsonian drugs but may be observed occasionally with anticonvulsants also [2,3]. Fosphenytoin is a phosphate ester prodrug of phenytoin, has the similar pharmacological properties as that of phenytoin after enzymatic conversion with phosphatase [4]. Acute orofacial dyskinesia secondary to phenytoin treatment is very uncommon [5]. This reaction may take place at normal or toxic drug levels [6].

Rajasekharan C et al., reported a case orofaciolingual dyskinesia due to phenytoin; the difference from our case is that the patient was on oral phenytoin for the last 17 days before the development of orofacial dyskinesia and the child in our case developed orofacial dyskinesia after 11 days of IV administration of fosphenytoin. Also, that the patient presented with abnormal dyskinetic movements of face, perioral area, eyelids, nystagmus and choreiform movement of the tongue. García-Ramos R et al., also reported a case of phenytoin induced acute orofacial dyskinesia and in his case the patient exhibited choreic and dystonic movements of the mouth and tongue after few hours of receiving loading dose of phenytoin. The above reported cases were in elderly patients of age 60 and 80 years and in present case, occurred in an 11-month-old baby [5,7].

The incidence of anticonvulsant induced dyskinesia is significantly higher in patients with one or more of the risk factors such as polytherapy, focal brain lesion, mental retardation, toxic drug levels and concomitant neuroleptics [8]. The effect of phenytoin upon dopamine system is assumed to be one cause of provocation of involuntary movements. Phenytoin has been shown to possess dopamine receptor blocking properties in animal experiments [9]. Harrison MB et al., hypothesised that the differential effect of phenytoin on dopamine receptor subtypes can cause disturbance in the functional equilibrium of the basal ganglia output system that leads to orofacial dyskinesia [10]. In majority of cases, dyskinesia is resolved completely after phenytoin withdrawal [8,11]. Garcia-Ramos R et al., mentioned that multiple mechanisms of the phenytoin can induce movement disorders in the individuals but it is difficult to differentiate the mechanisms, with the currently available data. So he hypothesised that there will be an increase in dopaminergic and serotonergic activity in the striatum in case of phenytoin-induced dyskinesia and also an individual with underlying brain lesions or subclinical functional changes may be more likely to experience this drug-related dyskinesia [5].

In our case, the differential diagnoses were dyskinesia due to Hypoxic Ischaemic Encephalopathy or Encephalitis Sequelae or Fosphenytoin. As there was no MRI evidence of hypoxic damage, Hypoxic Ischaemic Encephalopathy was ruled out. Similarly MRI showed no evidence of encephalitis sequelae. The withdrawal of the Fosphenytoin brought about complete disappearance of all signs of orofacial dyskinesia within a short time. So the final diagnosis was made as fosphenytoin induced orofacial dyskinesia. The orofacial dyskinesia was probably due to fosphenytoin as assessed by Naranjo scale and the World Health Organisation (WHO) Uppsala Monitoring Centre causality assessment scales.

CONCLUSION

Although fosphenytoin induced orofacial dyskinesia is infrequent, there is a need to consider the adverse effects of fosphenytoin as a differential diagnosis in all patients with a movement disorder in the course of fosphenytoin treatment.

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