Case Report

Journal of Emergency Medicine Case Reports

Is Every Involuntary Movement Epileptic?

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Abstract

Introduction: Paroxysmal nonepileptic events are episodic changes in behavior, sensation, or consciousness that are similar to epileptic seizures but not associated with abnormal ictal brain electrophysiological discharges. Here, a case treated as epileptic seizure was presented in order to draw attention to paroxysmal nonepileptic events in differential diagnosis.

Case: A 4 years old girl sent to our hospital with the diagnose of status epilepticus due to change in her consciousness, contractions and abnormal movements in her body, arms and legs those started after taking 6 spoonfull syrup of Peditus® (Containing 120 mg paracetamol, 50 mg guaifenesin, 6.25 mg pyrilamine maleate, 5 mg phenylephrine hcl in 5 ml scale) and 5 Medikinet® 10 mg capsules (10 mg methylphenidate hydrochloride in 1 capsule). She was conscious and cooperate and has involuntary snake-like movements throughout her body on admission. The patient's movement disturbances thought as methylphenidate-induced choreoathetosis responded to given haloperidol treatment and any sign of poisoning were not observed in the patient's follow up.

Conclusion: Chorea side effects were observed in our patient but not any poisoning symptoms, who received a toxic dose of methylphenidate for her age. This suggests that methylphenidate, a central nervous system stimulant, may have therapeutic, toxic dose limits and side effects profile those associated with individual pharmacogenetic variations. Accurate distinction of chorea from drug-related paroxysmal nonepileptic events will ensure early effective treatment of patients and to protect patients from unnecessary drug risks.

Key words: Status epilepticus, Methylphenidate, Korea

Introduction

Epilepsy has an incidence of 40-50/100000 in the childhood age group and is characterized by spontaneous and repetitive seizures resulting from abnormal and excessive electrical discharge in cortical neurons[1]. The most important first step in the management of childhood epilepsy is to decide whether the event described is an epileptic seizure. Paroxysmal nonepileptic events (PNEs) are episodic changes in behavior, sensation, or consciousness that are similar to epileptic seizures but not associated with abnormal ictal brain electrophysiological discharges. While psychogenic seizures and cardiac events constitute the majority of PNEs; parasomnia (sleep gait, sleep terrors and nightmares), movement disorders, narcolepsy, breath-holding spells, Sandifer syndrome, and behavioral events are other types of PNE events. In the literature, it has been reported that PNE events constitute 23% of the patients followed up with a diagnosis of epilepsy in childhood with long-term video EEG[2]. Here, a case treated as epileptic seizure was presented in order to draw attention to paroxysmal nonepileptic events in differential diagnosis.

The Case

A four-year-old girl was referred to our hospital due to change in consciousness, convulsions, and abnormal movements in her body and limbs. Patient epicrisis revealed that the patient had taken 6 spoonfuls of *Peditus^{R}syrup* (5 ml spoonful containing 120 mg paracetamol, 50 mg guaifenesin, 6.25 mg prilamine maleate, and 5 mg phenylephrine HCl) by mistake ~1 hr before admission and was treated with gastric lavage and activated charcoal at the center of first admission. The patient was hospitalized and followed up, then began to have seizures, received two intermittent infusions of 0.25 mg/kg diazepam IV and 20 mg/kg phenytoin IV. Convulsions could not be stopped, and the patient was referred to our center with the diagnosis of status epilepticus. When patient anamnesis was further investigated, it was learned that the patient had also taken five Medikinet®10 mg altered release capsules (10 mg methylphenidate HCl in 1 capsule). The patient had no self or family history of epilepsy or movement disorder, and neuromotor development was appropriate for her age. At the initial evaluation

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Received: 28/08/2020 • **Accepted:** 26/12/2020
DOI: 10.33706/jemcr.787086

DOI: 10.33706/jemcr.787086
Journal of Emergency Medicine Case Reports 2021; 12(1): 1-3

of the patient, the airway was clear, spontaneous breathing and circulation were normal. Body weight was 20 kg (90p), vital signs were as follows: fever, 37.1°C; pulse, 131/min; respiratory rate, 24/min, blood pressure, 113/72 mmHg; conscious, and normal orientation and cooperation. Pupils were isocoric, light reflex was bilateral (+). The patient was able to speak meaningfully and regularly, and had involuntary snake like movements throughout the body (Video-1, Video-2). No pathology was detected in systemic examination of the patient. With the diagnosis of choreatetosis due to methylphenidate poisoning, the patient was administered with intramuscular 0.1 mg/kg haloperidol. Abnormal movements stopped within five minutes. Hemogram, kidney and liver function tests, cardiac enzymes, coagulation tests, and paracetamol levels were within normal limits and ECG was evaluated as normal. Patient was discharged without any problems after 48-hours of follow-up.

Discussion

Diazepam and phenytoin treatments were previously administered to our patient with the suspicion of epileptic seizures because of convulsions and abnormal movements in the patient's body, arms, and legs. Patient was referred with a preliminary diagnosis of status epilepticus because she did not respond to the treatment. Persistent snake-like movements were observed in the whole body, and the patient was able to respond normally to verbal stimuli with proper content and articulation. The gold standard in the diagnosis of epileptic generalized tonic clonic seizures is 24-hour video EEG monitoring. However, at first glance, PNE generalized movement disorders can be separated from generalized tonic clonic seizures with no change in consciousness. Difficulties in assessing the state of consciousness, especially in young children, can be misleading.

Chorea is defined as a short, involuntary, and hyperkinetic movement disorder. Many potential causes, including auto-immune processes, infections, hypoxic or ischemic injuries, mitochondrial diseases, and toxins, can be associated with chorea. Drug-associated choreiform movements have been reported due to methamphetamine overdose as well as poisoning with prescription Central Nervous System (CNS) stimulants, high-dose use for therapeutic purposes, or taking CNS stimulants with a second dopaminergic drug[3].

Methylphenidate, a psychostimulating drug, acts mainly by blocking dopamine and norepinephrine reuptake receptors in the synaptic gap, and can also block serotonin reuptake receptors. This leads to an increase of neurotransmitters in the extraneuronal space and prolongation of their effects[4]. At low doses, methylphenidate used in the treatment of Attention Deficit Hyperactivity Disorder (ADHD) reduces movement and impulsiveness by acting in the prefrontal cortex, increasing cognitive function, including attention and working memory. For 3-5 year-old children, methylphenidate treatment is recommended 5-30 mg/day with gradually increasing the dose[4]. It has been reported that doses up to 40 mg are well tolerated in this age range[5].

2-17% of patients may experience side effects such as insomnia, depression, decreased appetite, weight loss, headache, visual impairment, palpitations, and dizziness during methylphenidate treatment. Movement disorders such as tics, tourette syndrome, tremor, dyskinesia, and chorea are rare side effects[6].

It is suggested that excessive dopaminergic activation in striatum, caudate nucleus, or putaments is largely responsible for the choreiform movements[6].

Poisoning with methylphenidate produces symptoms similar to typical sympathomimetic agent toxicity. Psychiatric or neurological effects of varying degrees (e.g., headache, CNS excitation or depression, abnormal movements or rigidity, changes in mood or behavior, hallucinations, paranoia), cardiovascular effects (e.g., hypertension, tachycardia, chest pain) and sometimes gastrointestinal effects (e.g. vomiting, abdominal pain), or various laboratory abnormalities (e.g. high serum transaminases or creatine kinase or thrombocytopenia) can be seen. In some cases, hyperthermia, arrhythmias, and seizures have been reported[5].

The 4-year-old patient, who was referred to our center with preliminary diagnosis of poisoning and subsequent seizures, had received a single dose of 50 mg of methylphenidate. Except for choreiform movements due to methylphenidate, there were no identified signs or symptoms of intoxication during the 48 hour follow-up.

In the literature, the side effect of chorea associated with the use of methylphenidate in therapeutic doses or rapid dose increase for therapeutic purposes has been reported in children[5,6]. This condition is attributed to the prefrontal cortex alpha-2A adrenergic receptor gene polymorphism, which can increase the effectiveness of the drug, or the CES1 gene variation that delays the metabolism of the drug[7,8]. Our patient who had no history of consanguinity have a brother who was receiving 10 mg of methylphenidate daily due to ADHD and he had no side effects such as movement disorder etc..

Animal studies have shown that guaifenesin and phenylephrine taken by our patient with methylphenidate may exhibit anticonvulsant effects, and there is no data in the literature on the effects of their use with methylphenidate[9].

There are numerous studies recommending the use of haloperidol, a postsynaptic dopamine (D2) receptor blocker in the mesolimbic system, in motion disorders due to methylphenidate and other CNS stimulants[10]. Consistent with the literature, we observed that the symptoms regressed and do not recur with haloperidol use.

Conclusion

Even though the patient had received a toxic dose of methylphenidate for her age, there were no signs of toxicity in our patient. Therapeutic and toxic dose limits of CNS stimulants such as methylphenidate may differ individually depending on pharmacogenetic diversity. On the other hand, chorea should be kept in mind in the differential diagnosis of epileptic seizures from PNE events caused by CNS stimulants. Correct distinction will ensure early effective treatment of patients and protect them from unnecessary drug risks.

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