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CASE REPORT – OPEN ACCESS

Dyskinesia in a Prepubertal Boy After the First Dose of Methylphenidate and the Association of Focal Epileptiform Activity: A Case Report

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ABSTRACT

Background: Methylphenidate is a piperidine derivative stimulant drug. It inhibits the reuptake of dopamine and norepinephrine and improves the primary symptoms of Attention-Deficit/Hyperactivity Disorder. Methylphenidate may cause dyskinesias in children with Attention-Deficit/Hyperactivity Disorder, and concomitant irregularity in Electroencephalography may increase the likelihood of the neuropsychiatric side effects.

Case Report: A case of a 6.5-years-old boy who was admitted to the emergency room with unintended and uncontrolled behaviours after the first dose of this drug was presented. He was diagnosed with acute dyskinesia in the orofacial region and extremities, and then he was cured with biperiden lactate infusion in eighteen hours. Focal biphasic waves at right temporoparietal areas were recorded on his sleep-Electroencephalography.

Conclusion: In our case with both attention-deficit/hyperactivity disorder and epileptiform activity, dyskinesia occurrence after one single dose of 20 mg methylphenidate was discussed with the results of previous studies.

Keywords: Dyskinesia, methylphenidate, movement disorder, Attention-Deficit/Hyperactivity Disorder

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INTRODUCTION

Methylphenidate (MPH) is a piperidine derivative stimulant drug and most commonly used in the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children. MPH increases the availability of dopamine and norepinephrine via reuptake inhibition at the presynaptic level, mainly in the prefrontal cortex and striatal areas. Through this way, attention span, memory function, behaviour control and cognitive flexibility significantly improve (1).

MPH may cause adverse effects in the neuropsychiatric system and movement disorders are the most frequent ones among them (1). Movement disorders are usually characterized with impairments in intentional motor activity without loss of muscle strength, and may appear as postural instability or rigidity, irregularity or excess rhythmicity in involuntary motor activity. Movement disorders in childhood usually have hyperkinetic nature. They arise in different manifestations as tic, chorea, athetosis, ballismus, dystonia, myoclonus, stereotype, tremor (2), and the term "dyskinesia" may be used synonymously, for all them.

Below, we presented a case of a prepubertal boy who was admitted with acute dyskinesia symptoms and irregular Electroencephalography (EEG) findings after the first dose of MPH. Our aim in presenting this case was to draw attention to the coexistence of both conditions for the first time. If any association can be proven between them, EEG record before MPH treatment may be suggested to be useful for predicting the vulnerability to dyskinesia.

CASE REPORT

A-6.5-year-old boy was brought into the emergency department with unintended and uncontrolled movements. On physical examination, facial grimace, repetitive stereotypical behaviours, forced opening of the mouth, repetitive jaw twisting, lip sucking and intermittent stuttering were seen. He had slow and sequential dancing-like hand movements and intermittent leg swinging. Any other sign was not observed in detailed physical and neurological examinations.

On his anamnesis, his mother told that he was diagnosed with ADHD and modified- release methylphenidate (medikinet retard, MEDICE Arzneimittel Pütter GmbH & Co. KG, Germany) was prescribed as 20 mg/day. One hour after the first dose in the morning, sedation, lassitude and some phrases indicating deterioration in time and space orientation emerged and disappeared in 15 to 20 minutes without any treatment application. Eight hours after these complaints, lip sucking, irregular swallowing movements, jaw contractions were noticed. In addition, intermittent blurred vision, involuntary finger movements as if relieving the tingles on hands, non-fluent speech were added to his symptoms just before the hospital admission.

No abnormality was shown on biochemical analysis of blood, Electrocardiogram and Cranial-Magnetic Resonance Imaging. Sleep-EEG revealed focal biphasic waves at the right temporoparietal areas (Fig. 1). There was a speech delay on his anamnesis. Also, there was an epilepsy treatment history in his mother's grandfather.

He was diagnosed with acute dyskinesia in the orofacial region and extremities. Five mg of biperiden lactate was infused slowly in isotonic serum physiological replacement. His symptoms gradually diminished throughout the night and disappeared until noon in the next day. After all, he was discharged and directed to the child neurology and child psychiatry outpatient clinics with the prescription of carbamazepine in a daily dose of 20 mg/kg/day.

As for the one year later's prognosis, he was still using carbamazepine as 30 mg/kg/day. Focal biphasic waves at right occipital area were recorded on his Sleep-EEG (Fig. 2). Any other neurological symptom or any convulsion was not notified during this treatment period. No drug was used for ADHD because of parent disapproval, but ADHD symptoms were substantially under control depending on the treatments, such as parent counseling, behavioral therapy and school support. The patient's consent was obtained for this case report.

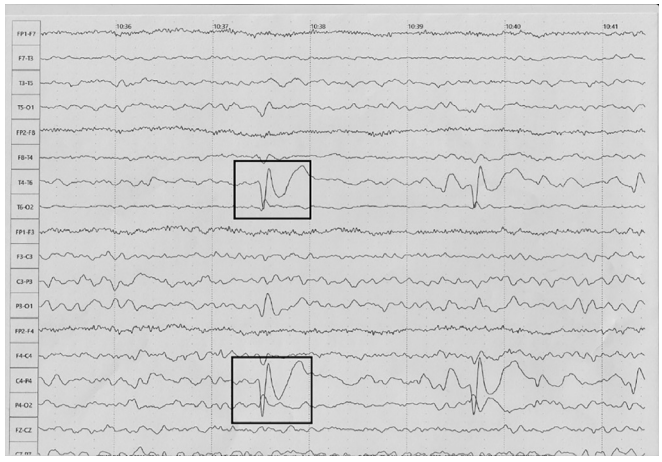

Figure 1. Focal biphasic waves at right temporoparietal area (sample of EEG recording in the emergency room)

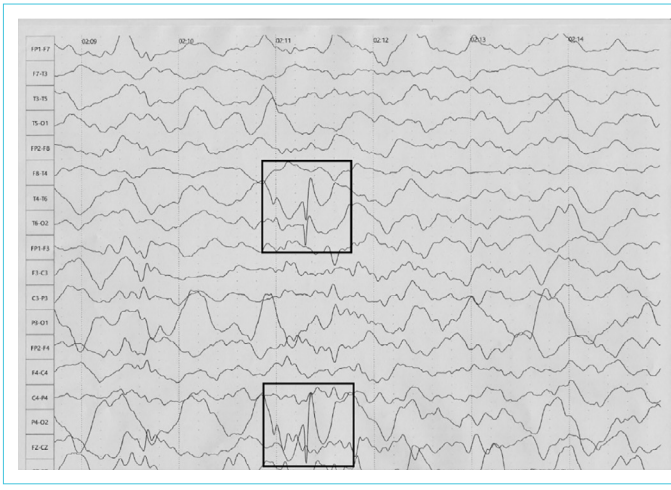

Figure 2. Focal biphasic waves at right occipital area (sample of EEG recording after the first year)

DISCUSSION

Basal ganglia are composed of the interconnected nuclei that are embedded in the hemispheres (striatum, globus pallidus), diencephalon (subthalamic nuclei) and mesencephalon (substantia nigra). These nuclei take inputs from the thalamus and the cerebral cortex also send outputs to the frontal lobe and the pedunculopontine area. Thus, basal ganglion has the potential to influence the voluntary motor movement, affective and cognitive function. Any damage in these nuclei may lead to the dysfunctions in the basal ganglia circuit and may evoke the different movement disorders, depending on the pathophysiology of the affected brain area (3).

Many conditions trigger movement disorders: medicines (psychotropics, corticosteroids, oral contraceptives, antiepileptics), infections, cerebral palsy, perinatal injuries (hyperbilirubinemia, hypoxia-ischemia), toxins (copper, alcohol), injuries of basal ganglia, inherited abnormalities, metabolic disorders (endocrine dysfunction, electrolyte abnormalities), autoimmune diseases (systemic lupus erythematosus, anti-phospholipid antibody syndrome) (2). Dyskinesias in a few hours after the first dose of MPH were rarely reported in prepubertal children (4, 5). Some cases were associated with autism symptoms, mental or developmental delays. However, how dyskinesia was triggered even after the first dose has not yet been proven clearly.

In basal ganglia, dopamine is the major mediator neurotransmitter and dopaminergic receptors are the essential modulators (3). MPH also works on the same pathway (1). Even one single dose of MPH was shown to increase the activation in basal ganglia, cerebellum and inferior frontal gyri in children (6). However, the relationship between MPH and dyskinesia could not be clearly identified, yet. Curtin et al. (7) showed that diseases of basal ganglia and cerebellum were 2.4 times more common in adults with ADHD than in healthy controls and stimulant treatment at the past increased this ratio to 8.6. However, they suggested that this increased risk may be related to the severity of ADHD phenotype or the stimulant treatment may facilitate the transition to degeneration on pathways relevant to the movement disorders.

Epileptic discharges are quite common in children with ADHD, and ADHD is more diagnosed in children with epilepsy. These discharges are most commonly recorded over the fronto-central areas, but other areas may also be involved less frequently, and focal distribution of the waves is usually higher than general distribution (8). In addition, an increase in slow-wave activity (theta and delta bands) and theta/beta ratio are the most prominent EEG abnormalities in children with ADHD (9).

The relationship between ADHD and EEG irregularity has been widely accepted, but the occurrence of dyskinesia after one dose of MPH in a prepubertal boy with both ADHD and focal epileptiform activity has not been previously reported. Our case is also compatible with the previous reports, which revealed that this coexistence was more common in the male sex, delayed speech and family history of epilepsy (10). Whether it is just a coincidence or the result of a common etiology; the coexistence of ADHD and

epileptiform activity may increase the likelihood of dyskinesia with MPH treatment.

In conclusion, our case has once again demonstrated that some patients may be more vulnerable to the movement disorders. Thus, EEG findings recorded before the treatment may reveal some clues that could be accepted as predictors to catch the children under risk. To discover the mechanisms that cause dyskinesia may also contribute us to understand both the brain areas relevant to ADHD and the action mechanisms of MPH, on the basis of the cortex and the basal ganglia pathways.

Informed Consent: Written informed consent was obtained from the mother of the patient.

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Conflict of Interest: The authors have no conflict of interest to declare.

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