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Febrile seizure during treatment with methylphenidate

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ABSTRACT

Methylphenidate (MPH) is the main psychostimulant drug for children and adolescents with ADHD. The long-acting stimulant of osmotic controlled-release oral delivery system (OROS) MPH has been designed to release gradually increasing concentrations of MPH over a period of 10-12 hours. Febrile seizure (FS) is a seizure associated with high body temperature, typically due to a viral infection. In this case report, a 17-year-old boy with a history of ADHD who experienced a febrile seizure while taking OROS-MPH is reported.

Keywords: Attention deficit hyperactivity disorder, febrile seizure, Methylphenidate, Adverse effect, Adolescent

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Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders among children, with a prevalence of around 5% of the worldwide-pooled population [1]. Methylphenidate (MPH) is the main psychostimulant drug used as firstline treatment for children and adolescents with ADHD. The long-acting stimulant of osmotic controlled-release oral delivery system (OROS) MPH has been designed to release gradually increasing concentrations of MPH over a period of 10-12 hours.

Febrile seizure (FS) is a seizure associated with high body temperature, typically due to a viral infection. Most FSs occur between six months and three years of age, with a peak incidence at 18 months of age [2, 3]. In this case report, a patient who experienced a febrile seizure while taking OROS-MPH is reported. The patient and his guardian has provided permission to publish these features of his case, and the identity of the patient has been protected.

Case Report

The patient is a 17-year-old boy with a history of ADHD. His prenatal, postnatal, and early developmental history was unremarkable. At age 10, he had visited another pediatric clinic with typical symptoms of ADHD. He was diagnosed with ADHD, and atomoxetine was started, but it was ineffective. Subsequently, OROS-MPH 18 mg/day was started and was increased to 36 mg/day in due course. Due to irritability and aggressiveness, risperidone 0.5 mg/day was added. Six months after starting risperidone, his irritability and aggressiveness had improved, and the risperidone was discontinued.

At age 12, he had two discrete episodes of generalized seizures. On both occasions, he had a common cold, and his body temperature rose above 38℃.

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He was diagnosed with FS by the pediatrician. At age 15, he came to our clinic and was prescribed OROS-MPH 36 mg/day. At age 16, he had a common cold, his body temperature rose above 38℃, and he experienced a generalized tonic-cyclonic seizure. It lasted 30-40 seconds with a loss of consciousness. He was sent to the emergency room of another hospital. His consciousness and spontaneous respiration were soon recovered. His physical and neurological examination was normal, and he was diagnosed with FS.

He came to our clinic a week later. He had no history of epileptic seizures, and there was no history of epilepsy or FS in first-degree relatives. He had no history of alcohol use, drug use, or head trauma. He did not have any other seizure risk factors. Blood biochemistry test results (fasting blood glucose levels of serum electrolytes, and renal and liver function tests) were normal. Electroencephalogram a week following the seizure was normal. Neither physical nor neurological disease was presented. The results of the brain magnetic resonance imaging were normal. The relationship between febrile seizure and MPH-OROS was not clear. MPH-OROS was discontinued due to the possibility it triggered the seizure. Seizures had not recurred during 9-month follow-up, and psychotic symptoms were under control.

Discussion

FSs are the most common type of convulsions in children and are generally harmless for children. Nevertheless, they can cause extreme parental anxiety, which is important to address. In the United States and Western Europe, they occur in 2-5% of children [4, 5]. But there is a higher prevalence in Asian populations, particularly among Guamanian (14%), Japanese (8%), and Chinese (1%) populations [3]. Approximately one-third of children who have had an FS will have a recurrence during early childhood, but less than 10% will have more than three recurrences [6]. The exact causes of FS are still unknown, but it is thought that a combination of genetic and environmental factors result in FS [7]. The release of high levels of cytokines during fever may alter normal brain activity, triggering seizures [8, 9]. There are other risk factors for FS: male gender, a family history of FS, an elevated peak body temperature, certain underlying causes of the fever, prenatal and natal complications, low serum calcium, sodium or blood sugar, microcytic hypochromic anemia, and iron and zinc deficiencies [10, 11]. Some studies have shown that some medications, such as theophylline, antihistamines, and antiallergics with antihistaminic actions, possibly have a role in prolonging FS, special attention should be given to the use of such medications in children with a history of FS, as stipulated by guidelines released in Japan [12].

Stimulants might lower the convulsive threshold [13]. Although, in the review article, the authors summarized the reports regarding the relationship between methylphenidate treatment and seizures or EEG abnormalities [14]. They mentioned that while the evidence is limited and unclear, the studies do not indicate evidence for seizures as an adverse event of methylphenidate treatment in children with no prior history. However, the type of methylphenidate release formulation (e.g. immediate or modified release) was often unreported, unclear, or reported as mixed in the studies summarized in this review. Therefore, more research is needed into the safety of long-term methylphenidate, especially OROS-methylphenidate, in children and young people at risk of seizures.

This case report does not allow us to make a definite conclusion on whether MPH-OROS treatment induces or causes a recurrence of FS. MPH-OROS could have played a role in the late occurrence of FS reviewed in this case report. The relationship between FS and MPH-OROS has not been investigated. Regardless, clinicians should be aware of the relationship between stimulants and FS, especially for patients at high risk of FSs such as members of some ethnic groups. Further research and investigation are needed.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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