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Manic Symptoms Due to Modified-Release Methylphenidate Use: An Adolescent Case

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TO THE EDITOR:

Stimulants, especially methylphenidate (MPH), are widely prescribed agents for the first line treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents.[1] Stimulant related psychosis and/or mania symptoms in children were firstly reported in three cases of "methylphenidate hallucinosis" and these symptoms occur in approximately 0.25% of children using stimulants, or about 1 in 400.[1,2] The terms "hallucinosis" and "toxicosis" usually indicate the transient psychotic-like or mania-like symptoms and distinguish them from the long-lasting symptoms of schizophrenia and bipolar disorder.[1] However, when the symptoms either continue or recur after discontinuation of the medication, the patients can be diagnosed as having schizophrenia or bipolar disorder.[1] In this paper, we report the occurrence of mania-like symptoms with modified-release MPH use in an adolescent with intellectual disability (ID).

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CASE

A-16-year old male was referred to our clinic with the complaint of attention difficulties, learning disabilities, and forgetfulness. He had difficulty in completing school works and dysfunction in academic performance. Developmental history revealed that he had marked delays in basic motor skills, social interaction, and speech. There was no physical illness, trauma, substance use, psychosis, or bipolar disorder in family and personal history. As a result of his psychiatric and psychometric examinations (WISC-R total score = 62), he was diagnosed with ADHD and mild ID. He had a weight of 62 kg and we initiated modified-release MPH 20 mg/day. One week after initiating MPH, he was admitted to emergency room with the complaint of hyperactivity, irritability, logorrhea, and sleeplessness. He was reported to speak loudly at faster pace and feel more energetic than usual. His symptoms began gradually on the fifth day of treatment. His psychiatric evaluation revealed euphoria, grandiosity, and incongruent affect. Young mania rating scale (YMRS) score was 32. His neurologic examinations, blood tests, electroencephalogram, and computerized tomography of brain were normal. MPH was stopped, however, his symptoms did not resolve spontaneously in a week. Thus, we initiated valproate 1000 mg/day and risperidone 2 mg/day gradually and his symptoms started reducing within two weeks. Approximately three months later, his symptoms improved significantly, YMRS score decreased to 6 and we stopped both valproate and risperidone.

DISCUSSION

Therapeutic doses of stimulants may cause psychosis and/or mania symptoms in a small proportion of treated children. The symptoms usually start shortly after the initiation of the medication or the dose increment. Presenting symptoms generally resolve within a week after discontinuation or the dose reduction.[3]albeit in a small number of cases. Signs and symptoms of adverse effects usually disappear on stopping the medicine. Data regarding the safety of methylphenidate in comorbid attention deficit hyperactivity disorder (ADHD In accordance with the literature, manic symptoms started within the first week of the medication in our case. There is a limited literature about the treatment options of continuing manic symptoms after discontinuation of MPH. Chakraborty et al. reported an 11-year-old girl who developed mania symptoms after starting MPH 15 mg/day. Her symptoms did not resolve with stoppage of MPH and they had to initiate valproate and olanzapine.[3]albeit in a small number of cases. Signs and symptoms of adverse effects usually disappear on stopping the medicine. Data regarding the safety of methylphenidate in comorbid attention deficit hyperactivity disorder (ADHD Similarly, the symptoms of our case continued after stopping MPH and required the use of valproate and risperidone.

Although stimulant related toxicosis is known to be an idiosyncratic reaction, some risk factors have been suggested. Premorbid ADHD, ID, and the use of high doses have been proposed to be risk factors.[4] Our case had ID along with ADHD, which could have predisposed him to develop this adverse effect. Many studies have suggested the efficacy of MPH for treatment of ADHD symptoms in children with ID. However, children with ID have been reported to be more susceptible to adverse effects of MPH, such as sleep problems and poor appetite.[5] Additionally, ID can also contribute to the continuation of adverse drug effects[3]albeit in a small number of cases. Signs and symptoms of adverse effects usually disappear on stopping the medicine. Data regarding the safety of methylphenidate in comorbid attention deficit hyperactivity disorder (ADHD and lack of resolution after stopping MPH might be related with ID in our case.

Although not clearly understood, psychotic/manic symptoms may be associated with the mechanism of action of MPH. MPH inhibits the reuptake of dopamine and noradrenaline in the striatal, frontal, and temporal regions. Increased dopaminergic and/or noradrenergic activity in these regions may be related with the emergence of the symptoms.[4]

Eventually, this case highlights the fact that therapeutic dose of modified-release MPH may cause mania-like symptoms in children and adolescents with ID, the symptoms may not resolve after discontinuation of MPH, and psychopharmacological interventions may require to control these symptoms.

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