

Methylphenidate-induced Exacerbation of Chorea in a Child Resolved with Switching to Atomoxetine

Ozalp Ekinci, Cemre Yaşöz, Selin Ayşe İpek Baş, Nazan Ekinci, Özge İpek Doğan

Department of Child and Adolescent Psychiatry, Medical Faculty, University of Health Sciences, Istanbul, Turkey

Choreiform movements have been reported with stimulant medications, especially in adults. There is only limited evidence on the management of such reactions in children with attention deficit hyperactivity disorder. Hereby, we present the exacerbation of chorea with long-acting methylphenidate use in a 6-year-old child with acute rheumatic fever which resolved with switching to atomoxetine.

KEY WORDS: Chorea; Stimulant; Atomoxetine; Attention deficit hyperactivity disorder; Child.

INTRODUCTION

Stimulant medications, including methylphenidate (MPH), are the first-line treatment for attention deficit hyperactivity disorder (ADHD). Previous reports have shown that stimulants may cause movement-related side-effects including tics, stereotypies, dyskinesia, and chorea [1]. Choreiform movements have been mainly reported in adults and with the use of higher doses of amphetaminergic compounds [2-4]. Since medication treatment is crucial for school-age children with ADHD, strategies should be established for the rare cases where stimulants cause and/or worsen chorea symptoms. Hereby, we present the case of a 6-year-old male with acute rheumatic fever (ARF) who had exacerbation of chorea after starting long-acting MPH which resolved with switching to atomoxetine (ATX).

CASE

A 6-year old boy was admitted to our clinic with the complaints of attention difficulties, hyperactivity, im-

pulsivity and aggression to peers. His psychiatric evaluation and the parent-rated and teacher-rated scales both indicated an ADHD-combined type diagnosis. Conners' Teacher Rating Scale Score (CTRS) on admission to clinic was 45 [5] while the Turgay DSM-IV Disruptive Behavior Disorders Rating Scale parent form (T-DSM-IV-S) [6] total score was 48 with a hyperactivity subscale score of 24 and an attention deficit subscale score of 24. His developmental history was reported to be normal. His medical history revealed that he had a streptococcal infection 14 months ago and subsequently had been diagnosed with ARF. As a symptom of ARF, he had Sydenham chorea and stiffness in hand joints but he did not have any cardiac or skin lesions. In his neurologic examination, Sydenham's chorea was evident with mild unintentional movements in the neck and arms. Since the diagnosis of ARF and Sydenham chorea, patient was on haloperidol 1.5 mg/day, valproate 500 mg/day and 1.200.000 IU benzilpenisilin once in 3 weeks. He had no previous admission to child psychiatry, no history of seizures or any other medical conditions.

For the treatment of ADHD, osmotic-release oral system (OROS) MPH was planned to initiate and the patient was referred to pediatrics department. After the approval of medication by pediatrics department, OROS MPH was started in the dose of 18 mg/day. Three days after MPH treatment, patient was admitted to our clinic with the complaints of worsening of chorea. In his clinical evalua-

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Address for correspondence: Ozalp Ekinci
Department of Child and Adolescent Psychiatry, Medical Faculty,
University of Health Sciences, Istanbul 34736, Turkey
E-mail: ozalpekinci@yahoo.com
ORCID: <https://orcid.org/0000-0001-9598-8944>

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tion, a marked increase in chorea symptoms was observed in arms. In addition, chorea symptoms were observed to emerge in legs, which were not present before MPH treatment. The Chorea Intensity Scale score was 12 on initial admission to clinic and increased to 27 after MPH treatment. Due to an exacerbation of chorea, MPH treatment was discontinued. At the 2-week-follow-up, patient's chorea symptoms resolved back to the level before MPH treatment. At this follow-up, the chorea intensity scale score was found to be 11. After the discontinuation of MPH, no additional medication was initiated for 2 weeks. Thereafter, ATX was started in the dose of 10 mg/day (0.5 mg/kg/day). Ten days follow-up on ATX treatment revealed a mild improvement in ADHD symptoms with no worsening in chorea symptoms. The chorea intensity scale score was 9; while CTRS score was 40 and T-DSM-IV-S total score was 36, with a hyperactivity subscale score of 19 and an attention deficit subscale score of 17. ATX dose was gradually increased to 18 mg and 25 mg/day in 3 weeks. Patient was reported to have moderate improvement in ADHD symptoms and no worsening was reported in chorea. The chorea intensity scale score was 9; while CTRS score was 37 and T-DSM-IV-S total score was 28. Figure 1 shows the changes in Chorea Intensity Scale scores during MPH and ATX treatments.

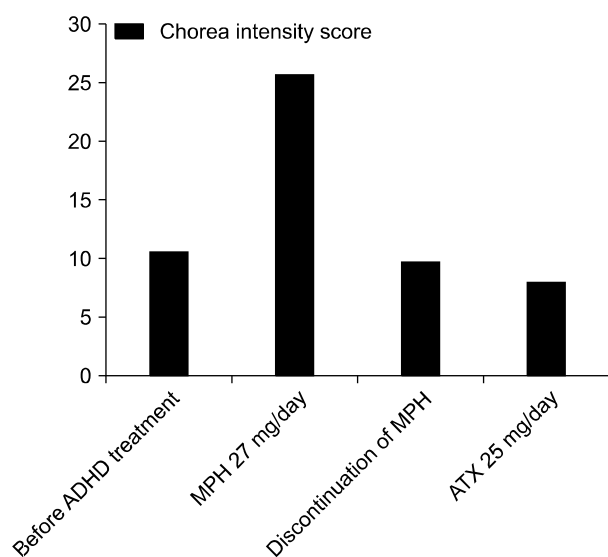


Fig. 1. Changes in Chorea Intensity Scale scores during treatments. ADHD, attention deficit hyperactivity disorder; MPH, methylphenidate; ATX, atomoxetine.

DISCUSSION

In this case report, the starting of long-acting MPH resulted in a marked exacerbation of chorea in a 6-year-old male with ARF. Thereafter, MPH was discontinued and ATX was initiated. ATX treatment was not found to be linked with worsening of chorea. Moreover, chorea symptoms were slightly decreased with ATX use. To the best of our knowledge, this is the first case which showed an exacerbation of chorea with MPH which resolved with switching to ATX. The mechanism of action of both medications should be taken into account when interpreting the adverse reaction.

There are only few case studies which reported chorea with stimulants in children with ADHD. One of the first reports was by Weiner *et al.* [7] which presented the case of a young child with ADHD who developed chorea in response to therapeutic dosing of immediate release MPH. Melvin and Heritary [3] reported a 10-year old female who developed chorea, presented by writhing, irregular hand movements and a twisting "dance-like" gait, with the increase of OROS-MPH from 36 mg to 54 mg/day. The adverse effect was reported to discontinue with the stopping of MPH and the addition of lorazepam [3]. Ford *et al.* [4] also reported a 10-year-old boy who accidentally ingested a high dose of lisdexamfetamine dimesylate that resulted in an acute chorea involving arms, legs, and trunk. In this case, haloperidol significantly improved chorea symptoms in approximately 48 hours [4]. The overview of the available literature indicates that both amphetaminergic compounds and MPH may cause choreiform movements. It is known that both formulations inhibit the reuptake of dopamine, while amphetamine increases the release of dopamine from vesicles more selectively [8].

Chorea is defined as a brief, involuntary and hyperkinetic movement disorder [9]. Many potential causes may be linked with chorea including autoimmune processes, infections, hypoxic or ischemic injuries, mitochondrial diseases, and toxins [10]. It has been suggested the excessive dopaminergic activation in corpus striatum, caudate or putamen are largely responsible for choreiform movements [3,4]. The primary central nervous system effect of MPH is increased dopaminergic availability, especially in the striatal regions [11]. In the present case, it may be suggested the use of MPH might resulted in an ex-

acerbation of chorea via increased dopaminergic activity in striatal regions.

It has been described that Sydenham's chorea is commonly associated with psychiatric symptoms, including obsessive-compulsive disorder, tic disorders and ADHD [12]. Antibodies against group A beta-hemolytic streptococcus which cross-react with basal ganglia have been demonstrated as the etiology [13]. The available literature indicates that the treatment of psychiatric disorders is challenging due to the high risk of motor-related side effects of psychotropic medications [12,14]. One earlier study found a high frequency of adverse reactions to central stimulants and suggested that Sydenham's chorea in childhood leads to a sensitivity to agents that augment central dopaminergic activity, which may be expressed as acute chorea [15]. The present case may be considered as an example of intolerance to dopaminergic medications.

ATX, a noradrenalin reuptake blocker, is the second-line medication treatment for ADHD [16]. The main actions of ATX were shown to be in the prefrontal cortical regions, while striatal regions are not generally affected. The previous research on ATX use in movement disorders suggests that the medication may be a relatively tolerable alternative in children with tic disorders [17]. In relation with its mechanism of action, there is also evidence that ATX may have benefits on the treatment of tics [18]. It has been shown that a subpopulation of patients with tics may improve under treatment with noradrenergic agents including tricyclic reuptake inhibitors [19,20]. Spencer *et al.* [20] has found ATX treatment associated with significantly greater reduction of tic severity in children with ADHD and Tourette syndrome. Since the neurobiology of tics and chorea are similar, a favorable tolerability and/or a degree of improvement may also be expected in chorea symptoms with ATX treatment. In line with this assumption, ATX use did not cause a worsening of chorea symptoms in the present case and a limited improvement was observed.

The management of stimulant-induced chorea has not been well established. In most of the available literature, stopping the offending agent and, if necessary based on severity of symptoms, administration of dopamine blocking agents or benzodiazepines have been recommended [21]. However, the continuation of ADHD treatment has not been mentioned. ATX, as presented in our case, may be suggested as a candidate treatment option in children

where stimulants are discontinued due to worsening of chorea. Future studies are needed to confirm the tolerability and efficacy of ATX in children with ADHD and chorea.

■ Conflicts of Interest

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

■ Author Contributions

Conceptualization: Ozalp Ekinci. Acquisition: Ozalp Ekinci, Cemre Yaşöz, Selin Ayşe İpek Baş. Writing—original draft: Ozalp Ekinci, Selin Ayşe İpek Baş, Nazan Ekinci. Review & editing: Ozalp Ekinci, Özge İpek Doğan.

■ ORCID

Ozalp Ekinci <https://orcid.org/0000-0001-9598-8944>
 Cemre Yaşöz <https://orcid.org/0000-0002-1192-3519>
 Selin Ayşe İpek Baş <https://orcid.org/0000-0002-0862-6142>
 Nazan Ekinci <https://orcid.org/0000-0002-1503-0654>
 Özge İpek Doğan <https://orcid.org/0000-0003-0572-5521>

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