JOURNAL OF
CONTEMPORARY MEDICINE

DOI: 10.16899/jcm.837023
J Contemp Med 2021;11(3):423-424

Case Report / Olgu sunumu

Methylphenidate-Induced Raynaud's Phenomenon In Two Cases With Attention-Deficit/Hyperactivity Disorder

Dikkat Eksikliği / Hiperaktivite Bozukluğu Olan İki Olguda Metilfenidat Kaynaklı Raynaud Fenomeni

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Abstract

Attention - deficit / hyperactivity disorder is a common neurodevelopmental disorder in childhood, for which there are several different treatment options. Among the suggested medications, methylphenidate (a central nervous system stimulant) is the first option in the treatment of ADHD. Psychostimulants are associated with various vascular problems including peripheral vasculopathy. This report describes two patients with ADHD who developed Raynaud's phenomenon during the modified-release methylphenidate treatment.

Keywords: Methylphenidate, Raynaud's phenomenon, ADHD

Öz

Dikkat eksikliği / hiperaktivite bozukluğu, çocukluk çağında çok sayıda farklı tedavi seçeneği bulunan yaygın bir nörogelişimsel bozukluktur. Önerilen ilaçlar arasında metilfenidat (bir santral sinir sistemi stimülasyonu) DEHB tedavisinde ilk seçenektir. Psikostimülanlar, periferik vaskülopati dahil olmak üzere çeşitli vasküler problemlerle ilişkilidir. Bu raporda, modifiye salınımlı metilfenidat tedavisi sırasında Raynaud fenomeni geliştiren iki DEHB hastası sunulmaktadır.

Anahtar Kelimeler: Metilfenidat, Raynaud fenomeni, DEHB

INTRODUCTION

Attention - deficit / hyperactivity disorder (ADHD) is characterized by developmentally inappropriate symptoms of inattention, hyperactivity, and/or impulsivity. Stimulants such as methylphenidate (MPH) have been demonstrated in clinical trials to reduce inattention and hyperactivity in children with ADHD.[1] MPH acts by blocking dopamine (DA) and norepinephrine (NE) transporters, thereby preventing reuptake of these catecholamines by the neuron following their release into the synaptic gap.[2] These drugs have been reported to be associated with several vascular diseases -that represent with necrotizing vasculitis- including secondary hypertension, cerebral vasculopathy, and erythema multiforme.[3,4]

Raynaud's phenomenon (RP) is a clinical syndrome characterized by recurrent episodes of vasospasm involving peripheral small vessels and is triggered by exposure to physical, chemical, or emotional stress.[5] Patients complain of pain and feeling cold concurrent with sudden pallor and/or cyanosis in their hands and/or feet. Females account for 60–90% of patients with this idiopathic condition.[6] In this report, two cases of RP induced by a high dose of modified-release methylphenidate treatment will be presented.

CASES

The first case is a 13-year-old boy who was admitted into our clinic with complaints of inattentiveness, untidiness, and low school success. Long-acting methylphenidate (OROS-MPH, Concerta©) 27 mg was started based on a diagnosis of ADHD after completion of a psychiatric evaluation; four weeks later, the dosage was increased to 36 mg/day due to partial response. Despite significant improvement in the ADHD symptoms, the treatment was stopped a month after because of a severe loss of appetite and weight. The patient was

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Received *(Geliş Tarihi)*: 07.12.2020 **Accepted *(Kabul Tarihi)*:** 12.03.2021

readmitted into our clinic two years later with similar complaints and was placed on a modified-release methylphenidate treatment (Medikinet© retard) at a dosage of 20 mg/day. At the next visit, the dosage was increased to 30 mg/day; this led to a reduction in the ADHD symptoms of the patient. However, while there were no side effects with the 20 mg/day dosage, the patient described feeling cold in both hands and feet which started one to two hours after each dose and lasted for seven to eight hours. The coldness in their hands was accompanied by paleness and then redness. The patient described no history of drug allergy or previous rheumatological disease. Considering the symptoms were similar to those of RP, the methylphenidate treatment was terminated and replaced with atomoxetine. There were no complaints of feeling cold in the hands and feet, nor appearance of redness with the treatment of atomoxetine.

The second case was a 16-year-old girl who was diagnosed with ADHD at a different health center when she was 11 years old. At the time of diagnosis, she was placed on a treatment of long-acting MPH 18 mg (OROS-MPH, Concerta©) which lasted for only two months. She was admitted into our clinic with symptoms of inattentiveness, and a modified-release methylphenidate (Medikinet© retard) treatment at a dosage of 10 mg/day was started after psychiatric evaluation. The dosage was increased to 20 and 30 mg/day at the next two visits, respectively. After the dosage was increased to 30 mg, she reported complaints of redness and cyanosis in her hands which began 20 to 30 minutes after drug intake. Her family and teacher also confirmed these symptoms. However, unlike the first case, she did not complain of feeling cold. These side effects were considered to be related to the Medikinet© retard treatment since they were not seen in the weekend recesses. The patient described no history of drug allergy or previous rheumatological disease. Considering the symptoms were similar to those of RP, the methylphenidate treatment was terminated and no other treatment was administered. The redness and cyanosis on the hands disappeared after termination of the treatment.

DISCUSSION

MPH is the first-line pharmacological treatment for ADHD.[7] MPH inhibits the dopamine and norepinephrine transporters in the neurons causing an increase in the extracellular dopamine and norepinephrine levels. Apart from its central effects, increased extracellular norepinephrine may cause vasoconstriction in the peripheral vascular system.[8]

RP is a peripheral vasculopathy characterized by transient ischemia in the hands and/or feet in response to cold or emotions.[9] Several psychiatric drugs (including citalopram, dextroamphetamine, and MPH) are associated with this phenomenon.[10,11] RP has been previously reported in child and adolescent patients on psychostimulant medications including short-acting, modified-release, and OROS MPH, and dextroamphetamine.[11,13] The authors of these reports stated that peripheral vasoconstriction may occur due to the dopaminergic and noradrenergic effect of the stimulants which may reflect clinically as RP.[11,13] However, none of the previous reports declared a similarity or discrepancy among the forms of methylphenidate in terms of development of RP. In our cases, although RP did not occur during the use of OROS-MPH (Concerta©), there were signs of RP with the modified-release form of MPH (Medikinet© retard). As far as we know, this report is the first to suggest that the vascular side effects of MPH may differ depending on the type of MPH used as indicated by these cases. Further studies are needed for comprehensive understanding of this condition.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

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

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version

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