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Case Report

Methylphenidate-Induced Menorrhagia in Twin Girls

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Abstract

Objective: Methylphenidate, a psychostimulant agent, is used in first-line psychopharmacological treatment in children and adolescents with attention-deficit/hyperactivity disorder. Common side effects associated with methylphenidate use in children and adolescents are insomnia, anorexia, headache, and nausea. Thrombocytopenia, nasal bleeding and menstrual bleeding disorders are very rarely reported during methylphenidate use. One of the least expected side effects during methylphenidate usage is menorrhagia.

Method: In this article, we report methylphenidate monotherapy-induced menorrhagia in two adolescent identical twins. To our knowledge, this is the first report of menorrhagia associated with methylphenidate use in children and adolescents.

Results: In both cases, menorrhagia has started after methylphenidate monotherapy and stopped after discontinuation. Other possible etiologies have excluded with clinical and laboratory evaluations. Naranjo Adverse Drug Reaction Probability Score was found 7, indicates probable side effect.

Conclusion: Menorrhagia is a rare adverse effect of methylphenidate use and clinicians should be aware of this phenomenon.

Key words: *Adverse Effects; Adolescent; Menorrhagia; Methylphenidate*

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Treatment of attention-deficit/hyperactivity disorder (ADHD) has a multidisciplinary approach including pharmacological agents and psychosocial interventions. Pharmacological treatment of ADHD includes both psychostimulant agents and non-psychostimulant ones. Methylphenidate, a psychostimulant agent, is the first line psychopharmacological treatment of ADHD in children and adolescents. It has been shown that methylphenidate has a significant effect on up to %70 or %80 of the children and adolescents who have been diagnosed with ADHD. Methylphenidate is a well-tolerated drug in most cases. Common side effects of this drug include insomnia, loss of appetite, headache, and nausea. It is also reported that methylphenidate has rare side effects such as urticaria, visual disturbances, gynecomastia, excessive sweating, muscle cramps, and hematological problems (1). Some side effects like thrombocytopenia, nasal bleeding, and menstrual cycle problems are extremely rare in the literature, only reported in case studies (2-5). One of the extremely rare side effects of methylphenidate is menorrhagia, which is part of menstrual cycle problems. Menorrhagia can be described as a menstrual bleeding period that lasts more than seven days or includes the loss of 80 milliliters (mL) or more blood per menstrual cycle (6). To our knowledge, methylphenidate–induced menorrhagia has never been reported before in the literature. In this paper, we report methylphenidate monotherapy-induced menorrhagia in two identical adolescent twins.

Case Report

Case 1

A 13-year-old girl applied to our clinic with problems in sustaining her attention in the lesson and complaints about leaving her seat in the class and fighting with her classmates. She has been evaluated with DSM-V-based clinical evaluation, Conner's Family and Teacher Rating Scales, and diagnosed with ADHD. The patient's weight was 45 kilograms. 27 mg/d Oral Release Osmotic System (OROS) methylphenidate monotherapy was prescribed for her. With OROS methylphenidate therapy, the severity of her symptoms decreased, her school success increased, her social interactions with her classmates were restored and Conner's Parent and Teacher Rating Scale points decreased significantly. However, after starting the consumption of the medication, her menstrual bleeding period became prolonged, and the volume of bleeding increased. She claimed that she had her first menstrual bleeding at the age of 11, had a regular menstrual cycle for the past six months, her bleeding period continued for 6-7 days and she used 3-4 peds per day before starting the consumption of OROS methylphenidate. With OROS methylphenidate usage for three months, her bleeding period continued for 12-13 days and she used 8-9 peds per day for three mens cycles, which is called menorrhagia. The patient visited the Istanbul University Gynecology&Obstetric Clinic for excluding potential etiologies of menorrhagia such as pregnancy, anovulatory cycles, polycystic ovary syndrome (PCOS), infections, thyroid dysfunction, thyrombocytopenia and von Willebrand Disease. No pathological etiology was found with gynecological examinations and laboratory and ultrasonography (USG) based evaluations. The patient's full blood count, liver function tests like alanine transaminase (ALT) and aspartate transaminase (AST), sedimentation rate, bleeding time (BT), partial prothrombin time (PT), activated partial prothrombin time (aPTT) and fibrinogen levels were normal. We continued OROS methylphenidate therapy during evaluations. For three consecutive months, the patient and her family claimed that she had used the drug every day, and her menorrhagia repeated in three consecutive menstrual cycles. After three months, other bleeding causes were excluded. Her twin also developed menorrhagia in her first menstrual bleeding after methylphenidate usage; therefore, we focused on the drug as the potential cause of menorrhagia. Then, despite the benefits for her, OROS methylphenidate consumption was discontinued. When the drug consumption was stopped, the next menstrual cycle returned to normal. The bleeding period continued for 6-7 days and she used 3-4 peds per day.

Case 2

Case 2, the monozygotic twin of Case 1, applied to our clinic two months after her twin's pharmacotherapy had started, because of "having the same social and academic symptoms and complaints as her twin". She was evaluated with DSM-V based clinical evaluation and Conner's Parent and Teacher Rating Scales, and was diagnosed with ADHD. OROS methylphenidate 27 mg/d was started for her, too. With pharmacotherapy, her academic success dramatically increased. As the patient stated, her normal menstrual periods are like her twin (bleeding period takes 6-7 days and she uses 3 or 4 peds per day). She claimed that in the first menstrual period after starting methylphenidate therapy, her menstrual bleeding amount doubled and her bleeding period extended to 14 days. With the data obtained from her twin, our clinical observation focused on methylphenidate as the potential cause of menorrhagia. The drug intake was stopped for Case 2 as well. Both cases were followed-up for three months. They had three menstrual cycles on the follow-up time, and their menstrual bleeding time turned back to their normal levels (for both cases, the bleeding period took 6-7 days and they used 3-4 peds per day). Neither case had another known medical illness, and they and their family claimed that they used no medical or herbal drug or product while they consumed methylphenidate. No other psychostimulant agent was prescribed for neither case. Their mother claimed that they have regular menstrual cycles every 28 days, with a bleeding period of six days.

Discussion

This report describes menorrhagia after methylphenidate usage for ADHD treatment in 13 years old twins. To the best of our knowledge, methylphenidate-induced menorrhagia in twins has never been reported before in any age group. Our report is the first report of methylphenidate-induced menorrhagia in twins. Some hematologic and gynecologic side effects such as thrombocytopenia, nasal bleeding, oligomenorrhea, and hypermenorrhea have been reported for methylphenidate before (2-5). In a previous study, a possible mechanism of methylphenidate induced thrombocytopenia was hypothesized to be related to peripheral thrombocyte destruction; but in our two cases, both twins' thrombocyte counts were normal (4). In another case report, methylphenidate-induced oligomenorrhea was reported. Increased dopamine in the brain was considered to be the link between methylphenidate and oligomenorrhea, and this increase could interrupt the secretion of the pulsatile gonadotropin-releasing hormone (GnRH) and the luteinizing hormone (LH) (3). In normal levels, dopamine functions as a co-agonist of adenosine diphosphate (ADP) associated aggregation and has a prothrombotic effect. But according to previous studies, in higher levels, dopamine serves as an anti-thrombotic agent. We believe that increased dopamine levels, modulated by methylphenidate, could lead to an anti-thrombotic state and induce menorrhagia. However, in the current report, we could not make further investigations on this mechanism (5, 7). In this study, observing the occurrence of menorrhagia in two identical twins after the consumption of methylphenidate and its stop with quitting the drug therapy caused us to think that this is linked with methylphenidate. It does not seem to be an idiosyncratic reaction and there could be a genetic predisposibility .

Menorrhagia is described as menstrual bleeding that takes more than seven days or involves 80 milliliters or more blood loss per menstrual cycle. The most common etiology of menorrhagia in the adolescent age group is dysfunctional uterine bleeding caused by anovulatory cycles. The most common causes of anovulation in adolescents are chronic diseases, eating disorders, illicit drug usage, polycystic ovary syndrome, and congenital adrenal hyperplasia (6-7). Menorrhagia could be originated from bleeding diathesis. Some inherited bleeding tendencies such as von Willebrand Disease, hereditary thrombocyte dysfunctions, coagulation factor deficits, hereditary thrombocytopenia and fibrinolytic cascade problems could lead to menorrhagia (6).

In our report, neither case had a reported medical illness nor a history of abnormal bleeding and their full blood counts; coagulation parameters like bleeding time, PT and aPTT; fibrinogen levels; liver function tests; and sedimentation rates were normal.

The Naranjo adverse drug reaction (ADR) probability scale offers a sensitive way to monitor ADRs. A score between five to eight corresponds to a probable side-effect level. The Naranjo ADR probability scale score in these two cases was seven, indicating a probable side effect. Therefore, methylphenidate was the most likely cause of menorrhagia in our cases (8).

Limitation

Our method has some limitations. It may be insufficient to support our hypothesis over 2 cases, further studies with bigger samples are needed to show correlation between methylphenidate and menorrhagia. Underlying mechanism could be related with genetic factors, such as liver enzyme profiles and drug-enzyme interactions. These interactions are not well known and there are no specific tests available for investigate genetic parameters.

Conclusion

There is not enough information about how methylphenidate could lead to menorrhagia. However, no matter what the pathophysiological mechanism is, clinicians should be aware of and careful about the occurrence of menorrhagia and other menstrual cycle disturbances with the patients treated with methylphenidate. Further investigations are required to unravel the link between menorrhagia, methylphenidate and genetic factors.

Conflict of Interest

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

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