Case report / *Olgu sunumu*

Successful management of methylphenidate related thrombocytopenia during ADHD treatment: a case report

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ABSTRACT

Methylphenidate is an effective and well tolerated agent frequently used in the treatment of attention deficit hyperactivity disorder. Thrombocytopenia is defined as a blood platelet count less than 150,000/mm^3, and is an important hematological side-effect capable of causing mild symptoms or severe complications such as intracranial hemorrhage. Thrombocytopenia may develop in association with various causes, including drug use. There have been very few case reports of thrombocytopenia developing during methylphenidate use, and to the best of our knowledge there have been no reports concerning the management of this side-effect. This report describes the development of thrombocytopenia likely related to methylphenidate therapy in an adolescent with attention deficit hyperactivity disorder and successful management with a safety switch to atomoxetine. ***(Anatolian Journal of Psychiatry 2020; 21(5):557-560)***

Keywords: *attention deficit hyperactivity disorder, methylphenidate, thrombocytopenia, atomoxetine*

Metilfenidat kullanımı sonrası trombositopeni gelişen bir ergen olguda atomoksetine güvenli bir geçiş: Olgu sunumu

ÖZ

Metilfenidat, dikkat eksikliği hiperaktivite bozukluğu tedavisinde sık kullanılan etkili ve güvenilir bir ajandır. Trombositopeni kandaki trombosit sayısının 150.000/mm^3'ten az olmasıdır. Trombositopeni, asemptomatik gidişten kafa içi kanamalar gibi ciddi komplikasyonlara neden olabilen önemli bir hematolojik sorundur. Trombositopenin ilaç kullanımı da dahil olmak üzere birçok nedene bağlı olarak gelişebildiği bilinmektedir. Metilfenidat kullanımı sırasında trombositopeni gelişimi ile ilgili az sayıda olgu bildirimi vardır ve bildiğimiz kadarıyla bu yan etkinin yönetilmesi ile ilgili herhangi bir olgu bildirimine rastlanmamıştır. Bu yazıda, DEHB'li bir ergen olguda olasılıkla metilfenidat kullanmaya bağlı trombositopeni gelişimi ve bu durumun atomoksetine güvenli bir geçiş yapılarak başarılı bir şekilde yönetilmesi sunulmuştur. ***(Anadolu Psikiyatri Derg 2020; 21(5):557-560)***

Anahtar sözcükler: *Dikkat eksikliği hiperaktivite bozukluğu, metilfenidat, trombositopeni, atomoksetin*

INTRODUCTION

Methylphenidate (MPH) is a safe and effective agent used as a first-line medication in the treatment of attention deficit hyperactivity disorder (ADHD).[1] The best known side-effects of MPH therapy are nausea, decreased appetite, weight loss, and sleep problems.[1] Rare side-effects including hallucination, hyper sexuality or inappropriate sexual behavior, cutaneous eruptions, obsessive compulsive symptoms and gynecomastia may also be seen.[2]

Thrombocytopenia is defined as a blood platelet count less than 150,000/mm^3.[3] This crucial adverse hematological effect may range from mild

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symptoms to severe complications such as intracranial hemorrhage.[3] Thrombocytopenia may develop for several reasons, such as infection, malignancy, and drug use, but particularly due to idiopathic causes.[3] In terms of medications, there have been reports of thrombocytopenia being caused by heparin, quinine, rifampin and carbamazepine.[3]

This report describes the development of thrombocytopenia likely related to MPH therapy in an adolescent with ADHD and successful management with a safety switch to atomoxetine. This article is presented since there have been few case reports of thrombocytopenia associated with MPH use and none, to the best of our knowledge, concerning a safety switch to atomoxetine.

CASE REPORT

An 11-years-old girl, was brought to our clinic by her family due to hyperactivity and rapid distractibility. Her history revealed an inability to focus on activities for more than five minutes, difficulty in participating in activities requiring concentration, hyperactivity, and frequent injuries resulting from hyperactivity. These symptoms had persisted since the pre-school period, and affected her functioning in both the domestic and school settings. Hyperactivity, rapid distraction, and poor thought content were determined at psychological examination. Myelodysplastic syndrome was present in the patient's medical history. At interview, she was assessed using the Clinical Global Impression Scale, the Ankara Developmental Screening Inventory (ADSI), and the Turgay DSM-IV Based Parent Scale. At psychometric evaluation, the patient's CGI score was 6 (severe). Her score on the attention deficit (AD) section of the Turgay Scale was 7/9, and her hyperactivity (HA) score was 6/9. The ADSI was compatible with 2 years 8 months-2 years 11 months. ADHD and intellectual disability were diagnosed based on DSM-5 diagnostic criteria following history obtained from the patient's family, psychological examination, and psychometric tests. MPH use was planned in the light of the existing symptoms, and the hematology department was consulted. The patient's platelet (PLT) count was 90.6 mm^3, no contraindication for MPH use was reported, and IR-MPH 5 mg/day was initiated. At blood tests performed at control examination in the second week, the PLT count decreased to 55.9 mm^3, and MPH therapy was discontinued. One month following discontinuation of MPH, the PLT count rose to 83.4 mm^3. Once the patient's PTC count had returned to basal values, the pediatric hematology and oncology department was consulted concerning starting atomoxetine therapy. The pediatric hematology and oncology department reported no contraindication for atomoxetine, and treatment was switched to this. At continuing controls, the patient's ADHD symptoms improved, her CGI score decreased to 3, and Turgay Scale values were DA 3/9 and HA 2/9, while no change was observed in platelet values. The patient was followed-up regularly at our outpatient clinic at two-month intervals over six months, and her existing state of well-being persisted.

DISCUSSION

MPH is an effective agent frequently employed in the treatment of ADHD in children and adolescents.[1] However, side-effects may sometimes occur during its use. In addition, there have been a few case reports of hematological side-effects developing in association with MPH therapy. Coskun et al. reported increased bleeding during the menstrual cycle in a teenager using MPH.[4] Similarly, Avcil et al. reported nasal bleeding in association with MPH therapy in an adolescent girl.[5] Bleeding developed in both patients, but platelet counts were normal, and the authors reported that bleeding was not associated with a decreased platelet count. Ercan et al. reported a decrease in platelet levels following MPH use in an adolescent patient with ADHD that these returned to normal after discontinuation but that platelets decreased again when the medication was resumed.[6] To the best of our knowledge, there have been only three case reports concerning the association between MPH and platelets.[6-8] MPH was discontinued after the development of thrombocytopenia in reported cases, but no information was encountered concerning the treatment of existing ADHD symptoms.

Thrombocytopenia may develop in association with several factors related to decreased platelet production (infection, vitamin deficiencies, or genetic causes) or increased platelet destruction (immune-mediated, platelet consumption, or mechanical breakdown).[9] Due to its frequent appearance, particularly in childhood, idiopathic thrombocytopenic purpura (ITP) is the first potential cause of thrombocytopenia that should be considered.[10] ITP cannot be definitely excluded in our case. The authors of other reports in the literature have also concluded that ITP could not be completely excluded. In addition, one patient scored 5 on the Naranjo scale, and

the side-effect observed was found to be 'probably' caused by the thrombocytopenia-MPH link.[11] Drug-related thrombocytopenia is classified as immune- or non-immune-mediated.[12] Non-immune-mediated forms frequently develop with the use of chemotherapeutic agents that suppress bone marrow, and of some antibiotics.[13] In immune-mediated thrombocytopenia, drug-dependent antibodies result in platelet destruction by adhering to the glycoproteins on their surface, and case reports have particularly reported development in association with agents such as quinidine, trimethoprim/sulfamethoxazole, and abciximab.[14] The mechanism by which MPH use results in thrombocytopenia is still unclear, although there are theories implicating peripheral breakdown. However, according to the annually updated Blood Center of Wisconsin Platelet Reactive Antibody Database, antibody production related to MPH use has not been detected. Antibody production is also known not to be detected in some immune-mediated thrombocytopenia.[15] Further studies are needed regarding the mechanism involved in the development of MPH-related thrombocytopenia.

A safety switch to atomoxetine was performed in the present case due to the emergence of a side-effect during MPH use. Warrer et al. described adverse effects as the most common reason for switching to atomoxetine during MPH therapy.[16] However, the number of studies regarding safety and effectiveness and switching to atomoxetine therapy is inadequate. The second author has published two case reports involving effective safety switches from MPH to atomoxetine. In the first case, treatment was switched to atomoxetine following development of gynecomastia likely associated with MPH use, after which the side-effect resolved and ADHD symptoms improved. Similarly in the second case, priapism developed following MPH therapy, but that side-effect was not observed when treatment continued with atomoxetine.

We think that it will be useful for clinicians to remember the possibility of thrombocytopenia, one of the rare side-effects of MPH use, and that atomoxetine should be considered as an alternative therapy in such cases.

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