



LETTER TO THE EDITOR

Abnormal vaginal bleeding related to risperidone

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Dear Editor,

Risperidone is an atypical antipsychotic with an affinity for D2 and 5-HT-2A receptors, used in treating various psychiatric disorders, particularly disruptive behavioral disorders (1,2). Risperidone is safe for children and adolescents; however, side effects such as headaches, weight gain, increased appetite, extended sleep, rhinitis, and upper respiratory tract infections may manifest during treatment (1). The literature documents adverse effects such as epistaxis, gastrointestinal bleeding, gingival bleeding, and hemorrhagic cystitis associated with this drug (3–8). This report presents a 15-year-old girl experiencing abnormal vaginal bleeding with risperidone treatment.

A 15-year-old female patient with Attention-Deficit/Hyperactivity Disorder (ADHD) was admitted to the clinic due to aggressive and impulsive behavior complaints. She was taking Osmotic Release Oral System-methylphenidate (OROS-methylphenidate), with which she had a 60-70% improvement in ADHD symptoms at 54 mg/day for four years. Based on the Conners' Parent Rating Scale, she scored 15 for attention deficit, 20 for hyperactivity, and 12 for Oppositional Defiant Disorder (ODD). The patient was diagnosed with ADHD and ODD by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.

The patient was started on risperidone 0.5 mg/b.i.d for ODD symptoms. She had heavy abnormal vaginal bleeding that began on the fourth day of risperidone treatment and lasted 18 days, although her menstrual period ended a week prior. Risperidone treatment was

discontinued due to abnormal bleeding. Three days after the discontinuation, the bleeding was regressed. Since her ODD symptoms persisted, risperidone 0.5 mg/b.i.d was resumed one week later, and the patient was closely monitored. On the fifth day of restarting risperidone, abnormal vaginal bleeding recurred. The patient was referred to obstetrics for consultation. She had no galactorrhea or symptoms of menstrual irregularity. Her complete blood count, routine biochemistry, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen hormones, prolactin (PRL), prothrombin time (PT), activated partial thromboplastin time (aPTT) values, fibrinogen levels, and abdominal ultrasonography were within the normal range. The patient had no personal or family history of bleeding disorders, physical trauma, or self-injurious behaviors.

Furthermore, she was not bleeding elsewhere. Aside from the prescribed treatment, she was not using any other herbal or medicinal drugs. The situation was considered a potential adverse effect of risperidone, leading to its discontinuation. Repeated assessments, including the abovementioned tests, consistently showed normal results during a medication-free follow-up period of one month. Since the patient's ODD symptoms persisted, aripiprazole was initiated at 5 mg/day and subsequently increased to 10 mg/day. For six months under the current treatment regimen, the patient did not report any complaints of bleeding. The patient and her parents granted written and verbal consent to publish the case.

Abnormal vaginal bleeding was evaluated using the Naranjo Adverse Drug Reaction Probability Scale,

How to cite this article: Gulcu Ustun NS. Abnormal vaginal bleeding related to risperidone. *Dusunen Adam J Psychiatr Neurol Sci* 2023;36:195-196.

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Received: May 17, 2023; **Revised:** June 18, 2023; **Accepted:** August 18, 2023

that assesses the potential association between side effects occurring during drug use and the drug itself (9). Accordingly, a reaction is categorized as “definite” if the score is nine or higher, “probable” if it falls within the range of 5 to 8, “possible” if the score lies between 1 and 4, and “doubtful” if the score is 0 or lower. The patient scored 8, indicating a “probable” correlation. The current adverse reaction was considered likely to be linked to risperidone due to reasons such as its occurrence after the drug’s use, its regression upon discontinuation of the drug, its recurrence upon re-administration of the drug, and the presence of reported instances of bleeding associated with risperidone in the literature. Additionally, the absence of alternative causes further supports this assessment.

Excessive vaginal bleeding has also been reported with methylphenidate (10). However, in this case, the bleeding had not occurred for four years during methylphenidate treatment. Therefore, the primary consideration was that the abnormal vaginal bleeding was unlikely to be attributed to methylphenidate.

Regarding bleeding associated with risperidone, potential mechanisms include thrombocytopenia and antagonism of the 5-HT_{2A} receptor (7,11). The patient’s platelet counts were within the normal range, indicating that thrombocytopenia cannot be attributed as the cause of vaginal bleeding. The antagonism of the 5-HT_{2A} receptor leads to the suppression of vasoconstrictors released from platelets and a subsequent reduction in platelet aggregation (12). This mechanism could explain abnormal vaginal bleeding. The absence of other medically justifiable causes for the bleeding, the chronological correlation between drug initiation and discontinuation, and the patient’s response hints at a possible causal relationship. Further studies in this domain are warranted.

To our knowledge, this case may be the first to represent risperidone-induced vaginal bleeding. This adverse effect presents a condition that impacts the patient’s adherence to the prescribed medication. Clinicians should consider this uncommon effect, seek essential consultations, and exercise caution when addressing it.

Informed Consent: The patient and her parents granted written and verbal consent to publish the case.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author declares no conflict of interest.

Financial Disclosure: The author declares no financial support.

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