CASE REPORT

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Vortioxetine-Induced Bleeding Tendency in a Young Woman with Depression: A Case Report

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ABSTRACT

Vortioxetine, which functions as a 5-HT3, 5-HT1D, and 5-HT7 antagonist, a 5-HT1A agonist, and a 5-HT1B partial agonist, is a recently launched antidepressant approved by the United States Food and Drug Administration for treating adult major depressive disorder. Although hematological adverse effects have been associated with antidepressants, massive bleeding is a rare but potentially life-threatening complication. In this case report, we present a young woman who experienced abnormal bleeding tendencies, with manifestations including tarry stools, ecchymosis, and massive uterine bleeding, while undergoing vortioxetine treatment. Bleeding tendency improved after discontinuation of vortioxetine, recurred upon re-challenging, and resolved again after discontinuing the medication. This case study highlights the importance of closely monitoring bleeding tendencies in patients undergoing vortioxetine treatment. Physicians should exercise caution and thoroughly review medication history, especially for patients presenting with unexplained bleeding.

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INTRODUCTION

Vortioxetine, a 5-HT3, 5-HT1D, and 5-HT7 antagonist, 5-HT1A agonist, and 5-HT1B partial agonist, is a new antidepressant approved by the U.S. Food and Drug Administration in 2013 for the treatment of adult major depressive disorder.[1] Despite its reliable efficacy, vortioxetine, as with other antidepressants, has recently been associated with noticeable adverse effects in clinical practice.[1] Specifically, bleeding tendencies have been noted since its introduction.[1-4] In our previous case report, a young man suffered from the rapid onset of hemoptysis within a few days of treatment with vortioxetine at an initial low dosage.[5] Our current presentation reports the case of a young woman with depression who, while being treated with vortioxetine at a higher dosage, developed abnormal massive uterine bleeding, stressing the importance of clinicians recognizing and addressing this severe adverse side effect.

Ethical committee approval was received from the TMU-JIRB (Taipei Medical University-Joint Institutional Review Board) (Approval No: N202301015, protocol version/date: Version 1.0 2022/12/29).

The ethical committee approved the study as a waiver of informed consent, provided that adequate anonymity and de-identification of the patient's personal information were ensured.

CASE PRESENTATION

A 25-year-old employed single woman, without a history of physical illness, misuse of illicit substances, or abnormal menstruation, was diagnosed with major depressive disorder at the age of 13. She has a history of non-suicidal self-injury at age 22 and no past suicidal attempts.

The patient visited our clinic in early 2022 with the chief complaint of depressed mood and sleep maintenance insomnia for 1 month, without significant psychosocial stressors. Other depressive symptoms included anhedonia, psychomotor retardation, difficulties concentrating, daytime fatigue, poor appetite, and feelings of worthlessness. At the time of her presentation, she obtained a total score of 23 on the Hamilton Rating Scale for Depression (HAMD-17), indicating moderate depression.[6,7] Subsequently, a recurrent major depressive episode was diagnosed. Before this visit, she had been treated with fluoxetine at a dosage of up to 80 mg/day for 6 weeks but with an unsatisfactory response. Thus, she preferred to switch to treatment with another class of antidepressants. Initially, vortioxetine was prescribed at a dosage of 5 mg/day, along with 0.5 mg of clonazepam at bedtime. We gradually optimized the vortioxetine dosage to the full dosage (20 mg/day) over the following 3 weeks.

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After 5 weeks of vortioxetine treatment, the patient complained of transient tarry stool and slight bruising on both thighs, indicating a probable vortioxetine-induced bleeding tendency. Given the concern that antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), can impair platelet function and increase the risk of bleeding by inhibiting the serotonin transporter expressed by platelets, a non-SSRI and non-SNRI antidepressant was considered.[8] Hence, we substituted vortioxetine 20 mg/day for bupropion 300 mg/day. Moreover, we checked her complete blood cell counts (CBC), prothrombin time (PT), partial thromboplastin time (PTT), renal function, and liver function, which were within normal limits.

At week 6, 1 week after discontinuation of vortioxetine and starting 300 mg/day of bupropion, the patient's tarry stool subsided. However, she developed bilateral hand tremors, which tremendously bothered her. Due to a previous unsatisfactory response to fluoxetine, the patient preferred to try a different non-SSRI antidepressant after discontinuing bupropion. After carefully evaluating the risks and benefits of trying another antidepressant versus re-challenging vortioxetine treatment, a shared clinical decision was made with the patient. Considering the patient's previous response to vortioxetine, with improvements in depressive symptoms and overall quality of life, she opted to retry vortioxetine instead of trying other non-SSRI and non-SNRI antidepressants. The decision was based on the superior efficacy and relatively tolerable side effects of vortioxetine, such as transient tarry stools and slight ecchymosis. After we explained the chall enge-dechallenge-rechallenge medical testing protocol, informed her of the potential risk of bleeding tendency with vortioxetine, and reassured her about vigilant monitoring of side effects, she consented to this switch in treatment.

At week 7, following 1 week of re-challenging with vortioxetine, the patient experienced prolonged menstruation with vaginal spotting. She visited a gynecologist, where gynecologic ultrasonography revealed no definite abnormality. Under the impression of vortioxetine-induced bleeding tendency, we replaced vortioxetine with agomelatine, a melatonin receptor agonist with no apparent risk of abnormal bleeding resulting from serotonergic effects on platelets, at a dosage of 25 mg/day.[9]

At week 8, abnormal heavy uterine bleeding persisted, requiring hourly changes of sanitary pads in the past week. In response, we discontinued all psychotropic medications and provided non-pharmacological interventions for depression, along with close clinical follow-up. Laboratory tests associated with bleeding tendency showed no prominent abnormalities. Additionally, we prescribed 250 mg of tranexamic acid, 3 times a day, to prevent further blood loss. The patient experienced no uterine bleeding or vaginal spotting in the ensuing weeks and exhibited partial remission of her depressive symptoms.

MAIN POINTS

- This case report demonstrates the adverse effect of abnormal bleeding tendencies, with manifestations including tarry stools, ecchymosis, and massive uterine bleeding, in a young woman treated with vortioxetine for depression.
- Vortioxetine-induced bleeding tendencies may manifest as heavy or prolonged menstruation.
- Bleeding tendencies should be vigilantly monitored when administering vortioxetine, especially in women with an active menstrual cycle.

DISCUSSION

This case report presents a young woman with major depressive disorder, exhibiting a vortioxetine-induced bleeding tendency. This is confirmed and supported by re-challenging with the same dosage of vortioxetine, which resulted in prolonged menstruation with abnormal massive uterine bleeding persisting for several weeks after discontinuing the suspected medication. We applied the Naranjo Adverse Drug Reaction Probability Scale to establish the causal relationship between vortioxetine and the patient's bleeding tendency.[10,11] Our case scored a 7 on the Naranjo Adverse Drug Reaction Probability Scale, indicating that vortioxetine was a probable cause of the adverse effects presented.[10,11]

The antidepressant-mediated bleeding tendency could be associated with impaired 5-HT-induced platelet aggregation amplification, a process that is linked to platelet 5-HT depletion due to medicated 5-HT reuptake inhibition.[3] Upper gastrointestinal bleeding or ecchymosis may have short-term adverse effects, as the patient had a normal platelet count, PT, PTT, and renal and liver functions. However, women are exposed to a higher risk of more severe side effects during menstruation, such as heavy abnormal uterine bleeding. Our patient demonstrated prolonged menstruation resulting from abnormal massive uterine bleeding, even though gynecological ultrasonography demonstrated no definite abnormality. Furthermore, the patient had no history of a pre-existing platelet disorder that may predispose her to this complication[3] or concomitant use of medications that would affect homeostasis.[1]

Existing studies regarding serious hematological adverse effects of vortioxetine reported dermatological presentations including pruritus, petechiae, and ecchymosis, although all 3 case reports were on middle-aged women.[2-4] In the younger population receiving vortioxetine treatment, we previously presented a young man who suffered from hemoptysis,[5] and herein present a young woman experiencing abnormal massive uterine bleeding.

Both patients were in their 30s. Our reports suggest that the non-dermatological adverse effects of vortioxetine should not be ignored in young adults, especially when treating women who have an active menstrual cycle.

In conclusion, abnormal massive bleeding may occur in patients treated with vortioxetine. Manifestations of the vortioxetine-induced bleeding tendency may include heavy or prolonged menstruation, which should be considered and closely monitored when administering vortioxetine, especially in women with an active menstrual cycle. Therefore, clinicians ought to balance the benefits and risks while administering vortioxetine, and close monitoring of clinical response and adverse effects in patients is crucial.

Data Availability Statement: The data that support the findings of this study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author upon reasonable request.

Ethics Committee Approval: This study was approved by the Ethics Committee of TMU-JIRB(Taipei Medical University-Joint Institutional Review Board) (Approval No: N202301015, Date:2022/12/29).

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