Received: 28 March 2024 | Revised: 18 May 2024 | Accepted: 22 June 2024

DOI: 10.1002/ccr3.9128

CASE REPORT

Clinical Case Reports Open Access WILEY

Feeling blue to seeing red: A case of escitalopram-induced epistaxis

Temitope Ogundare[1,2] | **Olumayowa Adesoji Ologun**[3]

[1]Department of Psychiatry, Boston Medical Center, Boston, Massachusetts, USA

[2]Department of Psychiatry, Boston University School of Medicine, Boston, Massachusetts, USA

[3]Department of Family Medicine, McMaster Univeristy, Hamilton, Ontario, Canada

Correspondence
Temitope Ogundare, Department of Psychiatry, Boston Medical Center, Boston, MA 02118, USA.
Email: ogundare@bu.edu

Key Clinical Message

Selective serotonin reuptake inhibitors are associated with an increased risk of bleeding, most commonly intracranial and gastric bleeding, especially in conjunction with anticoagulant use. Although uncommon, escitalopram is associated with epistaxis in a dose-dependent manner. Dosage reduction may be sufficient in management.

KEYWORDS

adverse drug events, antidepressants, epistaxis, escitalopram, SSRIs

1 | INTRODUCTION

Epistaxis, defined as bleeding from the nose, can be caused by local or systemic conditions such as neoplasms, trauma, inflammatory conditions, alcoholism, dryness in winter, and medications such as nonsteroidal anti-inflammatory drugs and oral anticoagulants.[1,2] Studies have shown that selective serotonin reuptake inhibitors (SSRIs) can increase bleeding risk, especially upper gastrointestinal bleeding and cerebral bleeding.[2,3] However, epistaxis has not been commonly reported. There have been a few case reports about escitalopram-induced epistaxis.[1,3] Bleeding risk is usually associated with other risk factors such as alcoholism, seasonal allergy, co-administration of other medications that affect coagulation, and those undergoing surgery.[1–4] We report a case of escitalopram-induced epistaxis in a 33-year-old female.

2 | CASE HISTORY/EXAMINATION

A 33-year-old woman with a psychiatric history of depression, PTSD, no prior inpatient hospitalization, no prior suicide attempt, and no significant medical history presented to the outpatient psychiatric clinic with complaints of depressed mood, insomnia, and anxiety. She endorsed a history of sexual assault and abduction with constant re-experiencing, intrusive memories and images, persistent sadness, sleep difficulties, and nightmares. She endorsed constant hypervigilance and inability to relax.

On further psychiatric review of the system, she endorsed auditory and visual hallucinations dating back to when she was a teenager. She described the auditory hallucinations as belonging to her mother, who is now dead, and some other unknown voices. She denied command auditory hallucinations. She endorsed seeing dead people

while awake, feels scared, but is aware that they are not real. She denied paranoia but mentioned that she believes some of her thoughts are being broadcasted to others and that some of her actions are not hers.

She constantly needs supervision and help with activities of daily living. She endorsed a positive family history of schizophrenia in her maternal uncle and two siblings. She denied a history of substance use. She has never been hospitalized but has turned to traditional medicine for a cure. She was previously married and endorsed interpersonal violence, has five children, and immigrated to the United States 5 years prior, currently living with an older brother and his family.

Before being seen at the outpatient clinic, she was seen at the community behavioral health clinic and was started on sertraline 50 mg daily and trazodone 25–50 mg at bedtime. Two weeks later, her medications were increased to sertraline at 100 mg daily and trazodone at 50–100 mg at bedtime. When she was seen a month later, she had stopped all her medications, both the sertraline and trazodone, because she complained that they made her feel like "I want to die." She was then started on mirtazapine at 7.5 mg at bedtime for a week and 15 mg subsequently. Two months after beginning mirtazapine, she reported some improvement with sleep but not depressed mood or PTSD symptoms, and escitalopram was started at 10 mg daily to augment mirtazapine. Over the next 2 months, escitalopram was increased to 20 mg daily, mirtazapine was kept at 15 mg daily, and Benadryl 25 mg at bedtime was added due to persistent sleep difficulties.

On evaluation at the outpatient clinic, a diagnosis of schizophrenia and PTSD was made. Aripiprazole was added to her medications and titrated over 3 months to 20 mg daily. She reported marked improvement in auditory and visual hallucinations but continued to complain of poor nighttime sleep and excessive daytime sedation.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT)

On her fourth follow-up visit, she complained of epistaxis, which started about a week prior. The bleeding started suddenly; she was unable to quantify the amount but mentioned that it was 'not much.' She was unable to provide additional information on how long the bleeding lasted but stated it occurred daily. She denied trauma, digital manipulation, cold, fever, bleeding gums, and bruising. She denied a prior history of epistaxis, allergic rhinitis, or septal deviation.

Physical examination was unremarkable. She denied dizziness. Blood pressure was 124/94 mmHg, pulse rate was 64 beats per minute, and respiratory rate was 12 cycles per minute.

A complete blood count showed WBC of 7000/μL, Hematocrit of 39.6%, Hemoglobin of 12.8 g/dL, APTT of 33 s, PT/INR of 12.8 s/1.14, and liver function tests of ALT of 21μ/L, AST of 18μ/L, alkaline phosphatase of 65μ/L, total bilirubin of 0.3 mg/dL, and total albumin of 4.6 g/dL. All tests were within normal limits.

Her medication consisted of aripiprazole 20 mg daily, escitalopram 20 mg daily, mirtazapine 15 mg daily, Benadryl 25 mg at bedtime, and melatonin 6 mg at bedtime. She was not on nonsteroidal anti-inflammatory medications or oral anticoagulants. Her bleeding diathesis was suspected to be due to escitalopram, and the dose was reduced to 10 mg daily, with a plan for ENT referral if the bleeding persisted.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

At the next follow-up visit, she reported that the epistaxis had resolved. Over a 6-month follow-up period, she did not experience epistaxis, and escitalopram-induced epistaxis was confirmed.

5 | DISCUSSION

In this case report, we presented a case of escitalopram-induced epistaxis, which subsided after the dosage reduction. The evaluation did not reveal any apparent cause of epistaxis. Reducing the dose resolved the epistaxis, similar to previous case reports of escitalopram-induced epistaxis.[3,4]

Increased bleeding risk is a well-documented side effect of selective serotonin reuptake inhibitors (SSRIs), with a meta-analysis estimating the risk of bleeding to be about 36% with a range of 12% to 64%.[5] Gastrointestinal bleeding and intracranial bleeding are usually the most commonly reported, especially when SSRIs are used in combination with NSAIDs and other anticoagulants.[3,5,6] SSRIs decrease nitric oxide production by inhibiting nitric oxide synthase, which leads to decreased platelet aggregation and increased bleeding.[7] They also inhibit the entry of serotonin from blood into platelets, which leads to reduced platelet aggregation and increased bleeding time.[8] Bleeding risk with SSRIs is related to binding affinity at serotonin receptors,[1,4] with higher affinity SSRIs such as fluoxetine, paroxetine, and sertraline having the highest bleeding risk.[1,9–11] Citalopram, fluvoxamine, escitalopram, amitriptyline, imipramine, and venlafaxine have intermediate affinity and a lower risk of

bleeding, while the lowest risk is with mirtazapine, bupropion, agomelatine, desipramine doxepin, nortriptyline, phenelzine, tranylcypromine, and trazodone.[1,9–11] There is no consensus on the timing of bleeding risk from SSRIs use, with some studies proposing that risk is highest in the first 30 days of use; however, the risk of bleeding has been estimated to be as late as 3 years after the onset of SSRIs.[9]

Epistaxis is rare with escitalopram use, with only a few case reports. In an open-label trial of escitalopram for a night eating disorder, one participant discontinued escitalopram due to epistaxis.[12] In another randomized control trial of escitalopram on preventing depression in patients with acute coronary syndrome, two cases developed upper gastrointestinal bleeding, menorrhagia, and epistaxis.[13] In the previous case reports, the patients developed epistaxis without other causative medications or other medical conditions predisposing to epistaxis, similar to this patient. In this case, the patient developed epistaxis after 6 months on 20 mg of escitalopram and 8 months of commencement of escitalopram. This was longer than previously reported, 2 weeks[1] and 2 months.[4] It is worth noting that in those cases, escitalopram dosage was increased rapidly over a short period compared to this case, which may account for the delay in the onset of epistaxis.

The paucity of case reports of escitalopram-induced epistaxis may be due to under-reporting, probably due to non-clinically significant bleeding, or because no connection was made between bleeding and concurrent use of escitalopram.[4] However, clinicians need to be aware of the increased risk of bleeding with SSRIs, especially in patients who are taking concomitant medications that increase bleeding risk, such as NSAIDs or anticoagulants. In addition, alcohol use has been shown to increase the risk of bleeding by decreasing platelet aggregation and release, increasing platelet destruction, and inhibiting platelet function.[14] Therefore, patient consuming excessive amounts of alcohol may also be at increased risk for bleeding when using escitalopram and should be counseled on reducing their alcohol intake. In patients at risk for bleeding, it may be prudent to prescribe SSRIs or other antidepressants with lower bleeding risk, such as mirtazapine or bupropion.

AUTHOR CONTRIBUTIONS

Temitope Ogundare: Conceptualization; writing – original draft; writing – review and editing. **Olumayowa Adesoji Ologun:** Writing – review and editing.

ACKNOWLEDGMENTS

No specific acknowledgments are required for this case report.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

No conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Temitope Ogundare https://orcid.org/0000-0001-7061-0013

REFERENCES

1. AlJhani SA. Escitalopram-induced epistaxis: a case report. *J Taibah Univ Med Sci*. 2021;16(6):938-942. doi:10.1016/j.jtumed.2021.06.004
2. Meirinho S, Relvas R, Alves G. Drug-induced epistaxis: an often-neglected adverse effect. *Curr Drug Saf*. 2018;13(2):74-83. doi:10.2174/1574886313666180213090943
3. McFarland D, Merchant D, Khandai A, et al. Selective serotonin reuptake inhibitor (SSRI) bleeding risk: considerations for the consult-liaison psychiatrist. *Curr Psychiatry Rep*. 2023;25(3):113-124.
4. Aggarwal A, Sharma RC, Sharma DD, Kumar R, Sharma DD. Probable epistaxis associated with escitalopram. *Prog Neuro-Psychopharmacol Biol Psychiatry*. 2010;34(4):709-710. doi:10.1016/j.pnpbp.2010.03.006
5. Laporte S, Chapelle C, Caillet P, et al. Bleeding risk under selective serotonin reuptake inhibitor (SSRI) antidepressants: a meta-analysis of observational studies. *Pharmacol Res*. 2017;1(118):19-32.
6. Yuet WC, Derasari D, Sivoravong J, Mason D, Jann M. Selective serotonin reuptake inhibitor use and risk of gastrointestinal and intracranial bleeding. *J Osteopath Med*. 2019;119(2):102-111.
7. Shen WW, Swartz CM, Calhoun JW. Is inhibition of nitric oxide synthase a mechanism for SSRI-induced bleeding? *Psychosomatics*. 1999;40(3):268-269.
8. Serebruany VL. Selective serotonin reuptake inhibitors and increased bleeding risk: are we missing something? *Am J Med*. 2006;119(2):113-116.
9. Bixby AL, VandenBerg A, Bostwick JR. Clinical management of bleeding risk with antidepressants. *Ann Pharmacother*. 2019;53(2):186-194.
10. Andrade C, Sharma E. Serotonin reuptake inhibitors and risk of abnormal bleeding. *Psychiatr Clin North Am*. 2016;39(3):413-426. doi:10.1016/j.psc.2016.04.010
11. Renoux C, Vahey S, Dell'Aniello S, Boivin JF. Association of selective serotonin reuptake inhibitors with the risk for spontaneous intracranial hemorrhage. *JAMA Neurol*. 2017;74(2):173-180.

12. Allison KC, Studt SK, Berkowitz RI, et al. An open-label efficacy trial of escitalopram for night eating syndrome. *Eat Behav*. 2013;14(2):199-203.
13. Hansen BH, Hanash JA, Rasmussen A, et al. Effects of escitalopram in prevention of depression in patients with acute coronary syndrome (DECARD). *J Psychosom Res*. 2012;72(1):11-16.
14. Wakabayashi I. Platelet count in men with a habit of alcohol drinking. *Platelets*. 2020;31(2):265-267.

How to cite this article: Ogundare T, Ologun OA. Feeling blue to seeing red: A case of escitalopram-induced epistaxis. *Clin Case Rep*. 2024;12:e9128. doi:10.1002/ccr3.9128