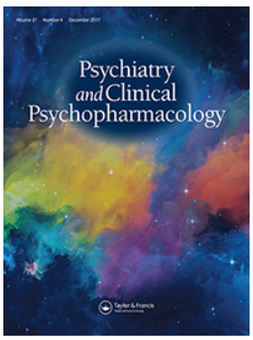

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CASE REPORT

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Fluoxetine-related ecchymosis treated with venlafaxine: a case report

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ABSTRACT

Selective serotonin reuptake inhibitors (SSRIs) are known to have a relatively favourable side effect profile. In recent years, there has been an emphasis on the risk of upper gastrointestinal bleeding in patients taking SSRI antidepressants. Although they may have some effects on coagulation profile, ecchymosis is a rare clinical manifestation of these effects. Here, we report a 25-year-old female patient who was diagnosed with major depressive disorder and manifested spontaneous ecchymoses on her legs rapidly following fluoxetine use. Her complete blood cell count, prothrombin time, partial thromboplastin time, bleeding time, and other hematological screening tests were within normal limits. After discontinuation of fluoxetine, her ecchymoses were resolved in two weeks. Ecchymosis did not recur after fluoxetine was discontinued, and the patient was switched to venlafaxine.

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KEYWORDS
Fluoxetine; ecchymosis; side effect

Introduction

Selective serotonin reuptake inhibitors (SSRIs), which are not superior to tricyclic antidepressants in terms of efficacy, are commonly used for the treatment of depression, anxiety disorders, and several other psychiatric disorders thanks to their favourable safety profiles [1]. Although SSRIs are relatively safe, they are known to be associated with several hematological side effects including bleeding. There are a growing number of studies reporting an increased risk of bleeding with the use of these agents [2]. In addition, similar to the other SSRIs, fluoxetine also rarely causes ecchymosis and the literature mostly includes case reports of this side effect [3,4]. Here, we report a case of depression who developed ecchymosis after the initiation of fluoxetine and was successfully treated with venlafaxine.

Case presentation

A 25-year-old female patient was referred to psychiatry outpatient clinic with complaints of fatigue, asthenia, difficulty in concentration, and loss of motivation for the past three months. The patient scored 26 points on the Hamilton Rating Scale for Depression. She was diagnosed with major depressive disorder based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition diagnostic criteria. The patient had no history of alcohol or substance abuse, and had no concomitant psychiatric diagnoses. She had no history of previous antidepressant treatments and was initiated on fluoxetine 20 mg/day. Three days after initiation of treatment, the patient developed bruises on both legs. Four days after the initiation of treatment, an ecchymosis of 3 and 5 cm in diameter around the knee on both legs was noted. The patient did not report any physical trauma to the ecchymosis sites. She had no bleeding or a colour change in urine or stool. She had no pain in the sites of ecchymosis. Her medical history revealed no drug use, food allergies, autoimmune or medical conditions which might have caused the lesions. Her family history did not reveal any spontaneous bleeding disorders or a hematological disorder. The patient had no lesions on the other parts of her body and, then, she was referred to hematology outpatient clinic for consultation. Her physical examination performed by the hematologist did not indicate ecchymosis on any other part of her body. Examinations and assays did not suggest any hematological pathology. In addition, laboratory investigations did not suggest any abnormality. Laboratory test results were as follows: hemoglobin: 14.3 g/dL; white blood count: 3:54 10E3/mm^3; platelets: 199.400/mm^3; mean platelet volume: 7:41; fluorine sedimentation: 12 mm/h; urea: 33 mg/dL; creatinine: 0.73 mg/dL; sodium: 140 mmoL/L; potassium: 4.6 mmoL/L; aspartate aminotransferase: 18 IU/L; alanine aminotransferase: 18/L; free T3: 3:19 pg/mL; free T4: 1:42 ng/mL; thyroid stimulating hormone: 1.80 mU/mL; international normalized ratio: 1:06; activated partial thromboplastin time: 35.7 sec; and partial thromboplastin: 13.1 s. The hematologist reported fluoxetine-induced ecchymosis. Upon cessation of fluoxetine treatment, ecchymotic lesions

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rapidly disappeared within 1–2 days and did not recur. Her depressive complaints, however, continued during this period. After the initiation of venlafaxine 75 mg/day, depressive complaints resolved within three weeks. Ecchymosis lesions did not recur after the initiation of venlafaxine. Venlafaxine treatment was continued for one year and her depressive complaints did not repeat; therefore, pharmacological treatment was discontinued at the end of one year. During follow-up, no hematological side effects were observed. Additionally, a telephone contact was performed with the patient two years after the most recent examination and she reported no ecchymosis or spontaneous bleeding, or she was not diagnosed with any hematological disorders.

Discussion

The use of SSRIs is known to be associated with increased bleeding risk. A recent meta-analysis demonstrated that SSRI use was associated with a 55% increase in the rate of upper gastrointestinal system (GIS) bleedings [2]. Although the exact mechanism through which SSRIs cause upper GIS bleeding is unknown, it has been suggested that they increase bleeding risk by inhibiting serotonin reuptake in the platelets or by increasing gastric acid secretion [5–7]. Moreover, preclinical studies have shown that platelets do not synthesize serotonin; therefore, it has been argued that SSRIs impair platelet functions by reducing serotonin levels in the platelets [2,6]. Inhibition of reuptake results in a decline in the level of serotonin in these cells, which plays a crucial role in platelet aggregation. In addition, SSRIs induce a decline in the release of dense granules further impairing the formation of platelet plugs, leading to reduced platelet aggregation and an increased propensity to bleeding [8]. The effects of SSRIs and the other antidepressants on platelet functions may vary. In a study investigating *in vitro* effects of serotonin-norepinephrine reuptake inhibitors (SNRIs) on platelet adhesion and coagulation, sertraline, citalopram, and reboxetine were shown to decrease platelet adhesion, while no effect of venlafaxine was demonstrated on this function [6]. Based on these data in the current literature, we switched our patient to venlafaxine, which is an SNRI agent believed to be more advantageous in terms of hematological side effect profile.

Although there is evidence of an increased bleeding risk, SSRIs are rarely associated with ecchymosis as a side effect. Previous case reports described development of side effects including ecchymosis and purpura related with the use of paroxetine and sertraline [9,10]. Nevertheless, most of the ecchymosis cases during the use of SSRIs, as reported in the literature, were indeed related with the use of fluoxetine [3,4,11]. Our case had normal platelet count and her activated partial thromboplastin time and bleeding times were within normal ranges, suggesting that fluoxetine acts by impairing platelet aggregation or inhibiting serotonin reuptake in the platelets without affecting platelet count or blood clotting factors [7]. Our case developed ecchymosis due to the use of fluoxetine and subsequently she was switched to venlafaxine, which is associated with a relatively lower risk of bleeding, compared to SSRIs. To the best of our knowledge, only one case of ecchymosis associated with venlafaxine treatment was previously reported in the literature [12]. After we switched our case to venlafaxine, ecchymosis did not recur.

Fluoxetine is a specific and potent neuronal reuptake inhibitor and it is often associated with a lower possibility of side effects, as it does not inhibit noradrenaline or dopamine reuptake [13]. Besides, fluoxetine is preferred for treatment of several psychiatric disorders as a safe agent, since its effects on the muscarinic, histaminergic, adrenergic, and serotonergic receptors are relatively less extensive, compared to tricyclic antidepressants. Other than nausea, irritability, and sleep disorders, fluoxetine was associated with a lower rate of side effects, compared to other SSRIs [14]. On the other hand, compared to other SSRIs, a higher number of case reports describing fluoxetine-related ecchymosis can be found in the literature [3,4]. The fact that our case rapidly developed ecchymosis on the third day after the initiation of fluoxetine treatment suggests that there is a casual relationship between fluoxetine and ecchymosis. Such a possible relationship is further supported by the absence of a spontaneous bleeding incident in the medical history of the patient and the rapid resolution of ecchymosis within days after the cessation of fluoxetine. Besides, the fact that our case did not experience any bleeding event during a period of three years after fluoxetine use indicates that fluoxetine itself directly caused ecchymosis, rather than exacerbating a hematological disorder.

In conclusion, while spontaneous ecchymosis is a rare side effect of fluoxetine, this possibility should always be kept in mind for certain patients. In clinical practice, monitoring skin lesions can be helpful to avoid advanced hematological complications in patients who are prescribed fluoxetine. A particular care must be given while initiating fluoxetine treatment in patients with history of a hematological disease or in individuals who have bleeding risk. The possibility of such untoward hematological side effects can be reduced preferring SNRIs over SSRIs in patients who are under the risk of ecchymosis, such as in the case described.

Disclosure statement

No potential conflict of interest was reported by the authors.

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