CASE REPORT

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Abnormal Uterine Bleeding Associated with Bupropion: A Case Report

Bupropion ile İlişkili Anormal Uterin Kanama: Olgu Sunumu

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Abstract

In the literature, many cases of abnormal uterine bleeding associated with selective serotonin reuptake inhibitors have been reported as a side effect of antidepressant treatment. However, abnormal uterine bleeding associated with bupropion, a norepinephrine-dopamine reuptake inhibitor, has been reported in only two case studies to date. A 28-year-old, oligomenorrheic female patient was admitted to the psychiatry department with the symptoms of depression. The patient was diagnosed with major depression and bupropion 150 mg/day was prescribed. After the initiation of the treatment, the patient experienced mild-to-moderate uterine bleeding, which was resolved with the discontinuation of the drug. In the patient's anamnesis, it was learned that the same side effect had developed with the previous bupropion treatment. A comprehensive examination of the patient suggested that this adverse effect could strongly be associated with bupropion. This case supports the view that antidepressants can cause bleeding abnormalities, in particular vaginal bleeding caused by bupropion usage. Physicians who prescribe bupropion should carefully follow up their patients to identify such adverse effects.

Keywords: Abnormal uterine bleeding, adverse effect, bupropion, case reports

Öz

Literatürde, antidepresan tedavisi yan etkisi olarak selektif serotonin reuptake inhibitörleri ile ilişkili çok sayıda anormal uterin kanama olgusu bildirilmiştir. Bir norepinefrin-dopamin geri alım inhibitörü olan bupropion ile ilişkili anormal uterin kanama bu tarihe kadar sadece iki olgu sunumunda bildirilmiştir. Yirmi sekiz yaşında, oligomenoreik kadın hasta, depresyon belirtileri ile kliniğimize başvurdu. Hastaya majör depresyon tanısı konuldu ve bupropion 150 mg/gün reçete edildi. Tedavinin başlamasından sonra hastada, ilacın kesilmesi ile düzelen hafif-orta derecede düzensiz uterin kanama gelişti. Hastanın anamnezinde daha önceki bupropion tedavisi ile de aynı yan etkinin gelişmiş olduğu bilgisi edinildi. Kapsamlı bir inceleme sonrasında, bu yan etkinin bupropion ile güçlü bir şekilde ilişkili olabileceği düşünüldü. Bu olgu, antidepresanların kanama anormalliklerine, özellikle bupropion kullanımına bağlı vajinal kanamalara neden olabileceği görüşünü desteklemektedir. Bupropion reçetesi yazan doktorlar, bu tür yan etkileri belirlemek için hastalarını dikkatle izlemelidirler.

Anahtar kelimeler: Anormal uterin kanama, bupropion, olgu sunumu, yan etki

Introduction

An increasing number of studies and case reports are involved in the literature associated with abnormal uterine bleeding (AUB) after treatment with various antidepressants. Most of these cases are associated with selective serotonin reuptake inhibitors (SSRIs) (1). A few cases of AUB have also been reported due to the use of venlafaxine, a serotonin norepinephrine reuptake inhibitor (2). To date, a case series of two patients with AUB associated with bupropion, a norepinephrine dopamine reuptake inhibitor, has been found in the literature. In this case series, it was reported that bupropion caused irregular and increased menstrual bleeding in one patient, and shortened cycles and secondary amenorrhea in the other patient (3). In this article, a patient who was treated with

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bupropion for depression and developed AUB as a side effect is presented.

Case Report

A 28-year-old woman was presented to our psychiatry clinic with the symptoms of depression, including feeling down, aversion, nervous temperaments, obliviousness, pessimistic thoughts and reluctance to social interaction. The patient was diagnosed with major depression. Her Beck depression scale (BDS) score was 24. In her anamnesis, it was learned that she had applied to a psychiatrist with the diagnosis of depressive disorder one year ago, and 150 mg/day bupropion treatment had been started, which had been increased to 300 mg/day at the 2nd month. The patient stated that she had AUB that had lasted for 15-20 days, except for menstrual bleeding, during the entire treatment, but she had not told her doctor about this. Within the sixth month of the treatment, the patient had stopped taking the medication due to the increased amount and duration of the bleeding. Fifteen days later, the patient's AUB had been resolved. She had had regular menstrual periods for the following 1 year. The patient, whose depressive symptoms had recurred after a one-year drug-free period, was admitted to the psychiatry clinic of our hospital this time. Based on her history, the patient was evaluated by the gynecology clinic of our hospital. No pathology was observed in the gynecological examination. We prescribed bupropion 150 mg/day. At the one-month visit after the initiation of the treatment, there was a reduction in her depressive symptoms and BDS score was fourteen. She also reported that, apart from normal menstrual bleeding, she had vaginal bleeding that lasted for four days. At the end of the third month, her depressive symptoms disappeared and she noted that the duration and intensity of her vaginal bleeding were the same as in the first month. Thereupon, the patient was evaluated gynecologically again. Her coagulation parameters and serum hormone levels were found to be normal. No pathology was observed as a result of the endometrial sampling performed under office hysteroscopy. After the fourth month, the patient discontinued her treatment because she thought she got better. Although we informed the patient on the potential risks of quitting the medication and strongly advised her to continue the treatment, she refused to receive it. We followed the patient for the next six months for depression and menstrual cycles. During this period, we observed that the patient's depression symptoms and AUB did not recur.

Discussion

Numerous mechanisms about how antidepressants can cause bleeding abnormalities have been suggested in previous research. Serotonin (5-HT) is important in platelet aggregation and the modulation of vascular tone. SSRIs block platelet uptake and endothelial metabolism of serotonin and use of these agents may result in bleeding and vasospastic complications (4). Serotonin is found in the reproductive tract of female mammals, including the ovaries, follicular fluid, mature oocytes, and cumulus cells, and its concentration changes during the menstrual cycle and it is involved in the modulation of follicular maturation (5). Antidepressants with serotonergic effects may cause vaginal bleeding due to their effects on gonadal hormones (1). With respect to this case, the above-mentioned case raises the question whether bupropion exhibits any serotonergic activities. A study with rats has provided evidence that all neurotransmitter levels (dopamine, norepinephrine, and serotonin) have significantly increased after bupropion injection (6). Medications that influence the dopaminergic and norepinephrinergic systems can presumably increase 5-HT transmission (7). These findings favor the notion that bupropion can demonstrate serotonergic effects and may cause bleeding abnormalities through modulation of gonadal hormones. We also explored the relationship between dopamine and norepinephrine reuptake and vaginal bleeding. An *in vitro* study demonstrates that the therapeutic concentration of the selective norepinephrine reuptake inhibitor desipramine inhibits serotonin uptake in platelets and that the 5-HT content in platelets is reduced by 38% compared to pretreatment levels in depressed patients (8). It has also been found that increasing dopaminergic neurotransmission can impair platelet functions, although the mechanism has not been clarified (9).

We have concluded that the AUB that developed in the patient might be related to the use of bupropion because, without an underlying organic reason, vaginal bleeding started after each bupropion use and was resolved after the discontinuation of the drug. More research is needed to fully understand how antidepressants cause bleeding abnormalities, and patients using bupropion should be carefully monitored for such side effects.

Ethics

Informed Consent: Informed consent form was signed by the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.K.V., E.E.K., Design: M.K.V., E.E.K., Data Collection or Processing: M.K.V., E.E.K., Analysis or Interpretation: M.K.V., E.E.K., Literature Search: M.K.V., E.E.K., Writing: M.K.V., E.E.K.

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