Acneiform eruption associated with the use of vortioxetine

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ABSTRACT
Acneiform is used to describe eruptions that resemble acne vulgaris, but are not aetiologically similar. A number of drugs that can be responsible for acneiform eruptions exist. Vortioxetine is a multimodal antidepressant molecule that shows an antagonistic effect to the 5HT1D, 5HT3, and 5HT7 receptors, a partial agonistic effect to the 5HT1B receptor and a fully agonistic effect to the 5HT1A receptor, and also is an inhibitor to the serotonin transporter (SERT). In this article, we report a female patient who developed acneiform eruption during vortioxetine treatment.

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Vortioxetine; antidepressant; depression; acneiform eruption; dermatologic side effect; adverse effect

Introduction
Vortioxetine is a multimodal antidepressant molecule that shows an antagonistic effect to the 5HT1D, 5HT3, and 5HT7 receptors, a partial agonistic effect to the 5HT1B receptor and a fully agonistic effect to the 5HT1A receptor, and also is an inhibitor to the serotonin transporter (SERT). The use of vortioxetine in animal models has been shown to increase extracellular serotonin, acetylcholine, norepinephrine, and histamine concentrations [1]. Vortioxetine is believed to enhance glutamatergic transmission through 5HT3 and 5HT7 receptors and thus have a therapeutic effect on cognitive functions [2]. Vortioxetine is a safe and tolerable drug in the treatment of the major depressive disorder. The rate of withdrawal because of adverse effects with vortioxetine 15 mg (6.8%) was similar to the rates reported in previous studies using vortioxetine doses up to 10 mg, that is 3–9% [3]. The number needed to harm, for discontinuation of vortioxetine due to an adverse event, was 36 (95% CI 24 to 70) [4]. At the end of the six-week study by Jain et al. [5], 18/597 subjects (3%) had discontinued the treatment due to adverse effects. There were no differences between the vortioxetine 5 mg and placebo groups with regard to the number of subjects who discontinued the study because of an adverse effect [5]. The most common adverse effects are nausea, and more rarely diarrhoea, constipation, dizziness, abnormal dreaming, flushing, general pruritus, bruxism, and night sweats can also be observed [6]. In this article, we report a female patient who developed acneiform eruption during vortioxetine treatment. The patient was given written consent to use her information and photograph.

Case
A 20-year-old female patient is single and a university student. About 4 months ago, venlafaxine 75 mg/day treatment was recommended according to her reluctance, unhappiness, insomnia, lack of study, and attention complaints. Her psychological complaints were partially receded after the medical treatment, however recently, due to her complaints as increasing weight, slower executive thinking processing, and forgetfulness, she applied to our clinic in order to change her medicine. It was learned in her medical history that, she started using the drug because of similar complaints after the stress factors that she experienced about 3 years ago and she has been using a number of antidepressants which she was not able to recall their names. There was no mental illness in her family history. Her Hamilton Depression Scale (HDRS) score was 13 points. The venlafaxine treatment was reduced and ended. For ongoing mental complaints, vortioxetine treatment was recommended with initially 5 mg/day, which has little effect on putting on weight and which has been developed with minor side effects on cognitive functions, and it has been suggested to increase vortioxetine dosage to 10 mg/day, after 1 week of usage. One month later, the patient’s depressive complaints were decreased and had an HDRS score: 11. During the fifth week of the treatment with vortioxetine, the patient had developed acne on both cheek areas on the face and did not care about this by relating it to her menstrual cycle but in the following days, the lesions spread to the larger area of the skin and she applied to the dermatology clinic as a result of bleeding due to scratching. The patient had no dermatological disease in her medical history. Due to the blood tests
results, asked by the dermatologist, were within normal limits, no additional disease or drug usage history other than vortioxetine the onset of drug use in the ana-
mnesis and the characteristics of the lesion the “acnei-
form eruption” was diagnosed, and withdrawal of vortioxetine and beginning of topical tetracycline treat-
ment was recommended. The patient, who was rec-
ommended to end the treatment, applied to our clinic. Fluoxetine 20 mg/day therapy was started
because of the continuation of the patient’s psychologi-
cal complaints and weight gain concerns. Withdrawal of the medication and topical antibiotic treatment
resulted in a decrease of old lesions on the face of the patient and prevention of new lesions to develop
during the use of fluoxetine.

Discussion

Acneiform is used to describe eruptions that resemble
acne vulgaris, but are not aetiologically similar. Acnei-
form eruption, which is diagnosed based on medical
history and clinical features, usually begins within
the first 1–3 weeks of drug use [7]. Acneiform eru-
tions are usually observed in adults, begins as an
cute disease, and characterized by pustules on the
face, neck, shoulders, chest, and back. Usually, come-
dones and cysts do not accompany. The lesions can
sometimes be itchy. After drug withdrawal, they
heal spontaneously depending on the half-life of the
drug [8].

A number of drugs that can be responsible for
acneiform eruptions exist. Examples of these medi-
cines include halogen-containing compounds (radio-
paque-contrast materials, sedatives, analgesics),
antiepileptics (phenytoin, carbamazepine, gabapen-
tin), antituberculosis drugs (isoniazid), lithium,
growth hormone, cyclosporin, medroxyprogesterone,
anabolic steroids (danazol, testosterone), and vitamin
B12 [9].

Dermatologic side effects due to vortioxetine are
redness of the face, neck, arms, and occasionally, upper chest, red or purple spots on the skin, itching
skin [10]. No published reports have been found about vortioxetine in the English publications; how-
ever, case reports of escitalopram [11], sertraline [12],
and duloxetine [13] are present.

A 32-year-old woman, diagnosed with depression,
developed pustular eruptions starting at the abdomen
and spread to the arms and legs, 2 weeks after escitalo-
pram use and the lesions decreased within weeks after
medication was discontinued and without additional
treatment needed [11].

In a 38-year-old patient who was diagnosed with
paranoid schizophrenia and had no active psychotic
symptoms, sertraline 50 mg/day was added to the
patient’s routine risperidone 8 mg/day treatment
when depressive symptoms were started, and
acneform lesions developed on the face 12 days later
and healed spontaneously within 5 days following
drug withdrawal [12].

A 43-year-old woman with depressive complaints
developed acne-like rashes on both cheeks, forehead,
and chest areas 1 month after the treatment initiated.
After a comprehensive evaluation by dermatology
consultant, acneiform eruption due to duloxetine
use was diagnosed and topical tetracycline prep-
paration was initiated, and duloxetine treatment was
recommended to be continued since the lesions will
take time to recover. At the 1-month follow-up
visit, the patient stated that the old lesions had
been regressed and no new lesions had been devel-
oped [13].

Two possibilities are emphasized for dermatological
adverse effects arising from selective serotonin
reuptake inhibitors (SSRI). The first possibility is that
individuals with hypersensitivity may develop these
adverse effects due to an increase in serotonin concen-
tration in the blood; however, the other possibility is
that may be these adverse effects are associated with
increased serotonergic activity in the dermal and epi-
dermal range rather than hypersensitivity [14]. The
mechanism of dermatologic adverse effects caused by
vortioxetine was not fully understood but can be
explained by serotonin.

Despite the fact that they are accepted as alternatives
to SSRIs and are a novel multimodal antidepressants,
they may be similar to SSRIs in terms of dermatologic
adverse effects.

Topical antibiotics such as topical benzoyl per-
oxide, fusidic acid, erythromycin, clindamycin are
used in the treatment of mild acneiform eruptions.
Systemic tetracycline and fusidic acid can be used in
the case of unresponsiveness of these treatments.
Oral isotretinoin is also quite effective, but it can
cause adverse effects such as paronychia and xerosis
in patients. Antihistaminic agents may be added to
patients with itches [15]. In our case, topical antibiotic
treatment was added as well as vortioxetine withdra-
wal because the lesions were widespread, itchy, and
haemorrhagic.

Our case is important because it is the first case
that develops acneiform eruption with vortioxetine
use. Dermatologic adverse effects may impair compli-
ance with treatment in patients using the drug,
especially with cosmetic concerns. Careful examina-
tions by physicians may be important for increasing
treatment compliance, in terms of the emphasis of
fewer dermatologic adverse effects of vortioxetine,
which was recently entered into the market, than
other antidepressants.

Disclosure statement

No potential conflict of interest was reported by the authors.
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