

Vortioxetine Induced Hypomania: A Case Presentation and Review of the Literature

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Antidepressant-induced hypomania/mania is a complex issue that can be seen in mood disorders but is not clarified. There are case reports in the literature regarding vortioxetine-induced mania and hypomania; however, there is insufficient data. Here, we aim to present a case of vortioxetine-induced hypomania in a major depressive disorder patient who previously used various antidepressants but did not experience hypomania or mania. Our case is expected to contribute to the literature.

KEY WORDS: Vortioxetine; Antidepressant; Hypomania; Drug-related side effects and adverse reactions.

INTRODUCTION

The antidepressant-induced hypomania/mania (AIHM) had been a contentious issue in the major depressive disorder (MDD) process. Antidepressants are likely to cause mood instability, revealing affective episodes. The incidence of AIHM in MDD range from 3.72% to 24.4% and can occur with all antidepressants [1-4].

It is not yet understood whether AIHM occurs due to the psychopharmacological effects of drugs or patients with previously undiagnosed bipolar disorder (BD). Some studies indicate that the potential risk factors for AIHM are female gender, having a younger age onset of depression, BD history in the family, having psychosis, severe depressive symptoms with hospitalization, and psychomotor retardation [4,5].

Vortioxetine is a novel strain multimodal antidepressant that positively affects cognitive functions in elderly patients with MDD [6,7]. It also causes less sexual dysfunction compared to other antidepressants [8]. Selective serotonin reuptake inhibitors (SSRIs) and seroto-

nin & noradrenaline reuptake inhibitors (SNRIs) are accepted to have a risk of hypomanic/manic switch. However, there is not enough evidence about vortioxetine-induced hypomania/mania [2,3]. Here, we aimed to present a vortioxetine-induced hypomania case, who had used various antidepressants (SSRIs and SNRIs) for recurrent depression in the past but had no hypomanic/manic shifts.

CASE

The 59-year-old female patient was married and had three children. Her depressive episode firstly started when she was 32 years old. She had used various antidepressants such as escitalopram, fluoxetine, paroxetine, and duloxetine due to recurrent depressive episodes in the last 27 years. The patient had been on 40 mg fluoxetine treatment for the previous two years. Due to sexual dysfunction and cognitive complaints such as amnesia, distraction, inability to focus, fluoxetine was discontinued by gradually decreasing from 40 mg in two weeks, and vortioxetine 10 mg was started. When the patient came to the outpatient clinic 20 days later, she complained of increased speech volume, distraction, increased energy, hyperactivity, euphoria, and decreased need for sleep in the last four days. Young Mania Rating Scale (YMRS) was applied, and the score was 15. There was no psychiatric or

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medical illness family history. Besides, there was no history of hypo/manic episodes associated with previous antidepressant therapies. Lab tests, complete blood count, renal function tests, hepatic function tests, electrolytes, and thyroid function tests were within the normal range. There was no extra medication, other life events, or stressor factors that triggered the patient's condition. We assumed that the patient had a hypomanic shift induced by vortioxetine. Therefore, we discontinued vortioxetine treatment. We observed for two weeks without any treatment. YMRS dropped to 5. Since the patient's depressive complaints recurred, Bupropion 150 mg was started. The patient benefited from the treatment. She had been followed for two years and had no hypomanic/manic shift. The written informed consent was obtained from our case for this case report.

DISCUSSION

Antidepressant-induced hypomania/mania means meeting the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) hypomania/mania criteria immediately after initiating antidepressants or increasing dose [9]. Here, we present a case of the hypomanic switch after vortioxetine treatment. The patient had taken fluoxetine, escitalopram, paroxetine, and duloxetine in the past. However, there was no hypomanic/manic switch with these agents before.

Vortioxetine is thought to work by blocking serotonin reuptake, while it differs pharmacologically from other SSRIs. At the same time, it works by directly stimulating different receptor profiles. Vortioxetine involves several pharmacological actions: serotonin (5-HT) transporter (SERT) inhibition and partial 5-HT_{1B} agonism, 5-HT_{1A} agonism, and 5-HT_{1D}, 5-HT₃, 5-HT₇ antagonism. Also, dopaminergic, noradrenergic, histaminergic, cholinergic, GABAergic, and glutamatergic systems can be regulated by vortioxetine [10,11]. There are four case reports on this subject in the literature. One of them reported a vortioxetine-induced mania in a patient with a previous BD diagnosis [12], while the other three reported vortioxetine-induced hypomania [13,14] and mania [15,16] in unknown BD history. A study conducted with 66 MDD patients reported that treatment was discontinued in 3 patients (12%) due to a manic switch [17]. Since our knowledge about this drug is limited, more studies are needed.

It is unclear whether the patient's hypomanic shift occurs in the disease's natural course or is triggered by vortioxetine. It has been reported that temporary mixed or agitated depression with antidepressants may occur [18]. A mixed presentation of depressive and hypomanic symptoms may occur in the treatment of MDD patients [19]. In DSM-5, the "mixed" specifier was added to the MDD, which consists of major depression based on the B criterion of BD (at least three hypomanic features) [20]. Clinical features of depression with mixed features and hypomania of BD are very similar, thus confusing [21]. In our case, the patient had a euphoric mood, vitality, increased speech volume, and energy; there was no depressive symptom after vortioxetine use.

It is known that patients may develop an "activation syndrome" in a few months of antidepressant therapy, characterized by agitation, akathisia, anxiety, insomnia, aggression, and impulsivity, suicidal thoughts and actions, hypomania/mania [22]. However, this syndrome is distinct from hypomania or mania. Euphoria and vitality seen in hypomania/mania, as in our patient, are not seen in activation syndrome [23].

Antidepressant discontinuation syndrome is one of the subjects of exclusion. Discontinuation syndrome symptoms appear mostly in medications with a shorter half-life and rapidly occur after discontinuation. It consists of headache, dizziness, nausea-vomiting, insomnia, loss of balance, sensory disturbances, hyperarousal states, myalgia, blurry vision, loss of memory and perception, cognitive impairment, loose bowels, depression, suicidal ideas [24]. Antidepressant discontinuation syndrome due to fluoxetine withdrawal was not considered in our case because fluoxetine is an antidepressant with a long half-life, and we had made a gradual dose reduction. Another reason is that the complaints of the patient did not match this syndrome. She did not have nausea, vomiting, depressive mood, suicidal thoughts, etc.

Hypomania or mania associated with rapid reduction or sudden withdrawal of antidepressant dose has been reported with SSRIs, tricyclic antidepressants, and monoamine oxidase inhibitors (MAOIs). Antidepressant discontinuation-related hypomanic/manic states can be explained by increased cholinergic and noradrenergic activity [25,26]. Also, decreased serotonin levels are associated with mania. As a result of the discontinuation of SSRIs, SNRIs, and MAOIs, serotonin levels may drop rap-

idly and cause mania [27]. In this case, fluoxetine was gradually reduced and discontinued within two weeks. Besides, the patient's hypomanic symptoms started shortly after vortioxetine initiation, and these symptoms disappeared entirely after discontinuation of it. Therefore, we believe that there was no hypomania in our case after dose reduction or complete discontinuation of antidepressant.

In DSM-5, AIHM belongs to the category of Substance/Medication-Induced Bipolar and Related Disorder. Our patient had not hypomania/mania history with various antidepressants. Vortioxetine treatment was initiated after fluoxetine treatment which was gradually reduced and discontinued. Afterward, our patient applied again with complaints of elevated mood, hyperactivity, increased amount of speech, insomnia. There was no previous history of mental disorder. There was no acute change in cognition, disturbance of consciousness that tends to fluctuate during a day, so delirium was not considered. Laboratory tests were within normal range. With the discontinuation of vortioxetine, complaints were resolved. Vortioxetine-induced hypomania was considered because there was no drug use other than vortioxetine.

Since the AIHM seen in MDD patients impacts treatment and prognosis, the factors that may cause this condition should be recognized. In conclusion, our knowledge about Vortioxetine associated with hypomania and mania is limited, and more clarification is needed. Clinicians should be aware of vortioxetine-induced hypomania or mania.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Ece Buyuksandalyaci Tunc, Serhat Tunc. Data acquisition: Ece Buyuksandalyaci Tunc. Formal analysis: Ece Buyuksandalyaci Tunc, Serhat Tunc. Funding: Ece Buyuksandalyaci Tunc, Serhat Tunc. Supervision: Serhat Tunc. Writing—original draft: Ece Buyuksandalyaci Tunc. Writing—review & editing: Ece Buyuksandalyaci Tunc, Serhat Tunc.

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