



Case Report **Neurochemistry**

Manic switch during vortioxetine treatment: New medicine, new issue

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ABSTRACT

Antidepressants have been linked to manic or hypomanic episodes in patient being treated for unipolar or bipolar depression. Knowledge of the risk of manic or hypomanic switch associated with a specific antidepressant assists clinicians in analyzing the risk-benefit ratio and finally prescribing an antidepressant of choice in a specific instance. Vortioxetine is now frequently utilized in clinical practice to treat unipolar depression. However, there is insufficient data on manic or hypomanic transition during vortioxetine treatment of unipolar depression. The purpose of this case report is to add to the existing literature on the vortioxetine-induced manic switch and the importance of considering risk factors before starting anti-depressants. Vortioxetine should be used with caution in patients with mood disorders.

Keywords: Antidepressant-induced hypomania, Mania switch, Vortioxetine

INTRODUCTION

Vortioxetine is a serotonin modulator and stimulator (atypical antidepressant) approved by the United States Food and Drug Administration in 2013 for the treatment of depressive disorder in adults.^[1] It has been available in India since 2018. It is a 5-HT₃, 5-HT₇, and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist, and inhibitor of the 5-HT transporter.^[2] Common side effects associated with vortioxetine are nausea, vomiting, constipation, flatulence, dizziness, xerostomia, and sexual dysfunction. In comparison to other antidepressants, it has a more pronounced therapeutic effect on cognitive domains such as executive functions, processing speed, attention, learning, and memory.^[3] Case reports and the naturalistic study which reported the rate of the manic switch at around 12% are part of the data, but it is scarce or limited at this time.^[4] A review of the literature reports four case reports of manic switches associated with vortioxetine. Among these four cases, three had a diagnosis of recurrent depressive disorder and the other had bipolar affective disorder, currently in severe depression.^[5-8] This case report highlights the case of Mania induced during vortioxetine use in a patient with a severe depressive episode.

CASE REPORT

Mr. X is a 33-year-old male, with a medical history of Non-Hodgkin's Lymphoma (NHL), with no past or family history of any psychiatric illness, premorbidly a stable individual, manifested

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in November 2022 with sadness of mood, decreased interest in past pleasurable activities, easy fatigability, lack of concentration in his work with frequent mistakes pointed out by his seniors, pessimistic view of future, and disturbed sleep and appetite for 3 months of duration. This was all in the backdrop of weight loss which he attributed to the possibility of recurrence of NHL and persistent stressor of primary infertility. His general examination revealed a thin build person (body mass index – 17.23 kg/m²) and systemic examination was essentially normal.

A mental status examination (MSE) revealed an ill-kempt person who walked at a slow pace and gait and had a down-cast gaze with reduced psychomotor activity. The speech was coherent and relevant but with increased latency and reduced rate, tone, and volume. He had a depressed affect with reduced range and a depressive cognition of hopelessness was present. There was no delusion/suicidal ideation/perceptual abnormality. His hematological and biochemical investigations were essentially within normal limits. His magnetic resonance imaging brain and positron emission tomography scan were also done in consideration of relapse of NHL/metastasis which was normal. Hamilton Depression rating scale score of 26 indicated severe depression. He was diagnosed and managed as a case of severe depressive episode and started on tab sertraline and gradually built up to 150 mg/day over 6 weeks and a short course of benzodiazepines. In view of minimal response with selective serotonin reuptake inhibitor (SSRI) for adequate dose and duration, his medication was cross tapered to Tab Vortioxetine 10 mg/day. He was given psychosocial intervention in the form of psychoeducation, problem solving skills, and cognitive behavior therapy (CBT). Gradually over a period of 3 weeks, he had a satisfactory response to treatment.

In January 23, he was noticed by his wife over a period of 2 weeks to be unduly cheerful, talking excessively in a loud voice with family members, expressing ideas of spending large amounts of money on the share market and building a villa which was unlike his usual self. He had exhibited disinhibited behaviors in front of others. His general examination and systemic examination were unremarkable. MSE revealed an ill-kempt individual who was over familiar with the examiner and psychomotor activity was increased. The speech was relevant and coherent but with decreased latency and increased in rate, tone, and volume with pressure of speech. The mood was described as “*very happy*” with elated affect. Thought generated an increased pace with inflated self-esteem. He had a decreased need for sleep, increased appetite, and energy, all in clear sensorium. His hematological and biochemical investigations were essentially within normal limits. Young Mania’s rating scale score of 34 suggested severe Mania. In view of the depressive episode and treatment emergent affective switch, he was diagnosed with a case of bipolar affective disorder, current

episode manic without psychotic symptoms. Tab Vortioxetine was stopped and he was started on Tab Quetiapine 300 mg/day and Tab Olanzapine 10 mg/day. Serial MSEs and ward observation showed gradual improvement in his mood, biodrives, and interaction with ward and family members. He was also given interpersonal social rhythm therapy and psychoeducation about illness. He was discharged in a euthymic state and advised to be adherent with medication. During subsequent follow-ups, he is in remission state and stable.

DISCUSSION

Antidepressant-induced hypomanic/manic (AIHM) switch occurs at a rate of 4–17% in unipolar depression and 10–39% in bipolar depression.^[9] Some researchers have proposed that female sex, early age, a family history of mental illnesses and atypical features, and three or more lifetime episodes of depression are probable risk factors for AIHM switch.^[10,11] Studies have shown that tricyclic antidepressants (TCAs) and Serotonin–norepinephrine reuptake inhibitors (SNRIs) have a high risk of manic switch in comparison to SSRI. Increased post-synaptic receptor sensitivity combined with high levels of catecholamines is one of the postulated hypotheses for manic transition in bipolar disorder.

There is a recent small naturalistic study that reported the rate of a manic switch with vortioxetine at around 12%.^[12] Vortioxetine has been shown to boost dopamine, norepinephrine, serotonin, acetylcholine, and histamine and this proclivity to elevate several neurotransmitters could explain the vortioxetine-induced manic switch.^[2] In the case report, there was vortioxetine induced switch in 3 weeks after the failure of the SSRI trial. Therefore, it is recommended to supervise patients who are prescribed vortioxetine for depression.

CONCLUSION

Vortioxetine is a novel antidepressant with a multinodal action on numerous neurotransmitter systems, including dopamine and norepinephrine. As in this example, the prevalence of manic switch in the literature shows that vortioxetine, like other antidepressants, may cause manic or hypomanic switch. It may be beneficial to check for risk factors and monitoring in order to lessen the possibility of a hypomanic or manic switch. Vortioxetine is a relatively new drug and has only four case reports related to the manic switch in the literature. The purpose of this report is to draw attention to the risk of AIMH with vortioxetine.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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