Delirium Associated With Olanzapine Therapy in an Elderly Man With Bipolar Affective Disorder

To the Editor: A typical antipsychotic medications are commonly used to treat symptoms of delirium. Olanzapine has been successfully used in the treatment of delirium. However, there have been few case reports of delirium associated with olanzapine. We report here a case of delirium associated with olanzapine therapy and discuss possible risk factors and underlying pathogenesis.

Olanzapine is a second-generation antipsychotic agent approved for management of schizophrenia as well as mania. The package insert for olanzapine includes a warning regarding possibility of adverse cerebrovascular events with its use in elderly patients with dementia.[1] It has also been reported that elderly patients have dose requirements similar to those of young adults.[2]

The antipsychotic olanzapine has been reported to be useful in the management of symptoms of delirium.[3,4] However, contrary to this, there are few reports of olanzapine-related delirium.[5–7] Because of its rarity, we hereby report a case of olanzapine-associated delirium developing in an elderly man with bipolar affective disorder.

Case Report

An 82-year-old married man working as a farmer had been suffering from bipolar affective disorder for the last 50 years. He had multiple episodes of mania and depression, which were treated with various psychotropic medications. He had been stable for the last 3 years, and hence had stopped all medications; and was only taking lorazepam 1 mg as needed for sleep.

He now presented with complaints of over-talkativeness, grandiosity, overactivity, decreased need for sleep, and excessive cheerfulness for the last 1 month. There was no associated history of seizures, urinary incontinence, fever, forgetfulness, or other symptoms suggestive of organicity. His personal and family history were nonsignificant. Medical history revealed him to be suffering from benign prostatic hypertrophy Grade I. Mental status exam revealed elated affect, increased psychomotor activity, grandiose ideation, and absent insight. His MMSE score was 25/30. A diagnosis of BPAD, currently manic episode, was made. He was started on divalproex 250 mg hs; olanzapine 5 mg hs, increased to 10 mg hs after 5 days; and lorazepam 2 mg hs. The patient, after taking the medications for about 2 days, reported excessive sleep, and, consequently, stopped divalproex. He continued olanzapine and lorazepam in the dose prescribed. However, after about 2 days on 10 mg olanzapine, family members noticed that he would get up at night at around 2.00 A.M. He would then start roaming around the house, would not recognize family members, would start saying that he should go to work, and was unaware of time and place. He would urinate in the wrong places. On occasion, he would start picking up the bed sheets or the pillow covers, saying that ants were sitting there, although family members did not see them. He would sometimes stand on the table and start speaking to himself or would try to reach for some invisible objects in the air. He would then go to sleep at around 5:00 A.M. and would get up at 9.00 A.M. He did not recollect the events of the night before. His daytime activities, however, started to decrease. These episodes continued regularly every night. A diagnosis of delirium was made, and the patient was investigated. Hematological investigations, including serum electrolytes and liver function tests were normal except for increased blood urea: 54 mg% (normal: 15–45) and increased serum creatinine: 2 mg% (normal: 0.5–1.0). A CT scan head was normal. Lorazepam was increased to 4 mg per day, and olanzapine was continued at the same dose. The manic symptoms decreased in intensity. The family members then stopped the olanzapine on their own; 2 days later, the family members reported improvement in delirium symptoms. He was now taking only lorazepam 4 mg per day, and showed improvement in manic symptoms as well as the abnormal behavior suggestive of delirium. Hematological investigations done after the improvement in abnormal behavioral episodes of delirium revealed similar findings.

Discussion

Our patient was diagnosed as a case of delirium per ICD-10 criteria.[8] The history given revealed features like fluctuating consciousness, impaired recent memory, disorientation, perceptual disturbances in the form of visual hallucinations, disturbed sleep–wake cycle,

"picking-up" movements, and sundowning phenomenon.

An increase in dose to 10 mg per day of olanzapine precipitated agitated delirium in our patient. The Naranjo Probability Scale[9] indicates that olanzapine was the probable cause of delirium. Although our patient had increased blood urea and serum creatinine, these persisted even after resolution of delirium. Delirium in our case responded to stopping the olanzapine treatment. The patient was not on medications other than lorazepam, which was begun long before the onset of delirium and continued even after resolution of delirium.

There was no other associated medical condition at the time of delirium. However, one of the limitations with our report is the lack of outpatient follow-up of the patient. Traditionally, delirium has been treated with typical antipsychotics, particularly haloperidol. However, with the increasing use of atypical antipsychotics, there have been several studies describing the successful use of these agents, especially olanzapine, for the treatment of delirium.[3,4,10,11]

Conversely, there have been few reports of delirium associated with olanzapine. Most of these have been in patients with other risk factors for delirium, such as combination with lithium; intoxication with olanzapine in a patient with metastatic lung cancer with intractable nausea; and in a case with mental retardation, seizure disorder, and acute cellulites.[5,6,12,13]

Similar to our case, there has been report of a 76-year-old man, also a bipolar-disorder patient, who developed olanzapine-related delirium.[7] However, this patient was on a higher dose of olanzapine (20 mg–30 mg per day), along with other psychotropic medications and had also developed systemic infection.

The anticholinergic property of olanzapine might have contributed to the pathophysiology of delirium induced by olanzapine.[14] Old age and impaired renal functioning could have predisposed to the development of delirium.

To conclude, one must be cautious while using olanzapine even in low doses, in elderly patients. Further research is warranted to identify the risk factors associated with olanzapine-associated delirium.

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